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Disclaimer:

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Contents

Contents

Contents

Plenary Sessions

Saturday, June 25 2022
Congress Opening Session

PLEN01-1

Where neuroscience meets neurology: blowing, expanding, and losing the mind

S. Greenfield

Founder & CEO of Neuro-Bio Ltd, Oxford, United Kingdom

The human brain becomes personalized by the post-natal development of unique configurations of neuronal connections that characterize its subsequent growth, personalizing it into what we would call a 'mind' that is in constant dialogue with the environment. We shall explore insights from neuroscience into (i) 'blowing' the mind; (ii) expanding the mind; (iii) losing the mind. (i) Since the 21st Century is delivering a vast range of new digital technologies that are transforming our environment in unprecedented ways, it follows that the human brain, and thus our minds, could also be undergoing unprecedented changes, particularly in the young where the appeal to live in the immediate sensory press of the moment has never been greater; (ii) Consciousness is the ultimate miracle, - and enigma. We will explore this deeply fascinating question from the perspective of neuroscience, using a wide range of examples from daily life such as waking up, walking the dog, dreaming, and experiencing pain to see how the following factors are key to every waking moment of the customer experience: intensity and synergy of the senses, extent of pre-existing associations, and arousal levels. (iii) When it comes to older age, one of the biggest problems of our time, is Alzheimer's Disease: a basic problem is that existing therapies target symptoms in the late stages, but don't arrest progression. However, we shall discuss a new approach identifying the pivotal basic mechanism as an inappropriate reactivation of a developmental process that becomes toxic in the context of the mature brain.
Disclosure: Nothing to disclose.

Sunday, June 26 2022
Presidential Symposium

PLEN02-1

Stroke systems and systematics

B. Norrving

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Of all diseases, stroke carries the 2nd largest burden on a global scale. But - few other diseases can match the potential of prevention and treatment of stroke, thanks to scientific advances during the last few decades. Stroke is highly preventable, with 10 modifiable risk factors accounting for 90 % of all strokes. It should be fully realistic to reduce the risk of stroke by one half, which is needed should the capacity of the health services not be flooded. By efficient stroke services (including pre-hospital management, stroke unit care, reperfusion therapies, rehabilitation) the prognosis after stroke can be substantially changed. Time has now come to implement a systematic approach that integrates current science with advocacy and policy actions. In Europe, the Stroke Action Plan for Europe (SAP-E) 2018 to 2030 has been launched and implementation has started. The SAP-E is the largest action ever taken in the stroke field. A similar initiative has been established in Latin America, and similar plans are underway in other regions. Globally, regionally, and nationally, stroke needs to be tackled in a systematic way in which professionals and health policy leaders join hands. In my Moritz Romberg lecture I will focus on the links between evidence based medicine and policy/advocacy issues in the stroke field, the importance that in the ICD-11 stroke is now appropriately placed under diseases of the nervous system, and the need for neurologists in taking the lead in implementing efficient stroke services in a systematic way.

Disclosure: Fees for serving on the DSMB of the THALES trial (Astra Zeneca).

PLEN02-2

The translational clinician: big gains from small observations

K. Bhatia

University College London, Department of Clinical and Motor Neuroscience, Institute of Neurology, London, United Kingdom

The legacy of Brown- Sequard was the recognition of classic clinical signs caused by a particular lesion of the spinal cord. In this context, in the modern era of advanced genetics, imaging data mining and artificail intelligence, the question arises whether there is still a role for the clinician in making relevant contributions as in the case of Brown-Sequard. In this presentation I will advance the case that indeed even in this era small clinical observations can lead to important discoveries which may have direct translational and therapeutic effects or advance the filed. The clinician still remains at the core of the pyramid of the specialised investigative techniques and in fact is required even more so in this era of genetic advances and data mining.

Disclosure: Nothing to disclose.

PLEN02-3

The Contribution of Neuropathology to Multiple Sclerosis Research

H. Lassmann

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The importance of neuropathology is generally seen in its contribution to the diagnosis of diseases of the nervous system, in particular in neuro-oncology. However, when it also includes in its analysis the three-dimensional extension of brain damage and the temporal sequence of lesion evolution and relates this to molecular changes using spatial transcriptomics and proteomics it offers the potential to decipher disease pathogenesis and to contribute to the development of effective and causative treatments. This has been achieved in multiple sclerosis research during the last decades. Neuropathology was essential to discriminate multiple sclerosis from other inflammatory autoimmune or demyelinating diseases, such as neuromyelitis optica spectrum disorders (NMOSD) or myelin oligodendrocyte glycoprotein antibody associated disease (MOGAD). It defined the hallmark of chronic progressive disease in MS patients as slowly expanding tissue damage around lesions and in the normal appearing white and grey matter. It showed that these changes occur in the course of a tissue resident immune response within the central nervous system, involving tissue resident effector memory cells and Plasma cells. Molecular studies in neuropathologically defined micro-dissected MS lesions, which were performed in comparison to lesions seen in other inflammatory and neurodegenerative diseases and which were complemented with classical immunohistochemical analysis, identified a cascade of microglia activation, oxidative injury, mitochondrial damage and subsequent virtual hypoxia as a major pathway of tissue injury in MS. The results of these studies were highly relevant for the identification of potential therapeutic targets in MS patients and the design of pivotal clinical trials.

Disclosure: Hans Lassmann recieved honoraria for lectures from Novartis, Merck, Roche, Sanofi Aventis and Biogen.

PLEN02-4

Brain Prize Lecture: The trigeminovascular system as a template for discovery in migraine

M. Moskowitz

Neurology, Harvard Medical School, Charlestown, MA, United States of America

Migraine entered the modern neuroscience era with a Lancet hypothesis in 1979 positing that trigeminal meningeal afferents and their peptide neuromediators were important to the genesis of migraine headache, and as such, targets for therapy. Subsequent research on the trigeminovascular system (TV) led to mechanisms relevant to actions of ergots, triptans and 5-HT1F receptor agonists. They also identified other therapeutically relevant constituent molecules, receptors and channels that populate TV afferents. Further research also identified an upstream trigger for headache in migraine with aura; cortical spreading depression (CSD), a slowly propagating intense depolarization of neurons and glia, is proinflammatory and releases noxious molecules that trigger overlying TV afferents and cause unilateral headache. CSD is also a target for some preventative drugs like anticonvulsants. Recently, imaging studies found an inflammatory signals within the meninges and skull were found in migraine with aura patients. A second related discovery found CSF within dural perivascular spaces that extend from the subarachnoid space into the bone marrow via bony channels. These newly discovered channels provide a migration route for CSF-containing inflammatory signals from brain via meninges to bone. Hence, skull marrow may act as a reservoir for activated inflammatory cells and signaling molecules as recently shown in other neuroinflammatory disorders (e.g. MS, stroke and trauma). This new body of information, inspired initially by interrogating the TV system, portends a bright future for novel migraine discoveries and therapeutic targets.

Disclosure: Nothing to disclose.

Monday, June 27 2022
Improving lives and reducing burden: What evidence do we need to implement?

PLEN03-1

Do neurology trials inform everyday clinical practice? If not, why not and what should be done to make sure that they do?

C. Clarke
Department of Neurology, University of Birmingham, Sandwell and West Birmingham Hospitals NHS Trust, Birmingham, United Kingdom

Evidence will be presented to suggest that the results of randomised controlled clinical trials in neurology inform everyday clinical practice after significant delays. The reasons for such delays and methods to tackle them will be discussed and the new field of Implementation Science introduced.
Disclosure: Nothing to disclose.

PLEN03-2

How do we ensure the appropriate development and implementation of diagnostic technologies in neurology, and what does the neurologist need to know?

C. Granziera
University Hospital and University of Basel, Basel, Switzerland

In this lecture, we will review some examples of recent diagnostic and monitoring technologies that are being/have been developed in neurology. We will then discuss the importance and the level of maturity of these exemplary technological developments for neurologists. Besides, we will provide an overview of the current gaps between the development/maturity of new technologies and their integration in clinical neurological practice. And finally, we will identify the domains where ad-hoc educational programs should be developed for neurologists in training in the near future.
Disclosure: Nothing to disclose.

PLEN03-3

Are guidelines a useful tool for improving outcomes in neurology?

M. Leone
IRCCS Casa Sollievo della Sofferenza, San Giovanni Rotondo, Italy

Clinical practice guidelines (GLs) translate scientific research findings into recommendations that can improve the quality of clinical decisions by reducing inappropriate practices. It is estimated that about 30–40% of patients receive treatments not based on scientific evidence, and 20–25% are either not needed or potentially harmful. GLs can help to overcome this gap between research and clinical practice, but the mere existence of GLs will not necessarily result in their implementation, leading to changes in practice. Despite the growing number of GLs, knowledge regarding appropriate strategies for their implementation remains sparse. Research identifying determinants of GLs implementation across various settings has highlighted several factors, commonly referred to as "barriers" to change. They include health professional factors such as knowledge, awareness, expectancy of positive outcomes, attitudes, as well as patient factors, such as applicability, patient preferences and behavior, and organizational and environmental factors. Therefore, GLs implementation strategies seek to address these potential barriers and try to overcome them, although no strategy effective in all circumstances has been identified. Furthermore, there are findings in favor of the idea that outcomes improve if clinical practice is evidence-based, although these findings could be specific to the setting and context of each study. In conclusion, the implementation of GLs in the clinical neurological setting remains a challenge. There is a need for further, high-quality research to gain a better understanding of which strategy works best and to evaluate the impact of GLs on outcomes, focusing on those relevant for patients.
Disclosure: Nothing to disclose.

PLEN03-4

How does the general neurologist find what is important and relevant in an era of information overload and increasing complexity?

B. Tettenborn
Kantonsspital St.Gallen, St. Gallen, Switzerland

Within the last years online methodology took over, almost everything is available in paperfree format. Together with this development the amount of content has increased enormously. What has been well reviewed textbook knowledge in the past is now looked up in the internet. But if you "google" something you have little guarantee regarding quality of content. What we all wish for is peer reviewed content. Previously, that was guaranteed by editors of textbooks or peer-review processes of international publications. Today exist many free-access online platforms making it difficult to find out which informations are relevant, objective, correct and without influence of pharmaceutical industry. Future format will be e-Learning platforms with editorial teams in charge for quality of content comparable to editorial teams in classical print format. The advantage of online format is the possibility of fast inclusion of new or revised content offering much more up-to-date knowledge than in classical textbooks. In the present lecture the pros and cons of different online formats are discussed and how one can prepare online for neurological board examinations as well as finding up-to-date reliable scientific content. The newly developed e-learning platform EANcampus will be presented with high-quality content on all educational and scientific levels: basic textbook knowledge, advanced content, guidelines and the newest findings on expert level in every neurological subtopic. The presented content is in accordance with the European Training Requirements for Neurology and in cooperation with all scientific panels and educational committees of the European Academy of Neurology.

Disclosure: Speaker is Editor-in-chief e-Learning EAN.w

Symposia

Saturday, June 25 2022
EAN/MDS-ES: Early detection and treatment of Parkinson's disease

SYMP01-1

How can biomarkers help us better define Parkinson's disease?

B. Mollenhauer

Paracelsus-Elena-Klinik, Kassel and Department of Neurology, University Medical Center, Goettingen, Germany

The diagnosis of Parkinson's disease is too late and inaccurate, especially in the first 5 years after diagnosis, which hampers the development of a causative treatment of α-synuclein (aSyn) aggregation disorders [i.e. Parkinson's disease (PD), multiple system atrophy and dementia with Lewy Bodies]. Biomarkers can be an imaging study, a functional measure and/or coming from biological fluids. Several cross-sectional and longitudinal single- and multicenter cohorts for biomarker analyses of PD have been established, including the single center DeNoPa- and BioFIND-cohort and the multicenter PPMI- and the Systemic Synuclein Sampling Study (S4). These cohorts enable biomarker research based on clinical phenotyping, imaging, blood/cerebrospinal fluid (CSF) biomarkers for biochemical analyses, microbiome studies and tissue analyses of peripheral pathology. To study prodromal aSyn aggregation disorders people with isolated REM sleep behaviour disorders are also recruited. Several biomarkers have shown to be interesting for diagnostic purposes of aSyn aggregation disorders, like CSF aSyn, that due to the overlap of single values and the lack of longitudinal change has limited clinical utility. Other biomarker (like neurofilament light chain) or technologies (like PMCA or RT-QuIC) show promising results. Due to the clinical heterogeneity of aSyn disorders, a panel of different biomarkers is needed for clinical practice and as outcome measure. Newer biomarker will have to be identified and explored, including inflammatory response and including cross-omics approaches.

Disclosure: BM has received honoraria for consultancy from Roche, Biogen, AbbVie, Servier, 4D Pharma PLC and Amprion. BM is member of the executive steering committee of the Parkinson Progression Marker Initiative and PI of the Systemic Synuclein Sampling Study of the Michael J. Fox Foundation for Parkinson's Research and has received research funding from the Deutsche Forschungsgemeinschaft (DFG), EU (Horizon2020), Parkinson Fonds Deutschland, Deutsche Parkinson Vereinigung, Parkinson's Foundation, Hilde-Ulrichs-Stiftung für Parkinsonforschung, and the Michael J. Fox Foundation for Parkinson's Research.

SYMP01-2

Imaging-based diagnosis of pre-motor Parkinsonism

N. Pavese

Clinical Ageing Research Unit Newcastle University Campus for Ageing & Vitality, Newcastle upon Tyne, United Kingdom

SYMP01-3

Biological vs Clinical Diagnosis of Parkinson's disease

T. Outeiro

University Medical Center, Goettingen, Germany

More than two hundred years after the description of a clinical syndrome observed by James Parkinson, Parkinson's disease (PD) is recognized as a complex entity that is not always easy to define. Based on a growing number of studies and owing to the advance of various technologies, clinicians, pathologists and basic science researchers have evolved a range of definitions and criteria for the clinical, genetic, mechanistic and neuropathological characterization of what, in their mind, constitutes PD. However, scientists and practitioners within these specialties have generated and used criteria that are not necessarily aligned between their operational categories, which may hinder progress in identifying distinct forms of PD, and ultimately how to treat them. Therefore, it is important to establish criteria for defining PD. In an initial effort, it is important to identify current inconsistencies between the definitions of PD and its diverse variants. Ultimately, it will be important to achieve a systematic and evidence-based integration of various diverse disciplines by looking at well-defined variants of the relatively common syndrome of PD in order to enable better stratification for therapeutic trials, a prerequisite for breakthroughs in the era of precision medicine.
Disclosure: Nothing to disclose.

SYMP01-4

Update on disease modifying treatments

A. Antonini

Department of Neuroscience, University of Padua, Padua, Italy

EAN/ECTRIMS: Scientific advances for immediate transition into clinical practice in multiple sclerosis

SYMP02-1

People with MS are at the center: Strategies to implement analogue and digital patient-reported outcomes in routine practice

C. Pot

Service of Neurology, Department of Clinical Neurosciences, Lausanne University Hospital and University of Lausanne, Lausanne, Switzerland

Multiple sclerosis (MS) remains the most common cause of non-traumatic neurological disability in young adults. Fortunately, the discovery of highly potent disease-modifying treatments (DMTs) over the last two decades has drastically changed the perspectives of persons with MS (pwMS), However the measure of the outcomes of the medical care is a challenge. Outcomes reported by the treating physicians are often not in adequacy with the expectations of pwMS as several of their complains are not captured by routine neurological examinations. This leads to misunderstanding of pwMS that do not feel at the center of their medical care. On the other side, treating physicians are confronted with measured outputs that are not best reflecting or predicting the evolution of MS disease. One illustrative example is the commonly used clinical EDSS scale. Thus assessing the efficacy of medical interventions and capturing disease activity in pwMS, with a special attention to the patient´s perspective, is a challenge. In the recent years, outcomes of a clinical intervention obtained using patient-reported outcomes (PROs) has gained more importance. PROs are captured directly from patients and include symptoms, function, health status and health-related quality of life. However, guidance on validation of PROs do not yet exist. In this presentation, I will discuss different strategies to implement analogue and digital PROs in routine practice.

Disclosure: C. Pot has received honoraria or consultation fees from Biogen, Novartis, Roche, Merck, Celgene, Sanofi. All the fees are received by the Lausanne University Hospital.

SYMP02-2

SARS-CoV-2 vaccines for people with MS and disease-modifying therapies: new immunological insights to help manage uncertainties in daily practice

B. Kornek

Department of Neurology, Medical University of Vienna, Vienna, Austria

The incidence of COVID-19 infection is people with multiple sclerosis is estimated between 1% and 11% with a mortality ratio of 1–4%. Higher age, the presence of certain comorbidities, a progressive disease course, higher EDSS scores and treatment with anti-CD20 antibodies are known risk factors for a severe disease course in MS patients. SARS-CoV-2 mRNA vaccines are highly effective in preventing COVID-19 associated hospital admissions related to the alpha, delta, and omicron variants. However, there are several uncertainties about safety and efficacy of SARS-CoV-2 vaccination in people with MS. For MS patients, it is recommended to get the SARS-CoV-2 vaccine as soon as it is available for them. However, the humoral response to vaccination may be attenuated or even abolished in the context of some disease-modifying therapies, such as anti-CD20 antibodies or sphingosine-1 phosphate receptor modulators. The extent of B cell repletion and the time from the last anti-CD20 treatment significantly influence the ability to develop SARS-CoV-2 specific antibodies following vaccination. In contrast, B cell depleted patients mount robust SARS-CoV-2 specific T cell responses in the absence of a humoral vaccine response. In this presentation, strategies to optimize SARS-CoV-2 vaccine responses in people with MS are discussed.

Disclosure: Honoraria for lecturing and advising Biogen, BMS/Celgene, Janssen, Merck, Novartis, Roche, Teva, Sanofi-Genzyme.

SYMP02-3

Getting Evidence into practice: The new EAN-ECTRIMS guideline "Update on the pharmacological treatment of people with multiple sclerosis"

M. Amato

University of Florence, Florence, Italy

The EAN-ECTRIMS guideline on the pharmacological treatment of people with Multiple Sclerosis was published in early 2018. Since then, several randomized controlled trials of newly developed disease modifying drugs but also high quality observational studies on "old" DMDs (Duchenne muscular dystrophy) have been published. It is for this reason that ECTRIMS together with EAN considered it was a good time to incorporate such clinical evidence in an update of the guideline. As for the methodology, PICO (patient, intervention, comparator, outcome) strategy was used whenever possible. A prioritized list of outcomes was drawn from the previous guideline and quality evaluation for each outcome was performed using the GRADE methodology. The questions addressed in the guidelines are divided in two types. A set of core questions , covering a range of topics relevant for the therapeutic strategy in patients with multiple sclerosis. These are the same (or slightly reformulated) questions included in the previous ECTRIMS/EAN guideline.The topics included are efficacy of disease modifying drugs, early treatment decisions, treatment response monitoring and treatment modifications, treatment suspension and disease reactivation, reproductive aspects. Then, a set of practical questions, covering topics usually encountered in the daily

clinical practice such as treatment safety and its monitoring, DMD switching strategies and long-lasting effect DMDs (i.e. Alemtuzumab and Cladribine). The publication of this updated version of the guideline is foreseen in the next few months.

Disclosure: Maria Pia Amato received compensation for consulting services and/or speaking activities from Bayer, Biogen Idec, Merck-Serono, Novartis, Roche, Sanofi Genzyme, Teva Pharmaceutical Industries and Celgene BMS; and receives research support from Biogen Idec, Merck-Serono, Roche, Pharmaceutical Industries and Fondazione Italiana Sclerosi Multipla.

SYMP02-4

Real-World-Evidence (Big data, registries): "game-changer" for regulatory and clinical views on when to start, switch and stop of disease-modifying therapies in MS?

M. Magyari

Danish Multiple Sclerosis Center and The Danish Multiple Sclerosis Registry, Department of Neurology, Rigshospitalet, Copenhagen University Hospital, Copenhagen, Denmark

Real-world data is an important supplement to evidence gained from clinical trials regarding the use of disease modifying therapies (DMT) in multiple sclerosis (MS). In the 'hierarchy of evidence' in scientific research, randomized controlled trials are the gold standard, however research based on the information that is generated in health care systems outside of a controlled trials have its advantages. Real-world research doesn't have the blinding and randomization, but uses data about real people, under real circumstances, includes cases without restrictions. Furthermore, real-world data can produce long-term outcome data and can contribute to identify predictors of treatment response and generate evidence about the comparative effectiveness and safety of DMTs. Strong evidence supports that early start of DMT is beneficial to postpone disability milestones. The same is true for switching to DMT with high efficacy when medication with moderate efficacy cannot stabilize the disease. Furthermore, starting with high efficacy DMT as first treatment contributes to longer time to disability accumulation. Evidence is sparse on disease stability when stopping treatment, as disability progression without relapses is no longer without treatment possibilities. As persons with MS age, the frequency of clinical and radiological relapses diminishes and are replaced by slow progressive disability accumulation, likely signs for ongoing neurodegeneration. Therefore, the potential benefits of de-escalation or stopping therapy should exceed the potential risks. Real-world studies conducted in unselected cohorts are essential to provide longitudinal information on the effectiveness, safety and tolerability of drugs and can contribute to defining predictive tools for personalized patient management.

Disclosure: MM has served in scientific advisory board for Sanofi, Novartis, Merck, and has received honoraria for lecturing from Biogen, Merck, Novartis, Roche, Genzyme, Bristol Myers Squibb.

EAN/ILAE: Getting evidence into practice in the management of epilepsies

SYMP03-1

Diagnosing Epilepsy

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Hospital Clinic Neurology, Barcelona, Spain

SYMP03-2

Medical treatment of Epilepsy

T. Marson
Unit of Neuroscience Research, University of Liverpool, Liverpool, United Kingdom

SYMP03-3

Surgical treatment of Epilepsy

K. Vonck
Department of Neurology, Ghent University Hospital, Ghent, Belgium

In patients with drug resistant epilepsy (DRE), continued drug trials with newer AED or combinations of drugs are unlikely to achieve seizure freedom. DRE patients should be referred to a specialized epilepsy center for a dedicated presurgical evaluation. Different types of surgical procedures are currently available including curative resective surgery (RS) and more palliative disconnective surgical procedures. In patients with focal seizures, RS is the first treatment modality that needs to be evaluated, as it is most likely to render patients seizure free. Resective epilepsy surgery is a treatment option for these patients only when the epileptogenic zone (EZ) can be identified and consequently resected. The EZ is defined as the brain volume necessary and sufficient for initiating seizures and whose removal or disconnection is necessary for abolition of seizures. The presurgical evaluation protocol consists of predominantly non-invasive localizing tests. Unfortunately no single test is able to directly and unequivocally define the EZ. Therefore information from the different individual tests of the presurgical protocol need to be combined and integrated to formulate a hypothesis on the location and extent of the EZ. Moreover the presurgical tests also need to assess possible overlap of eloquent cortex with the EZ preventing any RS causing additional functional deficit. At different time points in the presurgical evaluation a multidisciplinary team will meet and will discuss the results of the various tests to decide upon the most suitable approach for individual patients.

Disclosure: KV is a consultant for LivaNova, Synergia Medical, Precisis and the All Man Foundation.

SYMP03-4

Palliative care in epilepsy

A. Strzelczyk
Department of Neurology, University Hospital Frankfurt, Frankfurt, Germany

EAN/EANO: Getting evidence into practice: Biomarkers for the management of CNS tumors

SYMP04-1

The new WHO Classification 2021

A. Woehrer

Division of Neuropathology and Neurochemistry, Medical University of Vienna, Vienna, Austria

Published in 2021, WHO CNS5 has continued to translate new scientific knowledge into the classification of brain tumors, providing practical guidance to pathologists and clinicians. Building on the 2016 WHO CNS tumor update, it seeks to group tumors into biologically and molecularly defined entities with more homogenous outcomes, it introduces newly recognized brain tumor types, and addresses changes in the taxonomic structure. In the present talk, I will start from the high diversity among non-neoplastic glial and neuronal lineages and cell types in the brain, and how genetic and/or epigenetic alterations impact their developmental trajectories, and give rise to this broad spectrum of brain tumor types. I will then summarize the most important genetic and epigenetic alterations and how they have been harnessed to improve the current brain tumor classification. Ultimately, I will outline how these advances impact diagnostic and therapeutic practice and the many challenges they pose.

Disclosure: Nothing to disclose.

SYMP04-2

Molecular and imaging biomarkers in high grade gliomas

A. Hottinger

Brain & spine tumor Center, Lausanne University Hospital and University of Lausanne, Lausanne, Switzerland

Despite improved molecular diagnostics, surgical, radiotherapy and oncological techniques, high grade gliomas still present a dismal outcome. A shift toward personalized cancer treatment is therefore essential to establish a better overall prognosis for each patient and help select treatment modalities that are most susceptible to improve its outcome and discard those with minimal chances of success. Biomarkers have many applications, including initial screening, differential diagnosis, determination of prognosis and prediction of response to therapy. Given the critical role they play at all stages of the disease, it is essential that they undergo rigorous evaluation prior to incorporation into clinical routine. With the introduction of a molecular based WHO classification, revised in 2021, biomarkers play an even more important role in patients with high grade gliomas. Magnetic resonance imaging plays an undisputed central role to diagnose and monitor disease activity, help in therapy decisions and guide focused treatments. Positron emission tomography (PET) may also play an important role in treatment decision. In recent years quantitative and biomarker imaging have been maturing and reaching a level where they may demonstrate their clinical value and drive further discovery to define radiomic signatures of disease states. This presentation will review established biomarkers used in the neuropathological classification, including isocitrate dehydrogenase mutations, ATRX loss, 1p/19q codeletion, TERT mutation, CDKN2A/B, H3K27M and methyloma analysis. The clinical impact of established predictive markers for responses to therapy such as MGMT methylation status and novel markers such as BRAF mutations, NTRK gene fusions and others will be reviewed.

Disclosure: I have no conflict of interest in regards to this presentation

SYMP04-3

Molecular and imaging biomarkers in lower grade gliomas

R. Rudà

University of Turin, Turin, Italy

The new WHO classification of CNS tumors of 2021 reinforced the importance of molecular factors as biomarkers of prognostic and predictive value. Lower grade gliomas are now defined by the presence of IDH mutations, that represent positive prognostic factors regardless of tumor grade (2 versus 3) with median overall survival ranging between seven and ten years following standard treatments. Conversely, most IDH wild type gliomas of grade 2 or 3 have the molecular features of glioblastoma (grade 4) and poor outcome. Moreover, among IDH-mutated astrocytomas the homozygous deletions of CDKN2A/2B distinguishes a more aggressive subgroup. MGMT methylation is a well known molecular factor, that predicts the probability to respond to alkylating chemotherapy. Several biomolecular factors may now be identified by advanced neuroimaging techniques in vivo. The product of IDH mutations, 2-hydroxyglutarate, can be visualized by MRI spectroscopy, thus being useful for supporting diagnosis and monitoring of treatments. Similarly, glutamate and GABA can be visualized by MR Spectroscopy, thus being used to monitor the seizure activity. Last, PET with aminoacids is now the goal standard in the management of lower grade gliomas.

Disclosure: Nothing to disclose.

SYMP04-4

PET/MRI in Neuro-oncology

I. Law

Dept. of Clinical Physiology, Nuclear Medicine & PET, Rigshospitalet, Copenhagen, Denmark

Commercially available integrated PET/MR imaging was introduced for clinical use in 2011 combining the superior soft tissue contrast in MRI with the quantitative accuracy of PET. Hybrid PET/MR imaging systems offer the possibility of single-session multiparametric imaging by combining basic and advanced MR imaging techniques and any available PET radiotracer with the aim of improving overall diagnostic accuracy. Indications in neurooncology are dominated by either identifying malignancy in untreated suspect lesions or distinguishing true progression from treatment related damage. In gliomas the recommended PET tracers are radiolabelled amino-acids, such as O-(2-[18F]Fluoroethyl)-L-tyrosine ([18F]FET), that have high diagnostic accuracies in identifying active glioma tissue. Although all of the methods increase diagnostic accuracy, multiple regression analysis show [18F]FET to outperform any of the advanced MRI methods with no added advantage of combining methods except from increasing confidence. In paediatric neurooncology patients that require anaesthesia, PET/MRI may reduce trauma and cost by performing both simultaneously. The present PET/MRI systems are technically no longer at the forefront, and neurooncology patients may benefit from separate PET and MRI scans. New highly sensitive extended field of view total body PET/CT scanners (Siemens Quadra) allow short 2–5 min acquisitions with a higher PET resolution, that require no/short anaesthesia. PET/MRI in neurooncology is performed for the convenience of two scans in one visit and for standardised imaging, and there is presently no obvious added diagnostic value in the combination with advanced MRI. This allows for a focused work-up centred around standard PET and MRI imaging.

Example of multi parametric dynamic PET/MRI with [18F]FET DCE, DWI and EPSI spectroscopy. [18F]FET PET and standard MRI contribute most to diagnosis.

Disclosure: Nothing to disclose.

A 3-y-old boy with atypical teratoid/ rhabdoid tumor, WHO grade IV. Additional small residual tumor (red arrow) was identified only by [18F]FET PET. L. Marner et al., J Nucl Med 60, 1053 (2019).

EAN/ESRS: The burden of sleep disorders in neurology

SYMP09-1

Sleep and brain health

C. Bassetti

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Background: Brain health is essential for health, well-being productivity and creativity across the entire life. Its definition goes beyond the absence of disease embracing all cognitive, emotional, behavioural and social functions which are necessary to cope with life situations.
Methods: The EAN Brain Health Strategy responds to the high and increasing burden of neurological disorders. It aims to develop a non-disease, non-age centred holistic and positive approach ('one brain, one life, one approach') to prevent neurological disorders (e.g., Alzheimer's disease and other dementias, stroke, epilepsy, headache/migraine, Parkinson's disease, multiple sclerosis, sleep disorders, brain cancer) but also to preserve brain health and promote recovery after brain damage.
Results: The pillars of the EAN Brain Health strategy are: 1) Contribute to a global and international Brain Health approach (together with national and subspecialty societies, other medical societies, WHO, WFN, patients' organizations, industry, and other stakeholders); 2) Supporting the 47 European national societies, healthcare and policymakers in the implementation of integrated and people-centred campaigns; 3) Fostering Research (e.g. on prevention of neurological disorders, determinants and assessments of brain health), 4) Promoting Education of students, neurologists, general practitioners, other medical specialists and health professionals, patients, caregivers, and general public; 5) Raising public awareness of neurological disorders and brain health.
Conclusions: By adopting this 'one brain, one life, one approach' strategy in cooperation with partner societies, international organisations, and policymakers, a significant number of neurological disorders may be prevented while enhancing the overall well-being of individuals by maintaining brain health through the life course.
Disclosure: Nothing to disclose.

SYMP09-2

Sleep by and for the brain

P.-H. Luppi

Center of Neuroscience of Lyon, Bron, France

SYMP09-3

Epidemiology of Sleep Disorders in Neurology

E. Baldin

Epidemiology and Biostatistics Unit, IRCCS Istituto delle Scienze Neurologiche di Bologna, Bologna, Italy

Sleep wake disorders (SWDs), according to the latest International Classification of Sleep disorders-3, are identified in seven major categories: insomnias; sleep-related breathing disorders; central disorders of hypersomnolence; parasomnias; sleep-related movement disorders; circadian rhythm sleep disorders; others. Sixty specific diagnoses within these categories are included. SWD are very frequent in the general population. Epidemiological studies on SWD use different methods of ascertainment and different definitions. Therefore, the frequencies reported might show a wide range. The most common SWDs are sleep disordered breathing (SDB) (4.7–58.1%), insomnia (3–22%), and restless limb syndrome (1.2–18.3%). SWD are influenced by recognized factors as gender and age. SWDs can also represent the main or one of the manifestations of another neurological disorder, and they might present a bidirectional relationship with the disease itself. This bidirectional link can be seen with stroke. SDB (10–20% in general population and 50% of stroke patients) likely increases the risk of stroke and worsens its outcome. Rem Behavior Disorder (RBD) (1–5% in general population) is found in up to 75% of people with neurodegenerative diseases, in particular α-synucleinopathies, based on the duration of the follow up. The prevalence of insomnia in adults with epilepsy ranges from 36–74%, and a probable RBD can be found more frequently in elderly epilepsy patients (12%). About 70% of people with headache have a SWD. The main research gaps on determinants that influence the prognosis and the complex relationship between SWDs and other neurological disorders will be discussed.
Disclosure: Nothing to disclose.

SYMP09-4

Economic burden of sleep-wake disorders

R. Dodel

University Duisburg-Essen, Essen, Germany

Tuesday, June 28 2022
Migraine Cortical Spreading
Depression – from pathophysiology to
clinical expression

SYMP05-1

Pathophysiology of Cortical Spreading Depression

M. Sanchez Del Rio

Clinica Universidad de Navarra, Madrid, Spain

Cortical spreading depression (CSD) was originally described by Leao as a wave of depolarization that propagates slowly across the brain surface, leaving in its wake a suppression of spontaneous EEG activity. The wave of depolarization is manifested as a large shift in direct current (DC) potential and it is the result of a massive depolarization of glial cells and neurons, accompanied by significant fluxes in extracellular and extracellular ions. These ionic changes lead to marked cellular swelling, and alterations in the composition of the extracellular space. CSD seems to propagate largely via nonsynaptic mechanisms. Concomitantly to the electrical/ionic perturbation, vascular changes occur in parallel. An initial dramatic increase in blood flow is followed by a longer lasting hypoperfusion. CSD can be elicited by the application of chemicals (e.g. K^+) as well as mechanical (pin prick) or electrical stimuli to the cortex, thus facilitating the study of this phenomenon.

Disclosure: No conflicts of interest.

SYMP05-2

Cortical Spreading Depression is the main clinical initiation wave for all migraine types

A. Andreou

Headache Research, Wolfson CARD, Institute of Psychiatry, Psychology and Neuroscience, King's College London, London, UK; 2. Headache Centre, Guy's and St Thomas' NHS Foundation Trust, London, United Kingdom

The involvement of the occipital cortex, and of cortical hyperexcitability in migraine pathophysiology has been long recognized. Cortical spreading depression (CSD) is a phenomenon of cortical neuronal depolarisation and glial activation, followed by depression, and coupled to vascular changes. CSD is believed to be the underlying cause of migraine aura. However, cortical blood flow changes suggesting a functional role for the cortex have been also recorded in migraine patients without aura. Whether cortical hyperexcitability and CSD are responsible for the initiation of head pain, and what mechanism could be involved, is a contentious issue. Given the vast corticofugal connections to various subcortical structures, cortical hyperexcitability and CSD would be expected to influence the activity of various subcortical nuclei. In this seminar we will provide evidence from animal models on the effects of cortical stimulation and CSD in the thalamus and the hypothalamus, which are key brain nuclei involved in migraine pathophysiology. We will also discuss the effects of single pulse transcranial magnetic stimulation (sTMS), an approved cortical treatment for migraine, on CSD-induced changes.

Disclosure: Receipt of grants/research supports: eNeura; Receipt of honoraria or consultation fees: Allergan, AbbVie, eNeura, Eli Lilly; Participation in a company sponsored speaker's bureau: Allergan, AbbVie, eNeura, Eli Lilly; Stock shareholder: Neuresta; Sponsorship for educational and other events: ATI Technologies, Novartis, eNeura, Allergan, Zenith Scientific, TEVA; Advisory board for: Neuresta, Zentih Scientific.

SYMP05-3

Clinical expression and possible therapeutic possibilities

C. Lampl

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Cortical Spreading depression (CSD) is a neurophysiological phenomenon characterized by abrupt changes in intracellular ion gradients and sustained depolarization of neurons and glial cells in the cerebral cortex. Clinical disorders related to CSD vary in their presentation and severity, ranging from migraine syndromes, to severely disabling events. There are several clinical studies supporting CSD as the likely mechanism involved in the aura event of migraine. Migraine with aura occurs in 30–40% of patients diagnosed with migraine and is most commonly a visual disturbance, furthermore other auras including sensory and speech disturbance have been described. There is no evidence that acute anti-migraine drugs affect CSD due to the fact that they are not able to block or reduce aura symptoms. Diverse prophylactic drugs, which are efficacious for the prophylactic treatment of MwA and MwoA, have been shown to experimentally suppress SD susceptibility. In particuar, chronic daily administration of topiramate (TPM), valproate, propranolol, amitriptyline, and methysergide. Lamotrigine, a potent Na^+ channel blocker and glutamate receptor antagonist, has been demonstrated to affect MwA in open-label studies. Chronic treatment with this drug appeared to exert a marked suppressive effect on CSD, which is in line with its selective action on the migraine aura. To date, it has been found that CGRP-R antagonists exert a dose-dependent inhibitory effect on CSD. For this reason, it can be hypothesized that CGRP plays a determining role in CSD and its modulation may be effective for the preventive treatment of MwA.

Disclosure: Nothing to disclose.

EAN/ESO: New evidences to tackle major health issues in stroke

SYMP06-1

Detecting AF to prevent stroke: when how long, to whom and how much

G. Tsivgoulis

Second Department of Neurology, National & Kapodistrian University of Athens, Athens, Greece

Atrial fibrillation (AF) is the most common cardiac arrhythmia, affecting representing a frequent cause of first-ever and recurrent ischaemic stroke, with increasing prevalence and incidence worldwide. Identification of AF is critical because oral anticoagulation is highly effective for both primary and secondary stroke prevention. More specifically, in patients with cryptogenic stroke prolonged rhythm monitoring is likely to increase the detection rate of subclinical AF with potentially important therapeutic implications. Given its frequently asymptomatic and paroxysmal occurrence, AF can be difficult to capture by traditional short-term monitoring approaches. Currently, there are different diagnostic options for detection of subclinical AF following stroke, including: ECG at hospital admission; serial in-hospital ECGs; in-hospital continuous non-ambulatory and ambulatory (telemetry) monitoring, inpatient or outpatient Holter monitoring; and the use of external ambulatory ECG recorders, varying from short repeated intermittent ECG (e.g. thumb-ECG) to continuous wearable recorders or implantable loop recorders that can be utilized for long-term monitoring lasting for month to multiple years. The strengths and shortcomings of these diagnostic approaches will be outlined in detail. Specific diagnostic algorithms will be presented, while diagnostic and treatment individualization for AF detection following stroke will be highlighted.

Disclosure: Prof Tsivgoulis has received lecture fees and consulting fees from Medtronic. He has also received an unrestricted research grant from Medtronic.

SYMP06-2

Treating vascular risk to prevent dementia

H. Markus

Department of Clinical Neurosciences, University of Cambridge, Cambridge Biomedical campus, Cambridge, United Kingdom

57 million people worldwide suffered dementia in 2019 and this is predicted to increase to 153 million in 2050. While Alzheimer's is the most common individual pathology, most cases in the elderly have multiple pathologies including vascular disease, particularly small vessel disease. Increasing epidemiological evidence demonstrates that common cardiovascular risk factors account for a major proportion of dementia risk, not only vascular but also Alzheimer's disease. Targeting such risk factors represents a potential treatment opportunity which could have major implications on a global scale. As yet evidence that targeting risk factors reduces Alzheimer's risk is limited, but recent randomised controlled trial data has demonstrated that intensive blood pressure lowering reduces cerebral small vessel disease risk (the major cause of vascular dementia) and also appears to reduce mild cognitive impairment and dementia risk. Further large scale trials of other risk factor interventions to reduce dementia are badly needed. An alternative approach is to adopt multi domain risk factor prevention and this is being explored in the FINGERS trial.

Disclosure: Nothing to disclose.

SYMP06-3

Asymptomatic Carotid artery stenosis: stent, surgery and medical therapy

A. Halliday

University of Oxford, Oxford, United Kingdom

SYMP06-4

Stimulation for post stroke recovery

J. Dawson

Institute of Cardiovascular and Medical Sciences, College of Medical, Veterinary and Life Sciences, University of Glasgow, Glasgow, United Kingdom

The use of a paired vagus nerve stimulation (VNS) system for the treatment of moderate to severe upper extremity motor deficits associated with chronic ischaemic stroke has recently been approved by the U.S. Food and Drug Administration. This treatment aims to increase task specific neuroplasticity through activation of cholinergic and noradrenergic networks during rehabilitation therapy. Animals treated with paired VNS had greater recovery of impairment and in a functional task after stroke than those who had either motor training or VNS alone. Depletion studies suggest this is mediated via cholinergic, serotonergic and noradrenergic activation. Two pilot clinical studies and one pivotal phase III study have been performed using implantable VNS. The recent pivotal phase III trial showed that VNS paired with rehabilitation led to improvements in upper extremity impairment and function in people with moderate to severe arm weakness an average of three years after ischaemic stroke. In additional, considerable progress has been made in developing other neuromodulation based treatments such as transcranial magnetic stimulation (TMS), transcranial direct current stimulation (tDCS), pharyngeal electrical stimulation and sphenopalatine ganglion stimulation. Pharyngeal electrical stimulation may improve symptoms of dysphagia and facilitate decannulation following tracheostomy. Sphenopalatine ganglion stimulation may improve functional outcome in people with cortical ischaemic stroke who do not receive thrombolytic therapy. This talk will discuss these promising developments in neuromodulation technologies, highlighting areas for future study and how these techniques could be incorporated into clinical practice.

Disclosure: JD has received reimbursement for travel expenses from MicroTransponder Inc for attendances at conferences to present VNS trial data.

EAN/AE: Cognitive deficit and dementia: beyond neurodegenerative diseases

SYMP07-1

Cognitive impairment and falls in the frail elderly patient: impact of comorbidities and polytherapy

P. Ousset

Toulouse University Hospital, Gerontopole, Toulouse, France

The literature provides us with hackneyed evidence of the relationship between the existence of polypharmacy or commorbidities and the risk of cognitive impairment and falls in the elderly. Few studies, on the other hand, have focused on the possible role of "moderator" of the frailty syndrome on the occurrence of these traumatic events. We are going to try, in this presentation, to disentangle the complex interactions of these factors by relying on data from a few studies that have taken into account the status of frailty in the analysis of these major geriatric syndromes that are falls or cognitive decline and dementia. In this perspective, the preliminary results of the COGFRAIL study, carried out in our center, which explores the role of cerebral amyloid pathology, but also a range of nutritional, physical, biological or brain-aging marker in the development of cognitive frailty will be presented. Frailty, as defined by its operational criteria, represents a multidimensional syndrome characterized by diminished reserve and greater vulnerability to stressors. The interest of this syndrome is its potential reversibility, avoiding the occurrence of complications, of which falls and cognitive impairment are an example, and the entry for the elderly subject into an irreversible state of dependence.

Disclosure: Nothing to disclose for this presentation

SYMP07-2

Cognitive decline in neuroinflammatory diseases: the case of multiple sclerosis

P. Preziosa

Neuroimaging Research Unit, Division of Neuroscience, and Neurology Unit, IRCCS San Raffaele Scientific Institute, Milan, Italy

Cognitive impairment is a frequent and relevant manifestation of multiple sclerosis (MS), with a prevalence up to 65%-70% of cases and the involvement of several cognitive domains. Thanks to standardized neuropsychological tests, that are easy to be administered and sensitive to disease-related abnormalities, several studies have consistently demonstrated that cognitive dysfunction occurs in all MS clinical phenotypes, from the earliest phases of the disease, becoming more prevalent and severe in patients with the progressive forms of MS.

Cognitive impairment has a relevant impact on MS patients, their families and the society, due to its detrimental effects on quality of life, working employment and engagement in social activities. The application of advanced magnetic resonance imaging (MRI) techniques has shown that MS-related cognitive impairment can be explained by a disconnection syndrome caused by the accumulation of focal lesions and microstructural tissue abnormalities in cognitively relevant white matter tracts, together with a primary gray matter damage, including focal demyelinating lesions, microstructural abnormalities and irreversible tissue loss. Collapse of network functional efficiency plays an additional role. Despite all these findings, cognitive status is often only marginally evaluated during routine neurological examination for MS patients' monitoring. Similarly, the potential effects of disease modifying therapies (DMTs) and cognitive rehabilitation approaches on cognitive functions have been marginally investigated. During this talk, we will describe the patterns of MS-related cognitive impairment and discuss its pathophysiological substrates, which might represent the target for assessing the effects of DMTs and rehabilitative approaches on cognitive functions in these patients.

Disclosure: Dr. Paolo Preziosa received speaker honoraria from Roche, Biogen, Novartis, Merck Serono, Bristol Myers Squibb and Genzyme. He has received research support from Italian Ministry of Health and Fondazione Italiana Sclerosi Multipla.

SYMP07-3

The cognitive consequences of stroke: how to rehabilitate?

A. Verdelho

Department of Neurosciences, Faculdade de Medicina, IMM and ISAMB, University of Lisbon, Lisbon, Portugal.

Beyond motor and sensitive deficits, stroke survivors frequently present cognitive, affective, and behavioural changes. These changes are strongly associated with worse quality of life and difficulties when returning to usual daily-life activities. Nowadays, motor rehabilitation is widely accepted as a mean to promote motor recovery after stroke. Differently, intervention in cognitive and behavioural deficits is not recognized as a standard, partially due to lack of evidence from clinical trials. In fact, the issue is far more complex: non-motor symptoms after stroke may be difficult to identify, and, moreover, they are frequently overlooked by motor and physical difficulties. The first step to promote rehabilitation is to consider the hypothesis of cognitive deficits, and thus promote careful evaluation. Evaluation should include multiple domains testing (through detailed neuropsychological evaluation), impairment in functional abilities, and evaluation of premorbid abilities and functioning. As the clinical picture after stroke is dynamic over time, cognitive evaluation should take in consideration motor and sensory deficits after stroke, and integration of both interventions should be considered. So far, there is no evidence supporting any specific form of intervention.

Therefore, the decision must be individualized and take into consideration the patient preferences and available techniques. Intervention should be customized to patients` deficits. Planning should be tailored to patient current neuropsychological evaluation, previous status, but also availability of resources, taking into account physical limitations due to stroke.

Disclosure: Nothing to disclose.

SYMP07-4

The dementia-friendly Hospital: what is it and why we need it

J. Georges
Alzheimer Europe, Luxembourg, Luxembourg

Coma – what`s new?

SYMP08-1

Definition of coma – old and new perspectives

B. Rohaut

Department of Neurology, Groupe Hospitalier de la Pitié Salpêtrière, Paris, France

Coma is an ancient Greek word meaning « deep sleep ». Nowadays, coma is classically defined as a "state of unresponsiveness in which the patient lies with eyes closed and cannot be aroused to respond appropriately to stimuli even with vigorous stimulation". In this talk I will discuss diagnosis of coma, differentials from locked-in syndrome to brain death, and introduce some recent electrophysiological and brain imagery techniques that revolutionized our conception of disorders of consciousness.

Disclosure: I have no conflict of interest in relation to this presentation.

SYMP08-2

The biology of coma

D. Menon

University of Cambridge, Cambridge, United Kingdom

Understanding consciousness requires that we address key aspects of the framework that underpin consciousness. These include an exploration of whether specific anatomical sites in the brain are critical for consciousness. While the midline thalamic nuclei, rostral brainstem and insula have been implicated in this regard, their integration into neural systems allows the emergence of functions that go beyond the properties of individual components. These neural systems show clear anatomical connectivity, and some neuroanatomical subsystems are clearly more important in this context. However, the key attribute of the conscious brain is that the functional connections that subserve consciousness do not slavishly map to anatomical connections, but display modulations of functional connectivity in a more nuanced and dynamic fashion. Further, in addition to the quantity, the quality of information (characterized, for example by entropy) transmitted by these connections may be a critical signature of consciousness. These emergent functional connections correlate with behavior, which results in task related activity in cognate sites and systems. However, these connections are also affected, both in tonic and phasic ways, by neuromodulatory arousal systems, which have their focus in key brainstem nuclei, and are served by a range of neurotransmitters. Finally, there are key aspects of evolutionary biology that drive human consciousness, as exemplified by associations between human accelerated regions in the genome, and the development of key brain structures seen in human evolution.

Disclosure: Nothing to disclose.

SYMP08-3

Variability in the management of comatose patients

V. Rass

Department of Neurology, Medical University of Innsbruck, Innsbruck, Austria

Background: Although coma is commonly encountered in critical care, worldwide variability exists in diagnosis and management practices. We aimed to assess variability in coma definitions, etiologies, treatment strategies, and attitudes toward prognosis.

Methods: As part of the Neurocritical Care Society Curing Coma Campaign, between September 2020 and January 2021, we conducted an anonymous, international, cross-sectional global survey of health care professionals caring for patients with coma. Fleiss κ values were calculated to assess agreement among respondents.

Results: The survey was completed by 258 health care professionals from 41 countries. Among eight predefined items, respondents identified the following cardinal features, in various combinations, that must be present to define coma: absence of wakefulness (81%, κ=0.764); Glasgow Coma Score (GCS) ≤8 (64%, κ=0.588); failure to respond purposefully to visual, verbal, or tactile stimuli (60%, κ=0.552); and inability to follow commands (58%, κ=0.529). The most common clinical assessment tools used for coma included the GCS (94%) and neurological examination (78%). The most commonly used neurostimulants included amantadine (51%), modafinil (37%), and methylphenidate (28%). The leading determinants for prognostication included etiology of coma, neurological examination findings, and neuroimaging. Fewer than 20% of respondents reported routine follow-up of coma survivors after hospital discharge.

Conclusions: There is wide heterogeneity among health care professionals regarding the clinical definition of coma and limited routine use of advanced coma assessment techniques in acute care settings.

Disclosure: The authors have nothing to disclose.

SYMP08-4

Therapies to restore consciousness: what is available and what´s in the pipeline?

A. Thibaut

Coma Science Group, GIGA-Consciousness, University of Liège, Liège, Belgium

Severely brain-injured patients with prolonged disorders of consciousness (DOC) raise important issues regarding their management in particular with respect to their therapeutic options. As they are unable to communicate, these patients cannot take part in most of conventional rehabilitation programs. The current gap in therapeutic options in the field of DOC is presently challenged by recent clinical and neuroimaging data indicating that some DOC patients can benefit from rehabilitative interventions, even years after the brain injury. Even if some advances has been made recently, large sample randomised controlled trials are still needed to provide the requested level of evidence to develop clinical guidelines for the therapeutic management of patients with prolonged DOC. In addition, a better understanding of the therapies' neural correlates and the development of biomarkers of responsiveness are also warranted to facilitate the clinical translation of novel therapeutic options. During this lecture, I will give an overview of the current state of the art in the field of therapeutic options for DOC patients, including pharmacological treatments (e.g. amantadine, zolpidem, apomorphine) and (non-)invasive brain stimulation approaches (e.g. deep brain stimulation, transcranial current stimulation, repeated transcranial magnetic stimulation). I will also discuss emerging therapies as well as neuroimaging studies aiming to understand the underlying mechanisms of action of these therapeutic options. Finally, I will highlight the gaps that need to be filled to improve patients' management and develop guidelines.

Disclosure: Nothing to disclose.

Focused Workshops

Saturday, June 25 2022
EAN/MDS-ES: Hyperkinetic
movement disorders in children and
young adults – not to be missed

FW01-1

Tourette Syndrome

A. Cavanna
University of Birmingham, Birmingham, United Kingdom

Tourette syndrome (TS) is a chronic tic disorder characterised by the presence of multiple motor and vocal tics with onset during development. Tics are the most common hyperkinetic symptoms in childhood and co-morbid behavioural conditions (especially obsessive-compulsive disorder, attention-deficit and hyperactivity disorder, affective symptoms, and impulsivity) are present in the majority of patients. Although TS is no longer considered a rare medical curiosity, its exact pathophysiology remains elusive. Recent research on the brain correlates of the subjective 'urge to tic' has highlighted the role of extra-motor pathways within the brain mechanisms of tic generation. Advances in our understanding of the pathophysiology of TS can pave the way to the implementation of more effective treatment strategies for this heterogeneous neurobehavioral condition. Finally, the development of GTS-specific instruments for the assessment of health-related quality of life has allowed more standardised assessments across the lifespan, capturing the impact of both tics and behavioural co-morbidities.
Disclosure: A.E. Cavanna is the author of Pharmacological treatment of tics. (Cambridge University Press 2020).

FW01-2

Metabolic Hyperkinetic Movement Disorders

T. De Koning
Movement Disorders Groningen, University Medical Center Groningen, Groningen, The Netherlands

Metabolic hyperkinetic movement disorders are caused by genetic disorders affecting biochemical pathways. The first step in diagnosing these disorders is meticulously clinical phenotyping because in many patients multiple hyperkinetic movement disorders are present in combination with disorders of eye movement. The next step in the diagnostic process is next generation sequencing (NGS). Since metabolic disorders are all genetic disorders NGS is preferred over biochemical testing. The occurrence of hyperkinetic movement disorders and a diagnostic strategy is discussed in the presentation. Abstract Movement disorders represent an important proportion of the symptoms observed in neurology clinics. Such disorders can be caused by many different conditions, including acquired and genetic disorders. A group of these genetic disorders causing hyperkinetic movement disorders are formed by inborn errors of metabolism (IEM) or metabolic disorders. Here I will focus on the presence of metabolic hyperkinetic movement disorders in adults. IEM as the cause of neurological symptoms in adolescents and adults appears to be a largely neglected area, which leads to serious under-diagnosis of the IEM. However, the identification of these patients at the earliest stage of symptomatic disease is important to prevent further and irreversible damage to the brain and obtain optimal treatment results. Advances in the knowledge of the pathogenesis underlying IEM have led to specific treatments being available for more than 30 inherited rare metabolic movement disorders (Jinnah 2017). Although early recognition of IEM is important, it is frequently challenging. Presenting symptoms in adolescents or adults are different than in children with an IEM and include hyperkinetic movement disorders (dystonia, ataxia, myoclonus, tremor), disorders of eye movement, psychiatric signs and cognitive problems. In a significant proportion of patients multiple hyperkinetic movement disorders are observed and this in combination with abnormalities of eye-movement should raise the suspicion of an IEM. Meticulous clinical phenotyping is therefore of outmost importance as the first step in the diagnosis of adults with metabolic movement disorders. Historically, IEM were tested by means of biochemical procedures, but since all IEM are genetic diorders next generation sequencing (NGS) strategies are to be preferred as a first line diagnostic test of IEM in adults (Koens 2021). NGS has many advantages

above biochemical testing. First, the predictive power of biochemical tests in adults is likely to be lower than in children. This is because the biochemical defects are usually less severe in adults and thus more difficult to detect. Second, with NGS it is possible to analyze many genes simultaneously which is an advantange in heterogeneous conditions like IEM. Furthermore, the use of NGS is efficient, cost-effective and has led to more and unexpected diagnoses. Finally, most neurologists are not familiar with the range of biochemical tests that apply to specific IEM, and usually not all biochemical tests are available in every neurology clinic, whereas DNA diagnostic facilities are usually available. So, here I will discuss the clinical features of hyperkinetic metabolic movement disorders in adults, associated eye-movement disorders and a diagnostic approach on how to diagnose such patients in your clinic.

References: Jinnah HA, Albanese A, Bhatia KP, Cardoso F, Da Prat G, de Koning TJ, Espay AJ, Fung V, Garcia-Ruiz PJ, Gershanik O, Jankovic J, Kaji R, Kotschet K, Marras C, Miyasaki JM, Morgante F, Munchau A, Pal PK, Rodriguez Oroz MC, Rodríguez-Violante M, Schöls L, Stamelou M, Tijssen M, Uribe Roca C, de la Cerda A, Gatto EM. Treatable inherited rare movement disorders. Mov Disord. 2017 Sep 1. doi: 10.1002/mds.27140 Koens LH, de Vries JJ, Vansenne F, de Koning TJ, Tijssen MAJ. How to detect late-onset inborn errors of metabolism in patients with movement disorders - A modern diagnostic approach. Parkinsonism Relat Disord. 2021;85:124-132

Disclosure: Tom J de Koning is medical advisor for three charities (non-profit), Metabolic Power foundation (Stichting Stofwisselkracht), North Sea progressive myoclonus epilepsy foundation (Stichting Noordzeeziekte) and JanIvo Foundation. Tom J de Koning is medical advisor of and has shares in Ancora Health BV, a Dutch company offering life-style advises and preventive medicine. None of these disclosures relate to the content of the abstract or the presentation.

FW01-3
Genetic Hyperkinetic Movement Disorders

M. Carecchio

Movement Disorders Unit, Department of Neuroscience, University of Padua, Padua, Italy

Hyperkinetic movement disorders are a heterogeneous group of different diseases with onset in all ages of life. Underlying etiology includes all causes of movement disorders: vascular lesions, autoimmune processes, infections, neurodegeneration. Knowledge on the genetic causes of hyperkinetic movement disorders has significantly increased over the last decade, with particular expansion in the pediatric-onset group, thanks to the increasing availability of Next Generation Sequencing (NGS) techniques. New dystonia-related genes have been individuated, including KMT2B, VPS16, VPS41 and VPS11. Most of these genes cause an early-onset phenotyoe but later clinical presentations with a milder disease severity are emerging. Moreover, the association of dystonia and cerebellar atrophy has been linked to mutations in MED27 and TSPOAP1. The discovery of new genes has let to the identification of new molecular pathways in the pathogenesis of hyperkinetic movementjdisorders suche as a disregulation of the endolysosomal and autophagic system, leading to altered degradation of macromolecules and wasted cellular components. With regards chorea, relevant genes have also been published in the last decade, again in most cases with a pediatric onset. This talk will summarize the main recent genetic discoveries in the field of hyperkinetic movement disorders with a particular emphasis on complex phenotypes and clinical clues that suggest specific underlying genetic diagnoses both in adults and children.

Disclosure: Nothing to disclose.

How do we ensure the timely generation of evidence that will improve lives and reduce burden?

FW02-1

Covid-19: Benefits and pitfalls of rapid implementation during a pandemic

J. Sellner
Department of Neurology, Landesklinikum Mistelbach, Mistelbach, Austria

FW02-2

Multiple Sclerosis: Is neurology following or leading in the development of prognostic biomarkers?

J. Kuhle
Multiple Sclerosis Centre and RC2NB, Neurologic Clinic and Policlinic, Departments of Head, Spine and Neuromedicine, Biomedicine and Clinical Research, University Hospital Basel and University of Basel, Basel, Switzerland

Large heterogeneity in disease course make prognostic biomarkers in MS important tools to personalize treatments. Despite the need, large gaps remain between exploratory biomarkers proposed in many studies and biomarkers integrated into routine clinical practice. Recently, the presence of oligoclonal IgM bands has come into focus of interest as they have been reported to be associated with a more active inflammatory disease phenotype both in relapsing and progressive MS. Serum neurofilament light chain (sNfL) is the leading example of the development of an accessible prognostic biomarker in clinical practice in neurology over the past years. Based on >10,000 control serum samples, we have established a reference data base covering seven decades of life. In MS (>10,000 serum samples), sNfL Z scores/percentiles based on control persons identified a gradually increased risk for future acute and chronic disease activity. sNfL Z scores/percentiles outperformed absolute raw sNfL cut-off values. We provide an application for the calculation of sNfL percentile/Z-score values enabling the interpretation of individual measurements by physicians. It remains to be shown if usage of reliable reference values for sNfL and careful adjustment for other factors will be sufficient to detect clinically relevant signals contributing to 'pure' disease progression. Preliminary data demonstrate value of serum glial fibrillary acidic protein (GFAP) concentrations as a biomarker for disease progression in MS versus sNfL. Taken together, there is ample evidence that neurologists are truly leading the development of prognostic biomarkers in MS.
Disclosure: Jens Kuhle received speaker fees, research support, travel support, and/or served on advisory boards by Swiss MS Society, Swiss National Research Foundation (320030_189140/1), University of Basel, Progressive MS Alliance, Bayer, Biogen, Bristol Myers Squibb, Celgene, Merck, Novartis, Octave Bioscience, Roche, Sanofi.

FW02-3

Headache: New treatment paradigms; who defines them?

E. Wentz Loder
Department of Neurology, Brigham and Women's Hospital, Boston, MA, United States of America

Issues in the follow-up of glioma

FW03-1

Combining advanced MRI and PET

P. Lohmann

Institute of Neuroscience and Medicine (INM), Research Center Juelich (FZJ), Juelich, Germany

Neuroimaging techniques such as magnetic resonance imaging (MRI) and positron emission tomography (PET) provide valuable diagnostic information in the follow-up of patients with glioma. Particularly PET using radiolabeled amino acids, advanced MRI techniques such as perfusion-weighted imaging, diffusion-weighted imaging or MR spectroscopy, and combinations thereof demonstrated their potential for a non-invasive assessment of biological characteristics of brain cancer. Considering the growing complexity of neuroimaging data, advanced statistical methods from the field of artificial intelligence such as radiomics play an important role for clinical decision-making and have the potential to significantly impact diagnosis and response assessment in neuro-oncology. Further, the increasing availability of hybrid PET/MRI systems and the advent of ultra-high field MRI scanners operating at magnetic field strengths of seven Tesla or more opens new possibilities for improvements in metabolic imaging. The presentation summarizes the status of advanced MRI and PET, highlights the latest developments and methodological advancements, and envisions the future role of advanced neuroimaging in the follow-up of patients with glioma.

Disclosure: Nothing to disclose.

FW03-2

Does liquid biopsy matter?

M. Sanson
Department of Neurology, Pitié-Salpêtrière, Paris, France

FW03-3

Pitfalls and caveats during follow up.

M. Nowosielski
Department of Neurology, Medical University Innsbruck, Innsbruck, Austria

Magnetic resonance imaging (MRI) is the gold standard diagnostic tool during follow-up of gliomas. As new treatment concepts in brain tumors are rapidly evolving, the traditional methods of assessing tumor response are being questioned, as specific imaging phenomena due to drug related side effects occur. When interpreting brain tumor MR images, one has to recall that the various imaging features are the result of pathophysiologic processes, and tumor burden is depicted only indirectly. Contrast enhancement is the result of blood–brain barrier breakdown, and can be influenced by many non-tumor related conditions such as ischemia and epileptic seizures, as well as iatrogenic factors such as surgery, radiation, chemo- and immunotherapy, steroids, and anti-angiogenic drugs. These circumstances have to be considered in order to provide an accurate assessment of tumor activity. Misinterpretation may lead to a significant delay of adequate treatment of a progressive tumor or even lead to a discontinuation of an effective treatment. Moreover, patients with treatment-related changes misclassified as progressive disease present a major challenge for appropriate clinical trial enrollment and can adversely affect outcome interpretation. Reliable criteria to better determine response and progression are constantly under development also exploiting new functional MRI and positron emission tomography (PET) methods in order to more accurately differentiate between treatment-related effects and true tumor progression. The Response Assessment in Neuro-Oncology (RANO) working group, a multidisciplinary international group, was formed to improve response assessment and clinical trial endpoints in Neuro-Oncology.

Disclosure: Nothing to disclose.

EAN/IFCN-EMEAC: The role of clinical neurophysiology in the assessment and treatment of neurodegenerative disases with cognitive impairment

FW04-1

The relevance of subclinical epileptiform discharges in Alzheimer's disease

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Introduction: Hyperexcitability is a recognized contributor to the pathophysiology of Alzheimer's disease (AD). Subclinical epileptiform activity (SEA) is a neurophysiological sign of cortical hyperexcitability. There are only a few studies examining the effects of SEA on the progression of AD, and their results vary due to methodological differences. We aimed to determine the prevalence of SEA in AD compared to healthy elderly controls with the hypothesis that SEA is more frequent in AD than in cognitively intact individuals. Furthermore, we hypothesised that the occurrence of baseline SEA captured with electroencephalography might fasten the progression of the disease.

Methods: We investigated 52 Alzheimer patients with no history of epileptic seizures and 20 healthy individuals. All participants underwent a 24-hour electroencephalography, neurology, neuroimaging and neuropsychology examination. We enrolled 38 AD patients in a 3-year long prospective follow-up study with yearly repeated cognitive evaluation.

Results: SEA was recorded significantly (p:0.018) more frequently in Alzheimer patients (54%) than in healthy elderly (25%). Alzheimer patients who had SEA showed a 1.5-times faster decline in global cognitive scores than patients without epileptiform activity (p<0.001). The decline in cognitive performance scores showed a significant positive correlation with the number of spikes (r: +0.664; p<0.001).

Conclusions: SEA occurs in half of Alzheimer patients who have never suffered overt epileptic seizures. Alzheimer patients with SEA suffer accelerated cognitive decline with a strong relation to the frequency of spikes. These findings prove the prominent role of epileptiform discharges in the cognitive deterioration caused by Alzheimer's disease.

FW04-2

Probing neurophysiological vigilance systems in neurodegenerative diseases with cognitive impairment: resting state EEG biomarkers

C. Babiloni

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The talk will report recent findings of the present international PDWAVES Consortium testing the hypothesis of different abnormalities in cortical source activities and connectivity derived from resting state eyes-closed EEG (rsEEG) rhythms in patients with Alzheimer's disease dementia (ADD) as compared with those with dementia due to Parkinson's (PDD) and Lewy body (DLB) diseases.

The rsEEG rhythms were collected in 42 ADD, 42 PDD, 34 DLB, and 40 normal healthy older (Nold) participants. Exact low-resolution brain electromagnetic tomography (eLORETA) freeware estimated rsEEG cortical sources at delta, theta, alpha, beta, and gamma bands.

Results showed abnormal posterior source activities of rsEEG delta (<4 Hz) and alpha (8–12 Hz) rhythms in patients with ADD, PDD, and DLB, as cortical neural synchronization markers in quiet wakefulness. Compared to patients with PDD and DLB, those with ADD showed greater abnormalities in alpha sources and lesser in delta sources. Furthermore, abnormalities in interhemispheric and intrahemispheric eLORETA delta and alpha source connectivity were greater in the ADD patients than DLB and PDD patients, as cortical neural network markers.

The results suggest that compared with PDD and DLB patients, ADD patients may reveal a greater "disconnection cortical syndrome" in the regulation of quiet vigilance with possible clinical indications for non-invasive electromagnetic stimulations and other interventions at cortical network level.

Disclosure: No conflict of interest of the Speaker for this specific research study.

FW04-3

Transcranial stimulation in the diagnosis and treatment of dementia

A. Antal

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Physiological changes to the aging brain are highly variable, making it difficult to estimate a border between healthy and pathological functions and finding a method with which the conversion to cognitive decline can be monitored. As a consequence, the relationship between aging-related structural changes and cognitive function are not fully understood. In Europe cognitive decline reaches medical attention for about 5–25% of the elderly above 65 years as they suffer from Mild Cognitive Impairment (MCI). Around 46% of people with MCI develop dementia within three years; therefore, the early diagnosis and treatment of this condition is critical. Non-invasive brain stimulation techniques (NIBS) such as transcranial magnetic stimulation (TMS), transcranial direct current and alternating current stimulation (tDCS, tACS) offer useful insights into the functional integrity of intracortical circuits using electrophysiology and imaging measures. TMS measurements can be used to identify and monitor changes in cortical integrity and reactivity of inhibitory and excitatory neuronal circuits, therefore they can be useful for the early diagnosis of cognitive decline. Repetitive TMS, tDCS and tACS can be applied to modulate neuronal excitability and oscillatory activity, offering a therapeutic potential to slow down cognitive decline. During this talk, different methods and results will be presented regarding the use of TMS/rTMS and tDCS/tACS as potential therapeutic tools to improve network activity and cognitive function in the elderly and in cognitively impaired population. Challenges and limitations arising from the methodologies, intra-individual differences and biomarkers will also be discussed.

Rare causes of strokes

FW05-1

Monogenic small vessel diseases

H. Chabriat

Centre NeuroVasculaire Translationnel Hopital Lariboisiere Université Paris Cité INSERM U1141, Paris, France

Introduction: Since the 1990s, after the discovery of CADASIL, various cerebral small vessel diseases (cSVD) of hereditary origin have been identified. These genetic conditions have led to the discovery of important disease causing genes, to the development of multiple preclinical models and have shed new insights into the pathophysiology of cSVD in general.

Objectives: We propose to summarise the main characteristics of these different disorders and their variable phenotypes and to discuss their clinical course, imagingaspects and pathophysiology.

Synthesis: In such conditions, underlying alterations of key proteins and/or signalling pathways have been identified within the vascular wall. The different stages from molecular alterations up to pathological changes in the wall of arterioles or capillaries are now progressively deciphered.

Conclusion: We believe that the basic mechanisms underlying these hereditary cSVD are also involved in sporadic cSVD and that accumulating knowledge in the pathophysiology of these rare conditions should lead to new therapeutic approaches for preventing the progression of these disorders.

Disclosure: H. Chabriat has previously received fees from Hovid Company to participate to the steering committee.

FW05-2

Diagnosis and treatment of vasculitis

P. Berlit

German Society of Neurology, Berlin, Germany

Primary angiitis of the central nervous system (PACNS) is an inflammatory disease affecting exclusively small and medium-sized vessels of the central nervous system. CNS-vasculitis may also occur in systemic diseases like giant cell arteritis, Takayasu arteritis, granulomatosis with polyangiitis, or Behçet syndrome. The most common presenting symptoms of CNS vasculitis are multifocal symptoms associated with recurrent episodes of ischemia or hemorrhage, encephalopathy-related cognitive and affective abnormalities, and headaches. Diagnostic work up of CNS vasculitis includes MRI, CSF examination, digital subtraction angiography and brain biopsy. High-resolution, contrast-enhanced, compensated and fat-saturated MRI imaging of the cerebral vessel walls (black-blood imaging) may be of some value for the detection of CNS-vasculitis. Patients with normal CSF findings are unlikely to have CNS vasculitis. Brain biopsy should be performed in suspected PACNS. Important differential diagnoses include reversible cerebral vasoconstriction syndrome, moyamoya angiopathy and infectious vasculopathies (VZV, SarsCoV2, borreliosis, bacterial endocarditis). The adherence to diagnostic criteria and the avoidance of inappropriate therapies are essential. Treatment recommendations for CNS-vasculitis include glucocorticoids in combination with cyclophosphamide or rituximab; however, randomized clinical trials of PACNS treatment do not exist. Induction therapy is recommended for 6 to 12 months. After remission is achieved, treatment may be continued with substances as mycophenolate mofetil, methotrexate, or azathioprine. Repeated clinical, CSF- and neuroradiological monitoring is needed to determine the individual duration of maintenance therapy.

Disclosure: No conflicts of interest.

FW05-3

Moya-moya arteriopathy

A. Bersano

Fondazione IRCCS Istituto Neurologico Carlo Besta, Milan, Italy

Moyamoya arteriopathy (MA) is a rare but disabling cerebrovascular disease, affecting children and young adults, mostly female. It is characterized by a progressive steno-occlusive process of the terminal part of the internal carotid arteries (ICAs) and their proximal branches associated with the development of an unstable network of collateral vessels at the base of the brain (Moyamoya vessels). These MA vascular hallmarks are responsible for recurrent ischaemic and hemorrhagic strokes (80% of cases). Mortality rate has been estimated around 6.8-28.6% in hemorrhagic cases. Even though the pathogenesis of MA has not been elucidated yet, unbalances in angiogenic processes as well as genetic susceptibility have been invoked in the disease pathophysiology. Particularly, the susceptibility gene RNF213 was shown to be strongly associated with MA occurrence with a founder effect in East Asian patients. However, the role of this gene in Western patients is still unknown. The lack of data on the pathogenesis and the course of MA, mostly in Western countries, hampers the development of effective treatments, limiting the occurrence and/or progression of the disease. To date, direct and indirect surgical revascularization is the only available treatment reducing the incidence of ischemic and hemorrhagic strokes and improving cognitive deficits in pediatric and adult patients. However, no clear guidelines on the surgical timing or optimal procedure are available and therapeutic strategies largely depend on the surgeon's skills.

Disclosure: Nothing to disclose.

How to confirm a diagnosis of possible mitochondrial disease. An evidence-based approach

FW06-1

Mitochondrial red flags of the Central Nervous System

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A variety of clinical disorders are linked to mutations in both mitochondrial and nuclear genomes, leading to defective oxidative phosphorylation and ATP depletion, and clinically impairing multiple tissues and organs. This class of diseases still represents a challenge for neurologists, both in the diagnosis and treatment approaches. In this lecture, tailored for trainee clinicians and clinical scientists and practitioners with an interest in mitochondrial diseases, I will provide an update on recent developments in diagnostics and clinical presentation of CNS involvement in mitochondrial diseases, with an emphasis on red flags, applying an evidence-based approach.

Disclosure: Nothing to disclose.

FW06-2

Mitochondrial red flags of the Peripheral Nervous System

Y. Ng

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Mitochondrial dysfunction frequently affects the peripheral nervous system. Chronic progressive external ophthalmoplegia (CPEO) is a common clinical manifestation of adult mitochondrial disease. CPEO is characterized by progressive bilateral eyelid ptosis and complex ophthalmoplegia due to extraocular muscle weakness. CPEO can occur in isolation or is associated with proximal myopathy. There are marked genetic heterogeneities in CPEO, including single, large-scale mitochondrial DNA (mtDNA) deletion (sporadic), mtDNA point mutations (maternal inheritance), and nuclear genes involved in mtDNA maintenance (Mendelian inheritance). The age of disease onset, the association of other neurological and systemic features, and family history in patients presenting with CPEO are helpful clinal clues to guide further investigations. For example, childhood-onset CPEO and conduction heart defects are seen in single, large-scale mtDNA deletion. CPEO and mixed sensory and cerebellar ataxia are associated with POLG mutations, CPEO and prominent bulbar weakness and respiratory failure are commonly identified in TK2 deficiency. Peripheral neuropathy, especially in the axonal form, is another common finding in adult patients with mitochondrial disease. Sensory and/or motor polyneuropathy is a core feature of several mitochondrial syndromes, including neurogenic weakness, ataxia and retinitis pigmentosa, ataxia neuropathy spectrum in POLG disease and mitochondrial neurogastrointestinal encephalomyopathy. More recently, mitochondrial proteins involved in mitochondrial dynamics, such as mitofusin 2, are emerging as important causes of genetic neuropathy. In this workshop, we will use case illustrations to guide the participants on approaching adult patients presenting with CPEO, myopathy, and neuropathy. Specific therapeutic options for some cases will be discussed.

Disclosure: Nothing to disclose.

FW06-3

The diagnostic algorithm

C. Kornblum

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Mitochondrial diseases are some of the most common inherited neurometabolic disorders. Diagnostic confirmation and specific treatment are often challenging. The molecular genetic background is complex. The clinical phenotype is usually multisystemic with a preferential affection of skeletal muscle and other tissues with high energy demands. Mitochondrial diseases are characterized by a wide genotype-phenotype variability. Thus, the diagnostic pathway utterly depends on individual findings, e.g. the clinical phenotype, family medical history, and also specific requirements associated with the respective health care system. Diagnostic procedures may include blood tests, neurophysiological examinations, muscle and brain MRI, skeletal muscle biopsy, and molecular genetic analyses. In this presentation, we will focus on the most frequent clinical syndromes that can be overseen easily due to common diagnostic pitfalls: chronic progressive external ophthalmoplegia, Leber hereditary optic neuropathy, mitochondrial encephalomyopathy with lactic acidosis and stroke-like episodes, myoclonic epilepsy with ragged red fibers, and mitochondrial neurogastrointestinal encephalomyopathy. We will follow a didactic concept and step-by-step approach first presenting clinical key features like upper eyelid ptosis, stroke-like phenomena, myoclonus or cachexia and their broad differential diagnoses. Next, we will give an understanding of typical symptoms, hints and red flags of these mitochondrial syndromes completed by most recommended diagnostic pathways especially focusing on molecular genetic examinations.

Disclosure: Cornelia Kornblum received travel funding and/or speaker honoraria from Chiesi, Fulcrum Therapeutics, Novartis, Sanofi Genzyme, Santhera. She acknowledges financial support as advisory board member and/or primary investigator for Amicus Therapeutics, Fulcrum Therapeutics, Hormosan, Reneo Pharmaceuticals, Roche Pharma AG, Sanofi Genzyme, Stealth BioTherapeutics.

EAN/EANM: Translating the A/T/N system into clinical practice

FW07-1

Dual amyloid PET acquisition: a double window on neurodegeneration and amyloidosis

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FW07-2

New frontiers of Tau PET

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Pathological tau aggregates are involved in the pathophysiology of a number of neuropsychiatric disorders. So far, these tau pathologies could only be detected post mortem by histopathology. With the recent emerge of tau-targeting PET tracers, this has changed. It is now possible to non-invasively quantify the extent and localisation of tau pathology directly in the living brain. As such, tau PET imaging is an exciting addition to the existing fluid (CSF- or plasma-based) tau biomarkers. Here, an overview on the current knowledge with regard to tau PET imaging is provided. While most of the first-generation tau tracers suffer from relevant unspecific (with regard to tau) binding and limited effect sizes, [18F]flortaucipir was recently approved by the FDA to diagnose later stages of 3R/4R tau pathology in Alzheimer's disease (AD). Recently emerged, improved second-generation tracers like [18F]MK-6240, [18F]RO-948, [18F]PI-2620 and others already demonstrated the potential to detect earlier tau stages in AD. These tracers are also capable of differentiating, depending on their binding pattern, AD subtypes. In parallel, [18F]PI-2620 and [18F]APN-1607 showed potential to image 4R tauopathies like progressive supranuclear palsy and corticobasal degeneration. So far, none of the currently available tracers has shown potential to image 3R tau. Taken together, there is enormous energy and speed in the efforts to provide tau PET imaging to affected patients, both in research and clinical care. This new tool has great potential to broaden the portfolio of imaging biomarkers in neuropsychiatric disorders.

Disclosure: HB received speaker honoraria from Novartis/AAA, and reader honoraria frim LMI.

FW07-3

The emergence of neurodegenerative disease other than Alzheimer: a biomarker-based artifact?

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The ATN system describes the pathological status of a patient based on validated biomarkers that reflect amyloid (A) and tau (T) pathology as well as neurodegeneration (N). The pathological status can be assessed through cerebrospinal fluid biomarker analyses (ATN), amyloid or tau PET scans (AT) as well as FDG PET and MRI scans of the brain (N). Alzheimer's disease (AD) is defined as A+T+, irrespective of the N status. However, previous studies in autopsy-confirmed AD reported that up to 32% of subjects are T- based on cerebrospinal fluid (CSF) P-tau results. A significant proportion of AD patients is A- when only CSF Aβ1-42 is analysed. The ATN status might not exactly reflect the pathology in individual subjects, and one should wonder how many A-T+ or A+T- subjects still have AD. Can borderline CSF biomarker values contribute to these atypical profiles? These questions will be answered through a study of the ATN profiles in a cohort of 92 autopsy-confirmed AD patients and in a cohort of 65 clinically diagnosed MCI and dementia due to AD patients that underwent both lumbar puncture for CSF biomarker analyses and amyloid PET.

Disclosure: S.E. received unrestricted research funding from Janssen Pharmaceutica and ADx Neurosciences and served as a consultant for Biogen, Danone, Eisai, icometrix, Novartis, Nutricia, Roche.

Sunday, June 26 2022

Application of artificial intelligence to MRI in Multiple Sclerosis: from diagnosis to prognosis and monitoring.

FW08-1

Use of AI for MRI analysis: principles and application

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FW08-2

AI & MS diagnosis and differential diagnosis

M. Rocca

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Traditionally the diagnosis and quantification of the disease burden in multiple sclerosis (MS) rely on visual patterns recognition by experienced clinicians, these tasks time-consuming and hardly reproducible. Given the amount of scientific data, the heterogeneity of disease courses and the broad therapeutic scenario, great effort has been devoted to the application of artificial intelligence (AI) in MS to anticipate the diagnosis and to predict long-term prognosis. Machine learning (ML) methods analyze data to obtain decisional patterns, whereas deep-learning (DL) tools perform an automated selection of the best problem-solving features. Both these approaches mainly benefit from large datasets, hence being useful in multicenter studies and for large-scale clinical application. ML and DL algorithms are able to automate repetitive tasks, to analyze more data in lesser time and to achieve higher accuracy and reproducibility than the human counterpart. The application of AI has obtained promising results in medical imaging field (especially that of MRI), allowing automated lesion and tissue segmentation, disease classification, and contrast synthetization from advanced sequences. Such an approach is also suitable for the developing world of "omics", where the analysis of large amounts of data obtained from a single patient is pivotal in the perspective of personalized-medicine. During this workshop, we will discuss uses and limitations of AI in MS and its potential applications in the context of MS diagnosis. Despite the encouraging role of AI, one cannot overemphasize the paramount importance of human supervision, in order to optimize their use and take full advantage of their potential.

Disclosure: MAR received speaker honoraria from Bayer, Biogen, Bristol Myers Squibb, Celgene, Genzyme, Merck Serono, Novartis, Roche, and Teva, and receives research support from the MS Society of Canada and Fondazione Italiana Sclerosi Multipla.

FW08-3

AI & MS prognosis and monitoring

A. Eshaghi

Department of Neuroinflammation and Department of Computer Science, University College London, London, United Kingdom

Artificial intelligence (AI) is a field of computer science that uses algorithms that can learn complex patterns in large data sets. It has the potential to be used as both a prognostic and a monitoring tool to facilitate the move towards personalized decision making in ways that would not have been possible before. The accumulation of extensive and high-quality data from real-world registries, imaging, "omic", clinical trials and real-time monitoring tools are precursors for a future in which AI may act as a decision aid for neurologists. In multiple sclerosis (MS), recent progress in AI may enable (1) optimized image processing, including MRI analysis, (2) prognostication to identify higher-risk patients who may require more effective treatments, and (3) a better understanding of mechanisms underlying disease progression and identifying treatment targets. Despite these advances, the translation to clinical care is non-existent. I will provide an overview of the recent progress in AI and its application to neurological disorders, with a focus on MS. I will discuss the future direction of AI research in MS and other neurodegenerative disorders, its limitations and its potential applications in areas that can be revolutionary but have so far been neglected.

Disclosure: In the past three years, Arman Eshaghi has received travel support from the National Multiple Sclerosis Society. He has received research grants from Biogen, and Roche through his institutions. He holds equity stake in Queen Square Analytics Limited.

EAN/MDS-ES: Recent advances in surgical treatment of movement disorders

FW09-1
Dystonia

R. Jech

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FW09-2
Parkinson's disease

E. Moro

CHU de Grenoble, Division of Neurology, Deparment of Psychiatry and Neurological Rehabilitation Service de Neurologie, CHU Grenoble, Grenoble, France

FW09-3
Essential Tremor

M. Contarino

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Although tremor is the most frequent movement disorder, and medical treatment is very often frustrating, not many patients with Essential Tremor (ET) are referred for surgical treatment. This could be partly due to the fact that surgical options are still poorly known among GPs and patients . Surgery can provide a very good benefit for ET. Usually distal postural tremor presents the best and most stable response, followed by proximal postural and kinetic tremor. Intention tremor often responds incompletely or temporarily. There are several surgical options for patients with ET: Deep Brain Stimulation (DBS) is the most frequently used, due to the advantage of a bilateral approach and adjustable parameters. Alternatively, lesional surgery can be performed by stereotactic radiofrequency coagulation, gamma-knife radiosurgery, or Focused Ultrasound (FUS). When considering surgical options, surgical risks (among which hemorrhage or infection) must be taken into account. Although the thalamic Vim nucleus is the most common target, other anatomical structures in the cerebellar pathways (such as the zona incerta or the posterior subthalamic area) can be targeted. Gamma-knife and FUS lesions are less expensive, require less intensive postoperative care and are non-invasive techniques with lower surgical risks, but are usually performed only unilaterally to minimize the risk of permanent side effects. A correct classification and characterization of tremor, as well as a case-by-case evaluation of the risk-benefit profile and patients' expectations are important to decide whether surgery is an appropriate choice, which surgical option is better, and when is the best time to propose surgery.

Disclosure: Travel support: BostonScientific. Advisory board: Medtronic (fees to institution). Consultancies: Medtronic (independent consultant for research and educational issues - fees to institution) Speaking fees: ECMT. Research support: Medtronic: unrestricted educational grant (to institution 2017–2020).

The challenge of neuroinfection continues, even more in in post-COVID times

FW10-1

What about - Vaccine preventable infections

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Neurointensive Care Unit, Medizinische Universität Innsbruck, Universitätsklinik für Neurologie, Innsbruck, Austria

Infections of the CNS are still associated with high morbidity and mortality. Over the last 3 decades community aquired bacterial meningitis has decreased significantly in middle and even low income countries by large immunization programmes. Vaccines against Haemophilus influenzae are available since the late 1980s, against pneumococci since the late 1990s and against different meningococci strains with the beginning of the 2000s. Since these immunsation programmes focused on young children and adolescents, bacterial meningitis is nowadays more an infection of the elderly and immuncompromised person with quite different pathogens as Listeria monocytogenes, gram negatives, staphylococci, fungi and also protozoa. Tickborne encephalitis is the most important viral encephalitis in Central and Eastern Europe. Vaccination programmes started in the 1980s have reduced the disease burden in Europe. Japan B encephalitis causes 20–30,000 deaths per year. Vaccination is recommended for special circumstances and travelling into the epidemic regions of South and South-East Asia. Vaccines against the toxin related neuroinfections tetanus and diptheria are part of most European childhood immunisation programmes and are nowaday rareties in our areas. But political instability and war situations with reduced access to health care and immunisation programmes can cause re-emergence of these diseases as it was seen in Syria 2013 and Ukraine in February 2022 when single cases of poliomyeltis had to be diagnosed.

Disclosure: Nothing to disclose.

FW10-2

What about infection in travellers, migrants and refugees

F. Carod Artal
Neurology department, Raigmore hospital, Inverness, United Kingdom

Several factors have been linked to emerging infectious diseases including new agents (coronaviruses, zika virus), extension of geographical areas (schistosomiasis, dengue, West Nile, zika virus), increase in incidence (HIV, tuberculosis) and travel/migration (Chagas disease, cysticercosis). According to the World Migration Report 2020, the number of international migrants reached 272 million globally in 2019, and nearly two-thirds were labour migrants. Epidemiological evidence about infectious diseases and neuroinfection among travellers, migrants and refugees will be reviewed. Traveller's diarrhoea, dengue fever and other tropical diseases are reported in travellers. Re-emergence of infections in Europe includes chikungunya, dengue and malaria. Migration of asymptomatic people spread American trypanosomiasis in non-endemic areas and cases have been reported in Europe, Japan, and North-America. Neurocysticercosis is a common cause of seizures among South American migrants in USA. Migrants may be asymptomatic carriers (Chagas, HTLV-1). The involvement of CNS may occur in viral infections (HIV, HTLV-1, dengue, zika), malaria, schistosomiasis (myeloradiculopathy), Chagas disease (encephalitis, stroke), etc. Refugees may be at slightly higher risk of infectious diseases including tuberculosis, HIV, hepatitis and schistosomiasis. Systematic reviews have found that tuberculosis and hepatitis B and C prevalence is higher among migrants arriving in Europe, and the prevalence of antimicrobial resistance and infections was higher in refugees and asylum seekers than in other migrant groups. Infectious diseases in migrants may be explained by a higher prevalence in migrants´ countries of origin, barriers to health care in host/transit countries, and poor living conditions. These factors are especially relevant in vulnerable populations (refugees, documented migrants).

Disclosure: I don't have any conflict of interest regarding this lecture.

FW10-3

What about infections in the immunecompromised

M. Romoli

Neurology Unit, Neuroscience Dept, Bufalini Hospital, Cesena, Italy

The number of immunocompromised patients has found a steady increase over the last decades. In 2013, a National Health Interview Survey estimated that 2.7% of the population was immunocompromised. Immunosuppression can have several causes, from disease targeting the immune system or solid organs, to drugs that have to put the immune system down to extend life and its quality. Depending on the nature of their immunosuppression, patients may be at risk for a variety of infectious complications, both common and rare. Atypical symptoms of infection are common among all classes of immunocompromised people: asplenia, HIV infection, solid organ transplant, biologic medications for autoimmune diseases, and cancer. Due to the nature of infection, response to treatment and underlying conditions predisposing to it, these infections can carry a poor prognosis. Empirical therapy depends on the type of immunodeficiency. In HIV-infected patients, the most common CNS infection is cerebral toxoplasmosis, whereas in other immunocompromised patients, aspergillosis, cryptococcal meningitis and tuberculous meningitis seem to be more prevalent. However, in up to 15% of cases multiple pathogens can be identified from specimens, therefore complicating targeted therapy. A systematic approach including early diagnosis, targeted antimicrobial treatment and early aggressive approach can have a role in improving outcomes.

Disclosure: Nothing to disclose.

Implementing evidence: What have we learned and what must we do better?

FW11-1

Stroke: Implementation in the acute and emergency setting

H. Christensen

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Implementing evidence in stroke is – at least 90% - all about organization of care. Stroke treatment and care are presently areas that are strongly evidence-based and where treatment benefits are well-document both on individual basis but also with a health economical approach. We do not only improve patient outcomes but also save money for societies when preventing and treating stroke. There are three major steps in ensuring access to acute stroke care. 1) In the prehospital phase, contact to EMS from patient or bystander is a prerequisite. Further, the paramedics shall correctly identify stroke and ensure swift transportation to an intuition providing acute stroke treatment and care. 2) On arrival in hospital, the stroke diagnosis shall be confirmed, and immediate reperfusion therapy provided, if indicated. Appropriate care must also be ensured for patients with no indication for reperfusion therapy, e.g., patients with ICH. 3) All patients with stroke must be directly admitted to a stroke unit. The organization of stroke care musk work seamlessly with the general organization of health care in the country or region, and there is no one size fits all – especially not in Europe where organization of health care varies significantly between countries as well as the availability of resources. Based on Action Plan for Stroke in Europe's 'Essentials of Stroke Care' essential interventions and existing approaches will be discussed. The importance of service quality trackers and certifications will also be discussed.

Disclosure: HC has received speakers honoraria form Bayer, Boehringer-Ingelheim, BMS, and Daiichi-Sankyo.

FW11-2

Rare diseases: Implementation when both expertise and high-quality evidence are scarce

M. Reilly

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Rare diseases are defined as diseases affecting less than 1:2,000 of the population. Although these diseases are individually rare, together they affect a significant number of patients seen in neurological practise. Rare diseases pose challenges diagnostically and therapeutically. Diagnostically there is often a lack of agreed criteria or lack of evidence to make a definitive diagnosis. Therapeutically for some disease like many of the genetic disease there are no effective therapies in clinical practise and for other disease like the inflammatory neuropathies there are therapies available but often without the high quality evidence needed to be confident they will work. As clinicians who see patients with rare diseases we still need to diagnose and treat these patients regardless of what evidence is available. For diagnosis strategies include the use of multidisciplinary meetings with experts across disciplines available to agree a most likely diagnosis. This is particularly useful in patients with challenging diagnoses that cross disciplines e.g. genetics and neurology, haematology and neurology. For treating rare diseases often multiple strategies are needed including individual expertise, thorough literature searches, multidisciplinary input, ongoing review of diagnosis and therapy trials in individual patients. For rare diseases collaborations in the establishment of registries and databases, development of expert diagnostic and treatment guidelines and innovative approaches to clinical trial design the most promising tools to obtain the high quality evidence needed. This lecture will explore this topic with case examples from a diagnostic and therapeutic perspective.

Disclosure: I do consultancy work for Alnylam, Inflectis, Eidos, Applied Therapeutics.

FW11-3

Epilepsy: Implementation in a chronic disease across the life course

B. Steinhoff

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Brain death, cardiac death and organ donation: What the neurologist should know

FW12-1

Brain death and organ donation: Legislation and practice in 25 different countries

D. Kondziella

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Brain death protocols around the world almost universally follow a three-step approach: Confirmation that the prerequisites for a brain death protocol are fulfilled, the clinical brain death exam itself, and confirmatory laboratory investigations if required. However, although brain death protocols must be adhered to, it is important to know that they vary widely in detail from country to country. For example, a recent study found as many different protocols as countries surveyed (n = 24). Thus, whereas 1h must pass between the two clinical brain death examinations in Brazil, the time interval in Luxembourg is 6 h. In Canada, legislation requires only one physician to perform the clinical examination, but at least four physicians are needed in South Korea. Digital subtraction angiography is needed in Denmark in certain situations, whereas in Japan EEG is mandatory. Even within the same country, e.g., the USA, guidelines and practices vary according to geography. Also, while in most countries a patient is declared brain dead based on the irreversible loss of activity of the entire brain ("whole brain death"), the UK and India, by contrast, have implemented the concept of brainstem death, i.e., evidence of the irreversible loss of brainstem activity is sufficient. This lecture highlights the variability of worldwide brain death legislations, with the objective to provide the audience with a thorough understanding of the pathophysiology of the dying brain, and the knowledge of how to avoid common pitfalls in the clinical brain death exam and the interpretation of confirmatory laboratory tests.

Disclosure: Nothing to disclose.

FW12-2

Organ donation after cardiac death: The role of the neurologist

R. Beer

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Organ donation after the circulatory determination of death (DCDD), previously known as "non-heart beating donation" or "donation after cardiac death" (DCD) is an alternative option in patients who do not meet formal brain death (BD) criteria, and accounts for a growing percentage of deceased organ donations. There are two broad categories of DCDD: Uncontrolled DCDD refers to organ donation following unsuccessful resuscitation. More frequently, this procedure is done in a controlled DCDD (cDCDD) protocol following the planned withdrawal of life-sustaining therapies (WLST). There is strong consensus that the decision to organ donation should be uncoupled from the decision to WLST and never drive the process of determining a prognosis that justifies the WLST. Here, the neurological expertise needed in the cDCDD process will be highlighted, especially emphasizing the role of the neurologist to evaluate the prognosis of patients with devastating brain injuries, high spinal cord injury, and terminal neurodegenerative disease before any end-of-life decisions are made. Further, the relationship between WLST, circulatory arrest and permanent cessation of brain function will be discussed. Moreover, the issues of proper palliative care to the donor during WLST, the preservation of dignity of the dying patient, as well as organ preservation measures will be covered.

Disclosure: Ronny Beer is neurological consultant to the Austrian National Office of Transplantation Affairs.

FW12-3

Cellular mechanisms in the dying brain: Scientific and ethical considerations

J. Dreier

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To inform the definitions of cardiocirculatory death, brain death and biological death, it is interesting to take a closer look at the pathophysiology of the brain's dying process. The time point at which the first neurons are irreversibly damaged is termed the commitment point. When cerebral circulation ceases completely, as after cardiac arrest without resuscitation attempts, the commitment point is usually reached 4–10 min after the onset of cardiocirculatory arrest. Death is electrocorticographically characterized by the negative ultraslow potential (NUP). The two most obvious electrocorticographic changes that typically occur before the NUP are depression of spontaneous activity and spreading depolarization. Notably, the term spreading depolarization describes toxic cellular changes that eventually lead to cell death, but the depolarization is not a marker of neuronal death per se, as it is reversible - up to a point - with restoration of the physiological cellular homeostasis. This means that resuscitation with complete recovery of neurological functions is still possible even if the spreading depolarization has already started. The typical pattern recorded in the ICU after cardiocirculatory arrest is a non-spreading activity depression followed a median of 80 seconds later by the appearance of a spreading depolarization. The typical electrocorticographic pattern during brain death development is impressively different from this. It largely resembles the pattern also recorded when the electrodes are placed directly over a just-developing cerebral infarction. Characteristic here is a cluster of spreading depolarizations that first causes spreading and persistent activity depressions and eventually shows the transition to NUP.

Disclosure: Nothing to disclose.

EAN/WMS: The role of real-world evidence data in therapeutic decisions.

FW13-1

Opportunities and challenges in using real-word data to treat neuromuscular disorders

M. Molnar

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Real-world data (RWD) is any data that is collected in the clinical care, as opposed to data collected within a clinical trial that are not representative of real-world care and outcomes. The most important types of RWDs in healthcare are: 1.) Clinical data from electronic health records and case report forms (demographics, family history, comorbidities, treatment history, outcomes). 2.) Patient-generated data from patient-reported outcome surveys. 3.) Public health data. 4.) Health economics data. RWD is aggregated into real-world evidence (RWE) through robust analytics. RWE is becoming critical to establish effectiveness, long-term drug safety, quality of life, resource use, and to determine the impact of a healthcare intervention on the treatment pathway of local population. It can also determine the effect that a healthcare intervention has on outcomes for patients who may be excluded from randomized controlled trials. The collection of RDWs is a new challenge for clinicians. They have the be able to design protocols, answering meaningful clinical questions. to define which data elements can be collected and define and calculate clinically relevant outcomes. In many cases EHRs might not contain all of the data what we wish to have. In the new era we need computable phenotypes, standardized data schemes and data transfer protocols, interoperability with proprietary health information systems. This presentation will give you general insight how to prepare computable phenotypes, standardized data schemes and data transfer protocols which are supporting the implementation of the data driven precision medicine.

Disclosure: Dr. Maria Judit Molnar has nothing to disclose.

FW13-2

How real word outcomes influence the therapeutic decisions in muscle disorders.

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A therapeutic decision generally should require demonstration that it improves a clinical outcome or a validated surrogate for such an outcome. Improving survival, improving exercise capacity or function, preventing hospitalization, or improving quality of life, are all important treatment goals and have a direct impact on patients and their family. Nevertheless, clinical outcome assessments (COA) are not always feasible and healthcare professionals often rely on patient reports to guide management. For this reason and because COAs are generally not performed in a home environment, patient reported outcome measures (PROMs) and Real-World Data (RWD) are emerging in use and value, and can complement the evidence from randomised clinical trials, support innovative study designs to inform therapeutic decisions. Specifically, when combined with emerging technology and wearable devices, which offer the means to achieve remote, possibly continuous, longitudinal monitoring of a patient's physical activity. More importantly, Patient Generated Data (PGD) can contribute to all traditionally defined COAs and patient reports to improve the quality of clinical decision making. PGD is creating new hopes for patients and their families and is defined as "health-related information created, recorded, or gathered by or from patients, family members or other caregivers to help support and manage disease state". Challenges remain, as there are limited PROMs that reflect patient experience or have been properly constructed for the vast majority of rare diseases and the real-world evidence on progression and the burden of disease has not been collated and used to inform the base parameters of therapeutic decisions.

Disclosure: I am or have been a chief/principal investigator for trials sponsored by Biogen, Genethon, Sanofi Genzyme, Sarepta Therapeutics, Novartis Gene Therapies, Roche and a sub-investigator for many other commercial studies. I received speaker honoraria from Sanofi Genzyme. I am or have been on advisory boards for Astellas Gene Therapies, Biogen, Edgewise Therapeutics, Kate Therapeutics, ML Bio Solutions, Roche, Sanofi Genzyme, Sarepta Therapeutics, Vertex and Wave Therapeutics. I have/had research collaborations with Ultragenyx, Sarepta Therapeutics and Sanofi Genzyme.

FW13-3

How real world data guides SMA management

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Spinal muscular atrophy (SMA) is a lower motor neuron disease caused by mutations of SMN1 gene. Natural history studies delineated SMA1-4 types defined by the age of onset of symptoms, maximal motor function achieved and prognosis. SMA1 is the most common genetic cause of infantile mortality, while patients with SMA2-3 have normal or near normal life expectancy, but present with progressive, often severe muscle weakness. Improvement of multidisciplinary care resulted in improved survival; currently 30-50% of SMA patients in most populations are adults. Since 2017 three disease modifying therapies (DMTs): nusinersen, risdiplam and onasemnogene abeparvovec were approved by EMA, all after clinical trials conducted in pediatric or young-adults populations. There is increasing need for real-world data (RWD) on long term efficacy and safety of DMTs in SMA patients in patient's cohorts reflecting the whole age and severity spectrum. Results of observational studies provide valuable evidence of efficacy of DMTs in children and adults. Although most dynamic improvement is seen in pediatric SMA, RWD demonstrate improved function even in severe SMA1 adult patients. RWD demonstrates evolution of SMA phenotype and need for revised standard of care in the DMTs era.

Disclosure: Speaker honoraria, travel support and Advisory Board Biogen, PTC, Novartis/Avexis, Roche, PI in SMA clinical trials (Roche), reasearch institutional support (Biogen).

The human functional connectome in neurological diseases – relationship to pathology and clinical progression

FW14-1

The human functional connectome in neurodegenerative diseases

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IRCCS San Raffaele Scientific Institute & Vita-Salute San Raffaele University, Milan, Italy

Magnetic resonance imaging (MRI) is playing an increasingly important role in the study of neurodegenerative diseases, delineating the structural and functional alterations associated with these conditions. Network-based analysis of structural and functional connections has provided a new technique to study the brain. Graph theory provides a powerful method to quantitatively describe the topological organisation of brain connectivity. With such a framework, the brain can be depicted as a set of nodes connected by edges. Distinct modifications of network topological organisation in the brain have been identified during normal ageing, whereas disrupted functional and structural connectivities have been associated with several neurodegenerative disorders, including dementia, Parkinson's disease and amyotrophic lateral sclerosis. These assessments are of special interest for their potential to characterize the signature of each neurodegenerative condition and aid both the diagnostic process and the monitoring of disease progression. All these findings allow us to investigate the different features of neurodegeneration. This aspect will become crucial when disease-modifying (personalized) therapies will be established.

Disclosure: M. Filippi Editor-in-Chief of the Journal of Neurology and Associate Editor of Human Brain Mapping, received compensation for consulting services and/or speaking activities from Almiral, Alexion, Bayer, Biogen, Celgene, Eli Lilly, Genzyme, Merck-Serono, Novartis, Roche, Sanofi, Takeda, and Teva Pharmaceutical Industries, and receives research support from Biogen Idec, Merck-Serono, Novartis, Roche, Teva Pharmaceutical Industries, Italian Ministry of Health, Fondazione Italiana Sclerosi Multipla, and ARiSLA (Fondazione Italiana di Ricerca per la SLA).

FW14-2

The human functional connectome in epilepsy

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Structural connectivity is an essential counterpart of functional connectivity underpinning and forming the anatomical basis of functional connectivity, derived from diffusion measures in white matter and grey matter atrophy. EEG patterns and resting state fMRI (rsfMRI) networks are complementary expressions of cerebral activity. Ictally, rapid spread of gamma power, correlated with resting-state functional connectivity suggests that physiological pathways act as pathways of seizure spread. Structural network dysfunction and abnormal brain wide communication contribute to cognitive difficulties in focal epilepsy. In temporal lobe epilepsy (TLE) with impaired memory, there was concordance between activations, topographic gradients and performance. In left TLE there was impairment of task-positive language networks. Right TLE showed altered connectivity for default mode network cortical regions. Naming involves the dominant posterobasal temporal lobe. Weaker functional connectivity between this and bilateral anterior temporal lobe, precentral gyrus and lingual gyrus during auditory naming, and to occipital cortex and right fusiform gyrus during picture naming was accompanied by decreased neurite dispersion and higher free water fraction of white matter tracts. TLE was associated with impaired coupling of functional and structural metrics, with more severe disturbance in left TLE. Abnormalities of intrinsic local connectivity is associated with seizure onset zone abnormal in focal epilepsy. In individuals with TLE who had FBTCS, there was greater task-related thalamo-temporal and thalamo-motor connectivity. In these patients there was also alterations of the structural network that may serve as an underlying structural basis or consequence of the greater seizure spread observed in FBTCS.

Disclosure: Nothing to disclose.

FW14-3

The human functional connectome in brain tumours

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Treatment strategies for Multiple Sclerosis: escalation, induction, combination

FW15-1
Escalation

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FW15-2
Induction

T. Ziemssen
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For the past 25 years, there has been an accelerating inclusion of new immunomodulating drugs in immunotherapy of multiple sclerosis (MS). Two different therapeutic approaches are widely used in MS: escalation and induction therapy. The concept of induction treatment followed by long-term maintenance treatment or no necessary treatment has attracted considerable attention. This approach seems to be suitable for patients with particularly aggressive disease, characterized by frequent relapses with incomplete recovery and the accumulation of focal lesions visible on magnetic resonance imaging. In addition, MS immunotherapies may also be classified in a different way, into treatments that are given continuously (chronic treatments) and medications that are applied intermittently (immune reconstitution therapies (IRT)). The principle behind the latter is depletion of the immune system that allows it to rebuild itself. Upon its reconstitution/resetting, the immune system regains the ability to respond to infections and survey the periphery for cancer. An IRT by definition is given at short intermittent courses and not continuously. IRT modalities were shown to induce long-term remission of MS that, in some cases, is close to the definition of a "cure. Haematopoietic stem cell transplantation, cladribine and the monoclonal antibodies alemtuzumab, rituximab and ocrelizumab are frequently categorized as IRTs. The risks of adverse events related to immune suppression (such as opportunistic infections and secondary malignancies) with IRTs are lower and front-loaded, whereas the common side effects of chronic immunomodulation are higher and accumulate with time.

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FW15-3
Combination

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The multifaceted pathogenesis of multiple sclerosis (MS) provides a multitude of targets for therapeutic interventions. Current therapies for MS are only partially effective. One potential strategy to increase treatment efficacy is the combination of two or more drugs with complementary mechanisms of action, which may result in additive or synergistic therapeutic effects. Various immunomodulatory, immunosuppressive, neuroprotective and regenerative agents may be considered for combination treatment regimens, which should be carefully tested in in-vitro experiments, animal models and appropriately designed clinical trials. Scientific rationale for combination therapy (CT) has been established by showing additive suppressive effects of glatiramer acetate and interferon beta on the in-vitro proliferation and proinflammatory cytokine secretion of T-cell lines specific for myelin basic protein. Amelioration of experimental autoimmune encephalomyelitis was achieved with combination of suboptimal doses of immunomodulators that were ineffective when used alone. Several immune abnormalities could be reversed in MS patients treated with various CTs, but clinical trials yielded mixed results, highlighting the complexity of CT in MS. Although no combination has reached the sufficient level of evidence that would allow its implementation in clinical practice so far, better understanding of the pharmacological properties of existing and new MS drugs and the rational development of new drug combinations make this goal achievable. Appropriate candidates for combination therapy should be carefully selected and fully tested for efficacy, safety and tolerability in well-designed controlled large clinical trials in order to provide definite evidence for the role of specific drug combinations in the treatment of MS.

Disclosure: Nothing to disclose.

Models for treatable inherited rare neurological diseases: from small molecules to biotechnological products

FW16-1

Cerebrotendinous xanthomatosis as a model of premature aging: early diagnosis and treatment

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Cerebrotendinous xanthomatosis (CTX) is a rare neurometabolic disorders with onset in early infancy, usually with siarrhea, cataract, tendon xanthomas and adult onset progressive neurologic dysfunction mainly characterized by dementia, ataxia, spasticity, psychiatric disturbancies, peripheral neuropathy, dystonia and parkinsonism, secondary to a metabolic defect in bile acids, with deficiency of chenodeoxycholic acid, and lipid abnormalities, with accumulations of cholestanol in serum and tissues in relationship to CYP27A1 gene mutation. Chronic treatment with chenodeoxycholic acid results in improvement of biochemical and clinical findings and when started in neonatal periodi s able to prevent the severe pathological changes. During the last 3 decades we have followed more then 70 patients with this disorders and we will report our data on the clinical and molecular heterogeneity, the efficacy of treatment and some speculations on what we learned by the scientific approach to this model of neurodegeneration. We will report also the data on a consensus article on the clinical approach of this disorder and on treatment. Expert opinion on diagnosing, treating and managing patients with cerebrotendinous xanthomatosis (CTX): a modified Delphi study. Stelten BML, et al and, Federico A.Orphanet J Rare Dis. 2021 Aug 6;16(1):353. The safety and effectiveness of chenodeoxycholic acid treatment in patients with cerebrotendinous xanthomatosis: two retrospective cohort studies. Verrips A.and Federico A. Neurol Sci. 2020 Apr; 41(4):943–949 The role of dentate nuclei in human oculomotor control: insights from cerebrotendinous xanthomatosis Rosini F, Federico A, Rufa A. J Physiol. 2017 Jun 1; 595(11):3607–3620.

Disclosure: Research grant obtained by Ledyant, London.

FW16-2

New strategies in enzyme therapy for neurometabolic diseases.

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FW16-3

Gene therapies for rare neurological diseases

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Rare neurological disorders are individually not common, however there are more than 7,000 of them. In the search for therapies aimed at the most upstream disease course modification, a number of generic approaches are emerging. They include direct gene editing repair using advanced molecular technologies, which are effective in cell and animal models but not yet ready for human disorders. However, replacement of mutated genes using viral vectors with the normal gene has now reached a level to be used for human disorders, including for example the easier anatomically accessible retinal diseases and metabolic disorders also affecting neurological function. Expression of mutation genes can be modified in different ways, which are now being developed as alternative to gene therapy in the strict sense. Clinical trials are underway with several strategies, including antisense oligonucleotides and interfering RNA delivered in the cerebrospinal fluid or directly in the brain. One advancing major effort is continuously being devoted to Huntington's disease and a first trial with a large cohort has reached its completion. The primary outcomes have not been reached and the drug application has had to be halted since progression in the treated group was more severe than after placebo. Many lessons have been learned to inform further development in the field. Furthermore, the gene expression modification approach is also started to be applied at gene known to modify the phenotype. Small molecules modifying gene expression with similar aims are also under assessment, also reaching clinical trial status.

Disclosure: Nothing to disclose.

EAN/EFIC: Managing cluster headache

FW17-1

Recent improvements in cluster headache pathophysiology

A. May

Dept. of Systems Neuroscience, University Clinic Hamburg, Hamburg, Germany

In recent years the understanding of the central and peripheral mechanisms playing a part in the pathobiology of cluster headache has increased substantially. The question whether a genetic alteration may be causal to the disorder arose when epidemiological studies revealed a certain familial clustering. First-degree relatives of cluster headache patients have an 18 times higher risk of developing the same disorder than the general population while the risk for second degree relatives ranges is between one and three times higher 3–7. Current evidence lists three key structures which need to interact for successful attack sequencing: An abnormal activation of the trigeminovascular system, the activation of parasympathetic nerve fibers (trigeminoautonomic reflex) and the hypothalamus 9. From a mechanistic point of view the role of the hypothalamus in cluster headache goes far beyond the simple transmission and modulation of nociceptive information on its way to cortical structures that process pain 10. Recently, the parasympathetic system came to the fore, based on the observation that functionally blocking the SPG ganglion stops cluster headache attacks and may even have a preventative effect. This lecture will focus on the pathophysiological basis of the TAC focussing on cluster headache and will delineate the central and peripheral aspects of this puzzle.

Disclosure: Arne May is Editor-in-Chief of Cephalalgia, nothing else to disclose.

FW17-2

Pharmacological management of cluster headache

R. Jensen

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Cluster headache is a relatively rare headache compared to migraine and tension-type headache but represent a fairly frequent neurological disorder. Due to the excruciating pain attacks and the lack of effective treatment it represents a major burden on the society and on patient's life.
Objectives: To present the newest therapy and recommendations for the treatment of cluster headache.
Methods: The databases PubMed (Medline), Science Citation Index, and the Cochrane Library were screened for studies on the effectiveness for cluster headache. Likewise, clinical.trials.gov were also searched. Recommendations are based on controlled trials, but also on some case-studies and case-series.
Results: With regards to acute treatment only nasal and subcutaneous triptans and/or oxygen have documented effect and here the episodic patients are more likely to respond than the chronic patients. As transitional treatment only steroids have an effect but are hampered by side effects. For prevention the drug of choice is still Verapamil and/or lithium but here the responder-rates are limited. The CGRP antibodies, that are very effective and well tolerated in migraine, have only proven some efficacy in the episodic but not in the chronic cluster headache. However, there are ongoing studies on this topic. Despite acute therapy is more effective in the episodic than in the chronic subforms, there is a significant lack of better acute and especially preventive therapies. Cluster headache represent significant disability and very high socioeconomic burden so more specific and effective therapies are urgently needed. The existing and emerging therapies will be reviewed and debated.

Disclosure: RHJ has given lectures for Allergan, Teva, Novartis, EliLilly and Lundbeck. At present RHJ is principal investigator for clinical trials conducted by EliLilly and Lundbeck.

FW17-3

Neuromodulation for cluster headache treatment

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Getting evidence into practice: The use of "big data" in neuroepidemiology

FW18-1

Reliability of administrative databases for neuroepidemiology research

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Healthcare administrative data are collected mainly with reimbursement purposes by financing agencies, however such databases are rich sources for neuroepidemiological research as well. In countries with a single payer health insurance system the population of the whole country is covered in such databases for years or decades, providing the option for nation-wide follow-up studies. The legal system of several countries allows the use of such databases for research after central anonymization, thus complying with the general data protection regulations (GDPR). If a permanent identification code is assigned to each person in the anonymization process, then follow-up and information on medication use are possible to obtain via data linkage. The completeness of case identification can be increased if not only the main diagnosis used for reimbursement in the diagnosis related group (DRG) system is considered, but all diagnoses of a single hospital case (e.g. associating diseases, complications, cause of death) are also recorded in the database. Hospital data may be combined with data from outpatient services using data linkage. During data analysis in epidemiological studies, strategies of disease specific case certification should be developed to decrease the rate of false positive cases. The method of case certification should apply a disease-specific approach with a predefined set of criteria in the database and also include a validation process in a smaller set of patients. The thoroughness of the administrative database and the lack of option for direct patient contact are the major limitations in epidemiological studies based on healthcare administrative data.

Disclosure: The authors have no conflicts of interst regarding the content of this abstract.

FW18-2

Estimation of occurrences and consequences of neurological diseases estimated by traditional epidemiological studies and by analyses of "big data"

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Determining the frequencies of neurological diseases, associations, causes, comorbidities, consequences, significance of associations and outcomes is central to disease understanding and significance of the diseases. Local and national registers are central to determining this. The use of these depends on data completeness, coverage, and the possibility of linking other data information, including registers covering medicine, morbidity, mortality, quality, education, and social factors. Here are examples of major neurological diseases including epilepsy, sclerosis, neurodegenerative diseases, and stroke with the possibility of determining the significance of the diseases for morbidity, mortality, and social factors. Further examples of the importance of treatment are given.

Disclosure: Nothing to disclose.

FW18-3

The value of big data projects in organising national neurological services

J. Kõrv

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"Big Data" is a tool to gather information from different databases and processes, allowing users to manage large amounts of data. There are various sources of medical big data, such as administrative claim record, clinical registries, electronic health records, imaging database, biomarker data, financial data, etc. These data are nowadays mostly in digital form and can be integrated. The combined effect of technological advances and healthcare systems change (electronic recording of patient data) facilitate research with big data projects. The value of big data projects in neurological services is more accurate diagnoses, personalized treatment, monitoring of patients, preventive medicine, better quality of medical services and patient outcome, estimation of trends, and the ability to reduce costs. There are challenges to handle a large amount of information and use it to make data-driven decisions. "Big data" approaches can use routinely collected clinical data (all consecutive health care records should be collected) or can be mined to answer novel questions. However, "Big data" does not necessarily mean better data because they are reliant on the original data and study design.

Disclosure: Nothing to disclose.

The present and the future of ultrasound and electrophysiological examinations in neuromuscular motor neurone disorders

FW19-1

Are EMG and ENG still useful in the myopathic pathology definition?

C. Crone
Neurophysiology, Copenhagen University Hospital, Copenhagen, Denmark

Patients with one neuromuscular disease may present with a clinical picture that 'mimicks' another. In that case EMG and nerve conduction studies often play a pivotal role in establishing the correct diagnosis. Three patients are presented and their neurophysiological examinations demonstrate that EMG can be indispensable in distinguishing between myopathy/neuropathy/motor neurone disease.

Disclosure: Nothing to disclose.

FW19-2

Are neurophysiology and nerve ultrasound complimentary to diagnose peripheral neuropathies?

S. Goedee
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Diagnosis of peripheral neuropathies is based on recognition of compatible clinical features and selection of appropriate ancillary investigative strategies. Electrodiagnosis has traditionally been main directive of the diagnostic work-up of patients with suspected peripheral neuropathies. However, there are several important pitfalls and fallacies that warrant caution for its use and appropriate interpretation. Nerve ultrasound is an emerging diagnostic tool, that allows non-invasive evaluation of nerve morphology at relatively low cost and high efficiency. Low test burden, flexible field of view and high sensitivity to detect relevant nerve pathology are important benefits of nerve ultrasound, effectively complementing electrophysiology by adding important diagnostic information. Several revised and updated consensus guidelines on peripheral neuropathies already include nerve ultrasound as important add-on strategy. We will address the basics of using electrophysiology and nerve ultrasound in diagnosis of peripheral neuropathies, including appropriate interpretation and show how these techniques can complement each other.

Disclosure: I have received research grants from Prinses Beatrix Spierfonds and travel grant and speaker fee from Shire Baxalta in past.

FW19_3

Muscle ultrasound in neuromuscular disorders: utility and limits?

O. Musumeci
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Muscle disorders (MD) are a heterogeneous group of disorders where muscle damage can variable determine fat replacement, fibrosis or inflammation. Muscle replacement may be manifested by an increase in echogenicity. Muscle US has a potential role for screening and diagnostic purposes in suspected neuromuscular disease but so far few studies have been evaluated its application. Until now, MRI is the most used technique for muscle imaging. Recently the use of muscle US have been considered because of some advantages of this technique, it is a non-invasive technique that can be performed repeatedly and in clinical setting in particular in children. Some studies have explored its application in inflammatory myopathies as inclusion body myositis (IBM). US have been used also to test respiratory muscles and in particular diaphragm function. Considering neuromuscular disorders diaphragm ultrasound (DUS) was used to evaluate diaphragm muscle weakness in amyotrophic lateral sclerosis (ASL) or Duchenne muscular dystrophy (DMD). A recent study evaluated the correlation between diaphragm thickness and mobility assessed by DUS with respiratory function in patients with Pompe disease. DUS provides an alternative useful and risk-free tool to supply clinical assessment of respiratory muscle weakness in these patients. The few studies on MD exploring this tool demonstrated that it is a non-invasive imaging technique that could be used as supportive diagnostic measure but some limitations have emerged regarding reliability and sensitivity.

Disclosure: Nothing to disclose.

Topical Symposia

Tuesday, June 27 2022

Myasthenia gravis: What is our current knowledge on diagnostics and therapy

SYMPTOP03-1

The clinical presentation and state-of-the art diagnostics in myasthenia gravis

A. Evoli

Department of Ageing, neurosciences, head-neck and orthopaedics sciences, Institute of Neurologia, University Cattolica del Sacro Cuore, Rome, Italy

SYMPTOP03-2

Current international treatment standards in myasthenia gravis

K. Claeys

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SYMPTOP03-3

Modern approaches and clinical trial data for the treatment of myasthenia gravis

A. Meisel

Department of Neurology, Universitätsklinikum Charité Berlin, Berlin, Germany

Oral Presentations

Saturday, June 25, 2022
Neuro-oncology 1

OPR-001

Patient and carer involvement in the formulation of the clinical questions: the Guideline on Palliative Care (PC) in Adults with Glioma

S. Veronese [1], A. Solari [2], E. Bertocchi [3], B. Lissoni [4], L. De Panfilis [5], G. Dalla Verde [1], R. Rudà [6], A. Silvani [7], R. Merli [8], A. Pace [9]

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Background and aims: In 2017, the European Association for Neuro-Oncology (EANO) published the guideline for palliative care (PC) in adults with glioma. The Italian Society of Neurology (SIN), the Italian Association for Neuro-Oncology (AINO), and the Italian Society for Palliative Care (SICP) joined forces to update and adapt these guidelines to the Italian context; and (herein presented) to involve patients and carers in the formulation of the clinical questions.

Methods: Semi-structured interviews with glioma patients and focus group meetings (FGMs) with family carers of deceased patients. Participants rated the importance of 10 pre-specified intervention topics produced by the guideline panel, shared their experience, and suggested additional topics. Interviews and FGMs were audio-recorded, transcribed, coded and analysed (framework and content analysis).

Results: We held 20 interviews and five FGMs (28 carers). Both groups considered communication and psychological support as the most important topics, and reported difficulties in dealing with behavior and personality changes. Patients emphasized the impact of focal neurological and cognitive deficits. Carers focused on the preservation of functioning via rehabilitation and social support. Both affirmed the importance of a dedicated health care path and patient's involvement in the decision-making process.

Conclusion: Interviews and FGMs were well informative but emotionally demanding. Participants confirmed the importance of the 10 intervention topics, with no additional issues identified. Our findings strengthen the importance of a comprehensive care approach, and of addressing the needs of both parties (patients and family carers).

Disclosure: Nothing to disclose.

OPR-002

MRI response assessment in glioblastoma patients treated with dendritic cell-based immunotherapy

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Background and aims: In this post-hoc analysis we compared response assessment criteria (MacDonald, RANO, Vol-RANO, mRANO, Vol-mRANO, iRANO) in newly diagnosed glioblastoma (GB) patients treated with tumor lysate-charged autologous dendritic cells (Audencel) and determined the differences in prediction of progression free survival (PFS) and overall survival (OS).

Methods: 76 patients with newly diagnosed GB enrolled in a multicenter phase II trial receiving standard of care (SOC, n=40) or SOC + Audencel vaccine (n=36) were included. MRI scans were evaluated using MacDonald, RANO, mRANO and iRANO criteria. Tumor volumes (T1 contrast enhancing as well as T2/FLAIR volumes) were calculated by semiautomatic segmentation. To detect differences in PFS among the assessment criteria Kruskal-Wallis-test, for correlation analysis Spearman test were used.

Results: There was a significant difference in median PFS between mRANO (8.6 months) and Vol-mRANO (8.6 months) compared to MacDonald (4.0 months), RANO (4.2 months) and Vol-RANO (5.4 months). For the vaccination arm, median PFS by iRANO was 6.2 months. There was no difference in PFS between SOC and SOC + Audencel using these various response criteria. The best correlation between PFS/OS was detected for mRANO (r=0.65) and Vol-mRANO (r=0.69, each p<0.001). 16/76 patients developed a pure T2/FLAIR progressing disease, 4/36 patients treated with Audencel developed pseudoprogression.

Conclusion: When comparing different response assessment criteria in GB patients treated with dendritic cell-based immunotherapy, best correlation between PFS and OS was observed for mRANO and Vol-mRANO. iRANO was not superior for predicting OS in patients treated with Audencel.

Disclosure: Nothing to disclose.

OPR-003

ABTR-SANO Real-World Pattern of Care Study on Glioblastoma in the Austrian Population. Final results from 2014–2020

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Background and aims: The Austrian ABTR-SANO Glioblastoma Registry is the first population-based assessment of patterns of care for patients with Glioblastoma across Austrian healthcare institutions. The primary aim is to assess the real world effectiveness of administered therapies.

Methods: Clinical data are collected via a common web-based IT platform "ABTR-SANO Net" since 2014. The database and the ongoing evaluation of clinical parameters, as well as interims analysis are provided in cooperation with a review board. First Outcome analysis, including patients from 2014–2020, was performed at the end of 2021.

Results: 11 centers across Austria are involved, and the data of 1,416 patients (m/f ratio: 1.35, median age: 66 years) were recently analyzed in detail. Age, extent of resection, as well as ECOG was associated with improved survival. Methylated MGMT Status also showed a moderate survival benefit. Patients with re-resection and re-radiation also exhibited improved survival, which however may be attributed to a selection bias. Second line treatment manly comprised of antiangiogenic treatment, followed by alkylated agents, re-radiation and re-surgery. Median overall survival of all patients was 344 days and clearly age dependent (best for <50 years, worse for >80 years)

Conclusion: This is the first population based outcome analysis of Glioblastoma in Austria. Results regarding prognostic markers and outcome are mostly comparable with international data. Robust population based data are important in order to monitor quality of health care, and to match the data with results from clinical studies.

Disclosure: Nothing to disclose.

OPR-004

Brain Tumour-Related Epilepsy: Impact of Grading and Treatments in a Cohort of Molecularly Defined Lower-Grade Gliomas

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Background and aims: Brain-tumour related epilepsy is associated with lower-grade gliomas (LGGs) in up to 70–90% of cases. Our study aims to identify which factors are related to seizure control in a large cohort of grade 2 and 3 LGGs patients.

Methods: We retrospectively collected clinical data of LGGs patients with history of BTRE. We retained information about seizure-freedom after surgery, adjuvant treatments, and at recurrence.

Results: 280 patients with LGGs diagnosed between 1988 and 2021 were included. Oligodendrogliomas IDH-mutant 1p19q-codeleted, astrocytomas IDH-mutant and IDH-wildtype were 106 (54.9%), 40 (20.7%), and 47 (24.4%), respectively. Grade 2 and 3 tumours were 199 (71.1%) and 81 (28.9%). Gross-total resection (GTR) accounted for 117 (41.8%) cases. In a multivariable model, seizure-freedom after surgery was positively related to age $\geq$40 years (OR 2,173, p=0.012) and GTR (OR 2,006, p=0.022), and negatively related to temporal lobe location (OR 0.440, p=0.007) and grade 2 histology (OR 0.271, p<0.001). Similarly, grade 2 histology and temporal lobe location were negative predictors of seizure-freedom after adjuvant treatments (OR 0.169, p<0.001, and OR 0.353, p=0.006, respectively). FLAIR response to adjuvant treatments (complete/partial vs stable disease/progression) was associated with seizure-freedom (84.2% vs 59.4%, p=0.040) regardless of tumour grade. Seizures were a symptom at recurrence in 134 (59.6%) patients. Previous RT significantly reduced the risk of seizures at recurrence (OR 0.343, p=0.010).

Conclusion: These data suggest that grade 2 histology increases the risk of seizure persistence after treatment among LGGs. Conversely, GTR and RT are associated with seizure control regardless of tumour grade.

Disclosure: I have no disclosures.

OPR-005

Abstract withdrawn

Cognitive neurology/neuropsychology

OPR-006

### Unravelling neural correlates of empathy deficits along Alzheimer's Disease continuum

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Background and aims: Empathy is the ability to understand (cognitive empathy) and to feel (affective empathy) what others feel. We aimed to assess empathy deficit and neuronal correlates along Alzheimer's Disease (AD) continuum: from Subjective Cognitive Decline (SCD), to Mild Cognitive Impairment (MCI) and to dementia.

Methods: 24 SCD, 41 MCI and 46 AD patients were included. Informer-rated Interpersonal Reactivity Index was used to explore cognitive (Perspective Taking-PT, Fantasy-FT) and affective (Empathic Concern-EC, Personal Distress-PD) empathy, before (T0) and after (T1) cognitive symptoms' onset. Cerebral FDG-PET SPM analysis was used to explore neural correlates underlying empathy deficits.

Results: PD-T1 score were higher in AD compared to MCI and to SCD (p=0.001). A positive correlation was found between PT-T1 and hmetabolic disfunction of right middle gyrus (MFG) in MCI and AD. In AD group, a positive correlation between PT-T1 and insula and superior temporal gyrus (STG) metabolism was detected. PD-T1 was negatively correlated with superior parietal lobule metabolism in MCI, and with STG metabolism in AD.
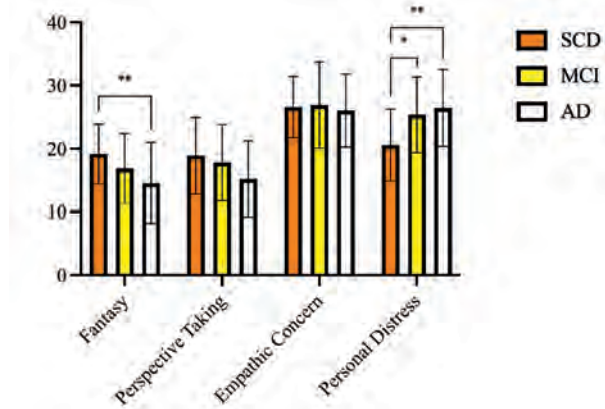
Current empathy assessed by Interpersonal Reactivity Index (IRI) in Subjective Cognitive Decline (SCD), Mild Cognitive Impairment (MCI) and Alzheimer's Disease (AD). *p<0.05; **p<0.01.
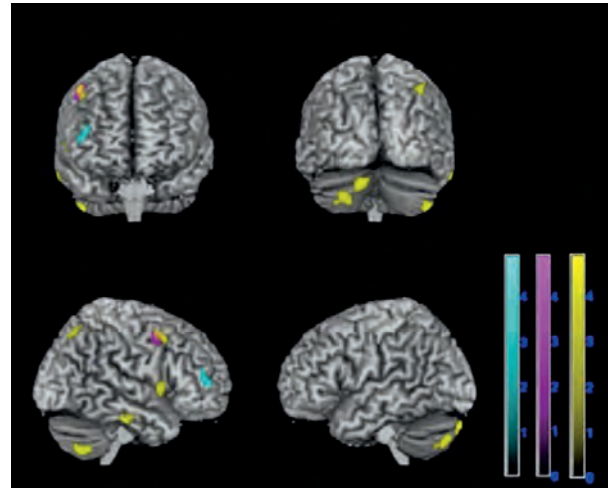
Positive correlation between cognitive empathy assessed by PT-T1 IRI subscale and brain metabolism in MCI and AD patients at 18F-FDG-PET SPM analysis. Colour grading: Cyan= MCI, Violet=AD, Yellow=MCI & AD.
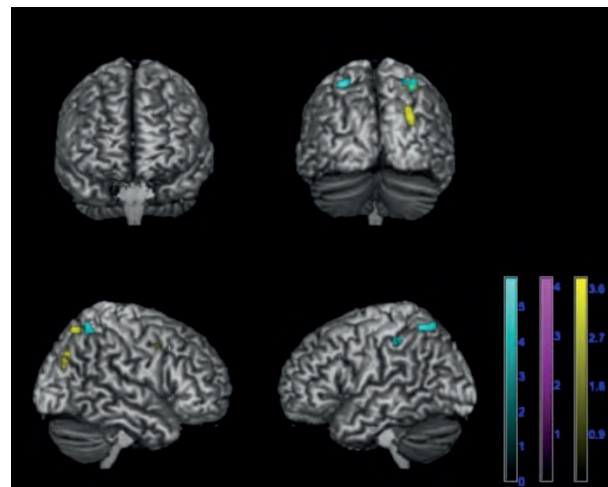
Negative correlation between emotional contagion assessed by PD-T1 IRI subscale and brain metabolism in MCI and AD patients at 18F-FDG-PET SPM analysis. Colour grading: Cyan= MCI, Violet= AD, Yellow=MCI & AD.

Conclusion: Impairment of cognitive empathy starts at MCI stage, while increase of PD starts from preclinical phases. Our study suggests the presence of a continuum, with a progressive involvement of structures involved in cognitive empathy starting from prodromal stage of AD. Heightened emotional contagion is probably related to derangement of mirror neurons systems in parietal regions in prodromal stage, and to impairment of temporal emotion inhibition system in dementia. Further studies are needed to clarify if empathy deficits might be a predictive feature of a cognitive decline driven by AD.

Disclosure: The authors have nothing to disclose.

OPR-007

Hippocampal microstructural integrity and speed of information processing in multiple sclerosis

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Background and aims: The contribution of hippocampal atrophy to cognitive impairment has been widely described in multiple sclerosis (MS). However, less is known about measures of microstructural damage, which could provide further insights on mechanisms of cognitive dysfunction. Aim of this study was to investigate the association between hippocampal microstructural integrity and information processing speed deficit (IPS) in MS.

Methods: 50 healthy controls (HC) and 117 MS patients underwent 3.0T MRI. Global and subregional hippocampal volumes were assessed with the cross-sectional pipeline of Freesurfer 6.0. Measures of microstructural integrity were obtained using diffusion tensor imaging (i.e, fractional anisotropy [FA], mean diffusivity [MD]) and neurite orientation dispersion and density imaging (NODDI, i.e, neurite density index, orientation dispersion index [ODI]). Symbol Digit Modalities Test (SDMT) was administered to assess IPS, and z-scores were calculated according to normative data. Age- and sex-adjusted linear models were used for between-group comparisons. In MS patients, hierarchical linear regression analysis was run to identify predictors of SDMT z-scores among clinical and MRI variables.

Results: Compared to HC, MS patients showed atrophy of the fimbria (p<0.001) as well as reduced FA and increased MD and ODI compared of the whole hippocampus (p<=0.004). Older age (delta R-square=0.189; p<0.001), higher T2-lesion volume (delta R-square=0.055; p=0.009) and higher MD of the fimbria (delta R-square=0.051; p=0.010) were selected as significant predictors of slower IPS measured with SDMT (adjusted R-square=0.273).

Conclusion: The integrity of the fimbria appears to be a critical anatomical correlate of information processing speed performance in MS.

Disclosure: Nothing to disclose.

OPR-008

Cognitive dysfunction in primary and secondary progressive MS: a multiparametric structural and functional MRI study

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Background and aims: Few cross-sectional studies have been focused on identifying patterns of cognitive impairment in progressive multiple sclerosis (MS) and possible differences between primary progressive (PP) and secondary progressive (SP) MS remain to be determined. Aim of this study was to investigate the contribution of structural and functional MRI abnormalities in explaining cognitive dysfunction in PPMS and SPMS.

Methods: Brain dual-echo, diffusion tensor, 3D T1-weighted, and resting-state (RS) MRI scans were acquired from 183 MS patients (60 PPMS and 123 SPMS) and 75 healthy controls. Cognitive assessment included the Brief Repeatable Battery of Neuropsychological tests; for all cognitive tests z-scores were calculated and used to derive a measure of global cognition (BRB-N z). Hierarchical linear regression analysis was run to assess the association of BRB-N z with clinical and MRI variables.

Results: Compared to PPMS, SPMS showed decreased fractional anisotropy (FA) (p=0.012) in the fornix, and lower RS functional connectivity within the basal ganglia network (p=0.005). No differences between PPMS and SPMS were found in mean BRB-N z (-1.0 and -1.1 respectively; p=0.46). In PPMS patients, decreased FA of the medial lemniscus (ΔR2=0.107; p=0.011) and lower normalized gray matter volume (ΔR2=0.287; p<0.001) were associated with lower BRB-N z (adjusted-R2= 0.364). In SPMS, decreased FA of the fornix (ΔR2=0.345; p<0.001) and lower normalized white matter volume (ΔR2=0.045; p=0.034) were associated with worse cognitive status (adjusted-R2=0.371).

Conclusion: PPMS and SPMS showed similar patterns and degree of cognitive impairment. However, different structural substrates contribute to explain cognitive dysfunction in these clinical phenotypes of MS.

Disclosure: Nothing to disclose.

OPR-009

Spatial correlations of gray matter atrophy and neurotransmitter maps explain clinical features in multiple sclerosis

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Background and aims: In multiple sclerosis (MS), clinically-relevant gray matter (GM) atrophy progresses in a non-random manner, possibly due to the preferential involvement of specific neurotransmitter networks. However, the associations among regional GM atrophy, neurotransmitter distribution and MS clinical manifestations still need to be fully explored.

Methods: Brain 3.0 T MRI scans were acquired from 286 patients with MS (PwMS) and 172 healthy controls (HC). Regional GM volume differences, the cross-correlations between regional GM atrophy and nuclear imaging-derived neurotransmitter maps and their associations with clinical disability, cognitive impairment, fatigue and depression were investigated using voxel-based morphometry and Juspace toolbox.

Results: Compared to HC, PwMS showed a widespread pattern of cortico-subcortical GM atrophy that was spatially correlated with serotonergic, dopaminergic, opioid, noradrenergic, cholinergic and glutamatergic maps ($p<0.003$). Cognitively-impaired vs cognitively-preserved PwMS had a widespread pattern of GM atrophy that was spatially associated with serotonergic, dopaminergic, opioid, noradrenergic, cholinergic and glutamatergic maps ($p<0.04$). Compared to mildly-disabled PwMS, those reaching Expanded Disability Status Scale>3.0 had significant atrophy of deep GM, fronto-temporal and cingulate cortices, hippocampi and cerebellum, which were associated with serotonergic, dopaminergic, and cholinergic maps ($p<0.02$). Compared to non-fatigued PwMS, those with fatigue had significant atrophy of fronto-temporo-parietal and cingulate cortices, hippocampi and cerebellum, which were associated with the serotonergic, dopaminergic, opiod and glutamatergic maps ($p\leq0.03$). No significant GM volume differences and associations with neurotransmitter maps were found according to depression.

Conclusion: GM atrophy in regions belonging to specific neurotransmitter systems may contribute to explain part of MS clinical manifestations, including locomotor disability, cognitive impairment and fatigue.

Disclosure: Nothing to disclose.

OPR-010

Cognitive reserve modulates the impact of frontal lobe damage on executive functioning in multiple sclerosis

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Background and aims: Early-life enriching experiences may influence frontal lobe maturation and may preserve executive function (EF) integrity in multiple sclerosis (MS). In this study, we investigated the interaction between cognitive reserve, frontal gray matter (GM) atrophy and white matter (WM) tract microstructural abnormalities and their associations with EF in MS patients.

Methods: Frontal GM volumes, lesional volume, fractional anisotropy, mean diffusivity, intracellular volume fraction and orientation dispersion index of frontal WM tracts were quantified in 93 MS patients and 27 matched healthy controls (HC). Cognitive reserve index (CRI), Wisconsin Card Sorting Test (WCST) and Word List Generation (WLG) of the Rao's battery were assessed. Interaction of structural MRI measures and CRI on cognitive performance were explored.

Results: MS patients vs HC showed significant diffuse frontal GM atrophy and WM tract microstructural abnormalities ($p<0.046$) and worse performances in categories and total errors of WCST and WLG ($p<0.034$). In MS, higher CRI was correlated with better WLG performance, WCST-categories, frontal gyri volumes and diffusivity measures of frontal WM tracts (r from -0.212 to 0.455; $p\leq0.046$). The combination of demographic, clinical and measures of frontal lobe structural damage significantly explained EF (WLG: $R2=0.44$; $p=0.022$; WCST categories: $R2=0.33$; $p=0.010$). Higher CRI explained a further portion of variance in WLG (WLG: $R2=0.50$; $p=0.002$; $\Delta R2=0.07$; $p=0.003$).

Conclusion: In MS, CRI is associated with higher frontal GM volumes and higher frontal WM tract microstructural integrity. CRI may contribute to preserve semantic verbal fluency and cognitive flexibility, possibly moderating the effect of frontal lobe structural damage on cognitive performance.

Disclosure: Nothing to disclose.

OPR-011

Functional Cognitive Disorder is a multisystem condition affecting reaction time and metacognition

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Background and aims: We hypothesised that FCD is characterised by heightened subjective mental effort, exhausted attentional reserve and metacognitive failure.

Methods: Stroop colour-word task in which attentional demand was varied by task difficulty (congruent/incongruent cues) and the presence of an auditory stimulus (passive/active listening to oddball-type paradigm). We measured subjective mental effort, objective performance, metacognition and EEG-based biomarkers of mental workload (including P300 suppression).

Results: We tested 19 patients with FCD and 23 healthy controls. FCD patients reported higher levels of depression, anxiety, fatigue, pain, sleep disruption, dissociation and obsessiveness. FCD was associated with slower reaction times; however the Stroop effect was similar in both groups. FCD patients reported greater mental workload and poorer self-rated performance when performing the congruent Stroop task in noisy conditions. However, accuracy did not differ between groups in any condition, suggesting that FCD patients are more prone to metacognitive error. Biomarkers of mental workload were similar in both groups, regardless of task difficulty.

Conclusion: In our sample, FCD was characterised by altered mood, somatic complaints, dissociation, and obsessiveness, suggesting syndromic overlap with mood disorders, chronic fatigue and pain. FCD was associated with metacognitive failure in that patients reported high subjective mental effort and poor self-reported performance but were just as accurate as controls. However, FCD patients were slower than controls, providing some objective support for the subjective "brain fog" commonly reported in this condition. We found no evidence of changes in EEG biomarkers of mental workload.

Disclosure: Nothing to disclose.

Cerebrovascular diseases: Acute stroke management

OPR-012

Absence of Susceptibility Vessel Sign in Patients with Malignancy-related Acute Ischemic Stroke

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Background and aims: Platelet and fibrin-rich composition of retrieved thrombi in patients with acute ischemic stroke (AIS) are associated with the absence of susceptibility vessel sign (SVS) on MRI and the presence of active malignancy. This study analyzed the direct association between SVS status and the presence of active malignancy in AIS patients that underwent mechanical thrombectomy (MT).

Methods: Single-centered, retrospective and cross-sectional study including consecutive patients with admission MRI treated for AIS with MT between January 2010 and December 2018. SVS status was evaluated on susceptibility weighted imaging (SWI). Adjusted OR (aOR) were calculated to determine the association between the absence of SVS and active and occult malignancy presence. The performance of predictive models with and without SVS status were assessed by calculating the areas under the Receiver Operating Characteristics curve (auROC).

Results: Of the 577 AIS patients with assessable SVS status, 40 (6.9%) had a documented active malignancy and 72 patients (12.5%) showed no SVS. The absence of SVS was strongly associated with active malignancy (aOR 4.85, 95% CI 1.94–12.11) and occult malignancy alone (aOR 11.42, 95% CI 2.36–55.20). The auROC of predictive models, including demographics and common malignancy-biomarkers, decreased from 0.85 to 0.82 when SVS status was excluded (Figure, p=0.07).
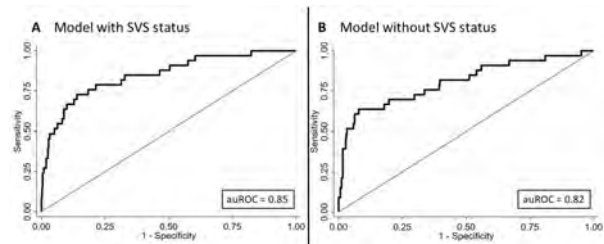

Figure – Comparison of predictive models for active malignancy with and without SVS status.

Conclusion: The absence of SVS on baseline MRI is associated with the presence of active and occult malignancy in patients with AIS eligible for MT. Considering SVS status may increase the chances of detecting paraneoplastic coagulation disorders and occult malignancy in patients with AIS.

Disclosure: Nothing to disclose.

OPR-013

Abstract withdrawn

OPR-014

Acute ischemic stroke in patients with active versus never cancer: characteristics, mechanisms, and stroke recurrence.

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Background and aims: Acute ischemic stroke (AIS) and cancer are important causes of disability and death. We aimed to estimate the rate of active cancer (AC) in a large cohort of consecutive AIS patients, and to assess demographics, risk factors, mechanisms, and long-term outcomes when compared with never-cancer (NC) AIS patients.

Methods: We retrospectively analyzed data from ASTRAL (Acute-STroke-Registry-and-Analysis-of-Lausanne) between 01/2003-10/2021. We defined AC according to the standard definition (Khorana, J.Thromb.Haemost, 2018) and included newly-diagnosed cancer within 12 months after the index stroke in the AC group. We performed univariate analysis comparing both groups regarding patients' characteristics, stroke mechanisms, and long-term functional outcomes. Other multivariate logistic regression analyses are ongoing and will be presented at the congress.

Results: Among 5,917 AIS patients, 44.3% were women and the median age was 73.8 years (IQR 21.3). We identified 396 (6.7%) AC patients and 5,521 (93.3%) NC patients. Whereas stroke risk factors were mostly similar between groups (Table), AC patients were more often men and presented with higher pre-stroke modified Rankin Scale scores. Compared to NC patients, AC patients had fewer traditional stroke mechanisms and more multiple/rare mechanisms [OR 7.3 (5.6–9.6)]. In unadjusted analyses, AC patients had a higher rate of stroke recurrence within 3-months as well as increased disability and mortality.

Variable	Study cohort (N=5917)	Active cancer (AC) (N = 396)	Never cancer (NC) (N = 5521)	OR (95% CI)	p-value
Age	73.8 (21.3)	74.3 (16.7)	73.8 (21.8)		0.039
Female sex	2623/5917(44.3%)	154/396 (38.9%)	2469/5521(44.7%)	0.79 (0.64 – 0.97)	0.024
mRS pre-stroke	0 (2)	1(2)	0(2)	1.3 (1.19-1.41)	0.026
Vascular risk factors					
Hypertension	1650/5916 (72.1%)	288/395 (72.9%)	3978/5521 (72.1%)	1.04 (0.83-1.31)	0.71
Atrial fibrillation	1716/5909 (29%)	106/393 (27%)	1610/5516 (29.2%)	0.9 (0.71-1.13)	0.35
Diabetes	1123/5911 (19%)	80/395 (20.2%)	1043/5516 (18.9%)	1.09 (0.84-1.4)	0.51
Dyslipidaemia	4421/5905 (74.9%)	274/393 (69.7%)	4147/5512 (75.2%)	0.76 (0.61-0.95)	0.015
Smoking	1389/5873 (23.7%)	105/389 (27%)	1284/5484 (23.4%)	1.21 (0.96-1.53)	0.16
Coronary disease	1098/5901 (18.6%)	79/391 (20.2%)	1019/5510 (18.5%)	1.12 (0.86-1.44)	0.41
Eject. fraction <35%	320/5917 (5.4%)	18/396 (4.5%)	302/5521 (5.5%)	(0.5-1.34)	0.43
BMI	25 (5)	24 (5)	25 (5)	0.95 (0.93-0.98)	0.008
Stroke etiologies					
Atherosclerosis	843/5558 (15.2%)	49/370 (13.2%)	794/5188 (15.3%)	0.85 (0.62-1.15)	0.29
Cardioembolism	1714/5558 (30.8%)	86/370 (23.3%)	1628/5188 (31.4%)	0.66 (0.52-0.85)	<0.001
Lacunar	578/5558 (10.4%)	26/370 (7%)	552/5188 (10.6%)	0.64 (0.42-0.96)	0.028
Dissection	227/5558 (4.1%)	3/370 (0.81%)	224/5188 (4.3%)	0.18 (0.06-0.57)	<0.001
PFO-related	191/5558 (3.4%)	3/370 (0.81%)	188/5188 (3.6%)	0.22 (0.07-0.68)	0.004
Rare, including cancer-related	325/5558 (5.8%)	94/370 (25.4%)	231/5188 (4.5%)	7.31 (5.59-9.56)	<0.001
Multiple	361/5558 (6.5%)	48/370 (13%)	313/5188 (6%)	2.32 (1.68-3.21)	<0.001
Embolic stroke of undet. source	788/5558 (14.2%)	37/370 (10%)	751/5188 (14.5%)	0.66 (0.46-0.93)	0.017
Undetermined, and/or incomplete work-up	531/5558 (9.6%)	24/370 (6.5%)	507/5188 (9.8%)	0.64 (0.42-0.98)	0.038
Recurrence 3 months	244/5904 (4.1%)	44/394 (11.2%)	200/5510 (3.63%)	3.34 (2.37-4.71)	<0.001
Mortality 7 days	537/5917 (9.1%)	42/396 (10.6%)	495/5521 (9%)	1.2 (0.86-1.68)	0.27
Mortality 3 months	829/5258 (15.8%)	110/350 (31.4%)	719/4908 (14.6%)	2.67 (2.1-3.39)	<0.001
Mortality 12 months	1170/4380 (24.4%)	165/305 (54.1%)	905/4075 (22.2%)	4.13 (3.26-5.23)	<0.001
mRS>2 at 3 months	2149/5028 (40.9%%)	194/350 (55.4%)	1955/4908 (39.8%)	1.88 (1.51-2.34)	<0.001

Table 1 : Patient characteristics and results. Continuous and ordinal variables are expressed as medians (with interquartile range, IQR), and categorical variables as absolute counts (with percentage). Results from the univariate analysis in the "AC" and "NC" groups are reported as odds ratio (OR) and 95% confidence interval (CI). "Mortality" refers to mortality for all causes. PFO: patent foramen ovale; mRS (modified Rankin Scale); BMI: Body Mass Index.

Conclusion: Among large contemporary cohort, 6.7% of AIS patients had AC, they were more often men and had worse pre-stroke function than NC patients. In addition, AC patients had more atypical stroke mechanisms, a higher rate of stroke recurrence, and increased long-term disability and mortality.

Disclosure: Nothing to disclose.

OPR-015

Perfusion imaging in large vessel occlusion stroke within 6 hours from onset: from time-window to tissue-window

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[2] Department of Diagnostic and Interventional Radiology, Lausanne University Hospital, Lausanne, Switzerland,
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Background and aims: Little is known on the role of perfusion imaging for patients treated within early (<6h) time window. We aimed to investigate whether pre-treatment perfusion parameters are associated with outcome in acute ischemic stroke (AIS) patients treated within 6 hours.

Methods: Based on the ASTRAL registry, we retrospectively included consecutive anterior circulation large vessel occlusion (LVO) AIS patients, treated within 6 h and with available baseline perfusion data. We assessed the absence of mismatch according to DEFUSE 3 and DAWN trials criteria, ischemic core and penumbra volumes, and perfusion/core ratio. We evaluated their association with 3-month unfavorable outcome (modified Rankin Scale, mRS>2) via univariate and multivariate logistic regression analysis.

Results: 262 patients were included: 83 (31.7%) and 168 (64.1%) did not meet DEFUSE 3 and DAWN criteria, respectively. Absence of mismatch according to DEFUSE 3 or DAWN criteria was associated with higher probability of unfavorable outcome (respectively 67.1% vs. 31.4%, aOR=2.69, 95% CI=1.22–5.90, p=0.014; and 50.0% vs. 28.9%, aOR=3.46, 95% CI=1.56–7.67, p=0.002; adjusted for age, pre-stroke mRS, baseline NIHSS, blood glucose, ASPECTS, collaterals, time-to-groin-delay, occlusion site and IVT). Ischemic penumbra volume (aOR=0.51, 95% CI=0.30–0.87, p=0.013) and penumbra/core ratio (aOR=0.75, 95% CI 0.60–0.95, p=0.015) were also independently associated with 3-month outcome, but not ischemic core volume (aOR=1.22, 95% CI=0.96–1.58, p=0.104).

Conclusion: The mismatch criteria for the extended time-window EVT are not met in a substantial proportion of early arriving patients and are independently associated with 3-month outcome. Further data confirming these results may suggest a paradigm shift in acute stroke management, from time-window to tissue-window.

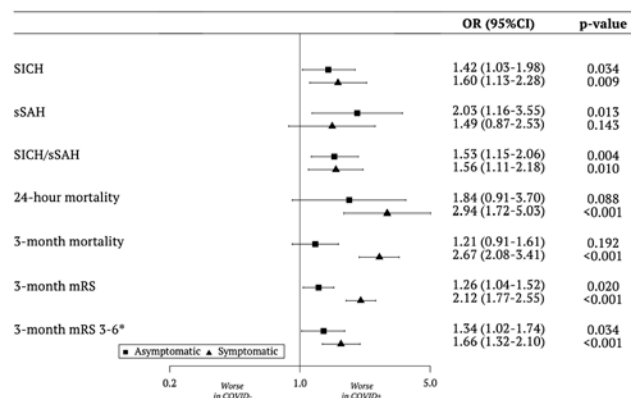**Disclosure:** The authors have no disclosures to report.

OPR-016

Effect of symptomatic and asymptomatic Covid-19 on safety and outcome of acute ischemic stroke treatments

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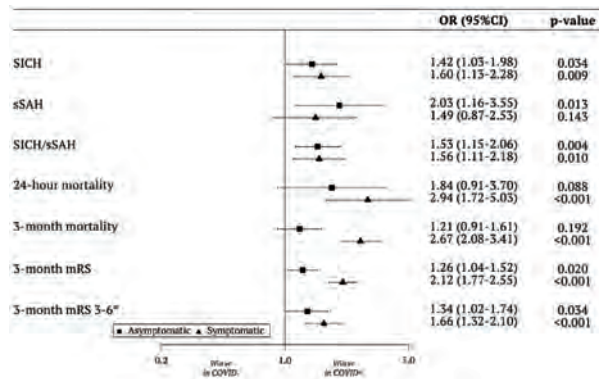
Background and aims: COVID-19 related inflammation, endothelial dysfunction and coagulopathy may increase the bleeding risk and lower the efficacy of revascularization treatments in patients with ischemic stroke (IS). The effect of these pathophysiological processes is possibly related to the disease severity. We aimed to evaluate the safety and outcomes of revascularization treatments in patients with IS and asymptomatic or symptomatic COVID-19.

	OR (95%CI)	p-value
SICH	1.42 (1.03-1.98)	0.034
	1.60 (1.13-2.28)	0.009
sSAH	2.03 (1.16-3.55)	0.013
	1.49 (0.87-2.53)	0.143
SICH/sSAH	1.53 (1.15-2.06)	0.004
	1.56 (1.11-2.18)	0.010
24-hour mortality	1.84 (0.91-3.70)	0.088
	2.94 (1.72-5.03)	<0.001
3-month mortality	1.21 (0.91-1.61)	0.192
	2.67 (2.08-3.41)	<0.001
3-month mRS	1.26 (1.04-1.52)	0.020
	2.12 (1.77-2.55)	<0.001
3-month mRS 3-6*	1.34 (1.02-1.74)	0.034
	1.66 (1.32-2.10)	<0.001

■ Asymptomatic ▲ Symptomatic

Methods: Retrospective multicenter cohort study of consecutive IS patients receiving intravenous thrombolysis (IVT) and/or endovascular treatment (EVT) between March-2020 and June-2021, tested for SARS-CoV-2 infection, with or without COVID-19-compatible

symptoms. By multivariate logistic regression analysis, we assessed the association of asymptomatic and symptomatic COVID-19 with bleeding complications and clinical outcomes. Study protocol was registered in ClinicalTrials.gov (NCT04895462).

Results: Among 15,128 revascularized patients from 105 centers, 853 (5.6%) were diagnosed with COVID-19, of whom 395 (46%) were asymptomatic and 454 (54%) symptomatic. 5,848 (38.7%) patients received IVT only, and 9,280 (61.3%) EVT (±IVT). As shown in Figure, the hemorrhagic complications similarly increased in both asymptomatic and symptomatic COVID-19 patients, while 24-hour and 3-month mortality was significant increased only in symptomatic COVID-19 patients. Compared to COVID-negative controls, 3-month disability was significantly worse in COVID-19 patients regardless the symptoms of the disease, but it was affected to a larger extent in symptomatic patients.

	OR (95%CI)	p-value
SICH	1.42 (1.03-1.98)	0.034
	1.60 (1.13-2.28)	0.009
sSAH	2.03 (1.16-3.55)	0.013
	1.49 (0.87-2.53)	0.143
SICH/sSAH	1.53 (1.15-2.06)	0.004
	1.56 (1.11-2.18)	0.010
24-hour mortality	1.84 (0.91-3.70)	0.088
	2.94 (1.72-5.03)	<0.001
3-month mortality	1.21 (0.91-1.61)	0.192
	2.67 (2.08-3.41)	<0.001
3-month mRS	1.26 (1.04-1.52)	0.020
	2.12 (1.77-2.55)	<0.001
3-month mRS 3-6"	1.34 (1.02-1.74)	0.034
	1.66 (1.32-2.10)	<0.001

■ Asymptomatic ▲ Symptomatic

Conclusion: Ischemic stroke patients with asymptomatic or symptomatic COVID-19 showed higher rates of intracranial bleeding complications and worse clinical outcomes after acute revascularization treatments than contemporaneous non-COVID-19 treated patients.

Disclosure: The authors have no disclosure to report.

OPR-017

Angiographic evaluation of no-reflow phenomenon in patients with acute ischemic stroke from large vessels occlusion

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Background and aims: Futile recanalization (FR) is defined as a 90-day mRS 3–6 despite successful recanalization (TICI 2b-3), and account for 29% to 60% of large vessel occlusion (LVO) ischemic stroke (IS) treated with mechanical thrombectomy (MT). Failure of early neurological improvement (fENI) describes patients successfully recanalized but not clinically improving at 24-hours or at 7-days. No-reflow phenomenon (NRP) is a possible cause of FR and fENI, described in global ischemia animal models and human myocardial infarction as deficient microvascular reperfusion. Evidence of NRP in IS patients is scarce. Aim of our study was to identify an angiographic marker of NRP and explore its association with clinical outcome.

Methods: We retrospectively analyzed 185 post-interventional digital subtraction angiographies of anterior circulation LVO IS patients treated with MT. We created a score, dividing middle cerebral artery territory in three segments. For each segment we gave 2 points if the capillary blush was present without any delay, 1 if delayed and 0 if absent. We called our score modified capillary index score (mCIS). We used ROC curve to define mCIS≤3 as cut-off and marker of NRP.
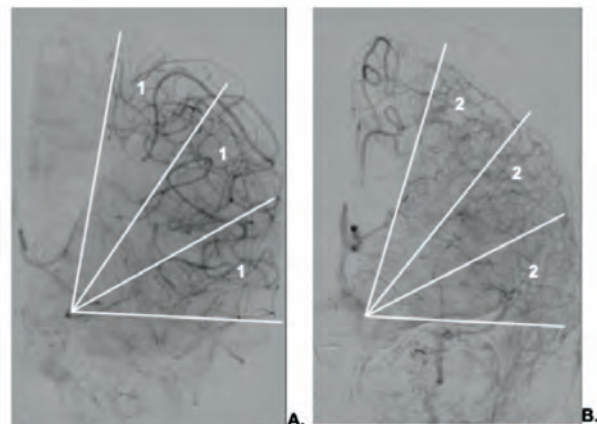
Post-interventional DSA showing on parenchymal phase (A) delayed contrast washout in all the 3 segments of MCA territory (mCIS 3) and (B) regular contrast washout (mCIS 6) (DSA=digital subtraction angiography; MCA= middle cerebral artery)

Results: NRP was present in 35.1% of patients. mCIS≤3 predicted fENI at 24 hours (aOR2.617, 95% CI1.192–5.745, p=0.016) and at 7 days (aOR4.601, 95% CI1.636–12.936, p=0.004), but not FR. Moreover, mCIS≤3 predicted hemorrhagic transformation (aOR 0.444, 95% CI 1.266–4.717, p=0.008).
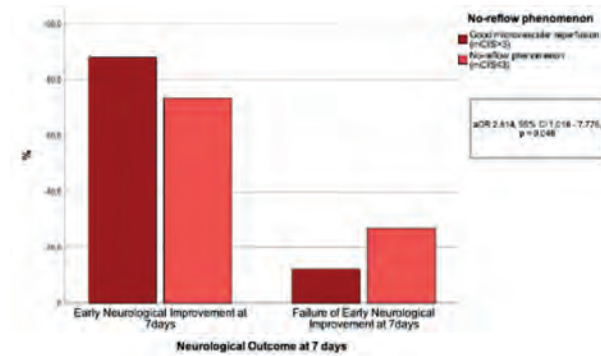
Conclusion: NRP is poorly investigated in IS patients. Our angiographic marker was able to predict early outcome and could help identifying patients for future research on NRP.
Disclosure: Nothing to disclose.

Muscle and neuromuscular junction disorder

OPR-018

FXR1-related congenital myopathy: expansion of the clinical and genetic spectrum

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Background and aims: Bi-allelic pathogenic variants in FXR1 have recently been associated with two rare congenital myopathy phenotypes: a severe form associated with hypotonia, long bone fractures, respiratory insufficiency, and infantile death, and a milder form characterized by proximal muscle weakness with survival into adulthood. We report eight patients from four unrelated families with bi-allelic pathogenic variants in exon 15 of FXR1.

Methods: The patients were recruited from the following centres: the Queen Elizabeth University Hospital in Glasgow, United Kingdom; Hospital de Basurto in Bilbao, Spain; Hacettepe University Children's Hospital in Ankara, Turkey and Hospital for Sick Children in Toronto, Canada. Whole exome sequencing was used to detect variants.

Results: Common clinical features were noted for all patients, which included proximal myopathy, normal serum creatinine kinase levels, and diffuse muscle atrophy with relative preservation of the quadriceps femoris muscle on muscle imaging. Additionally, some patients with FXR1-related myopathy had respiratory involvement and required BiPAP support. Other clinical features observed to varying degrees among the cohort were calf hypertrophy, scoliosis, joint laxity, contractures, and psychiatric symptoms. Muscle biopsy showed multi-minicores and type I fibre predominance.
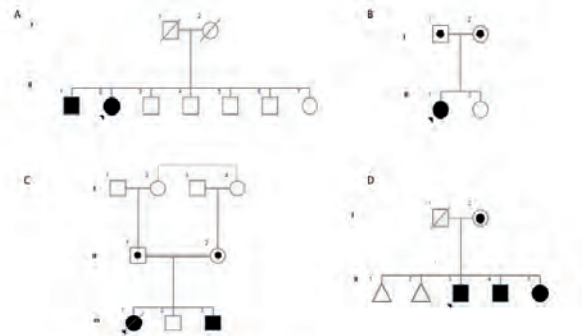
Pedigrees of all four families
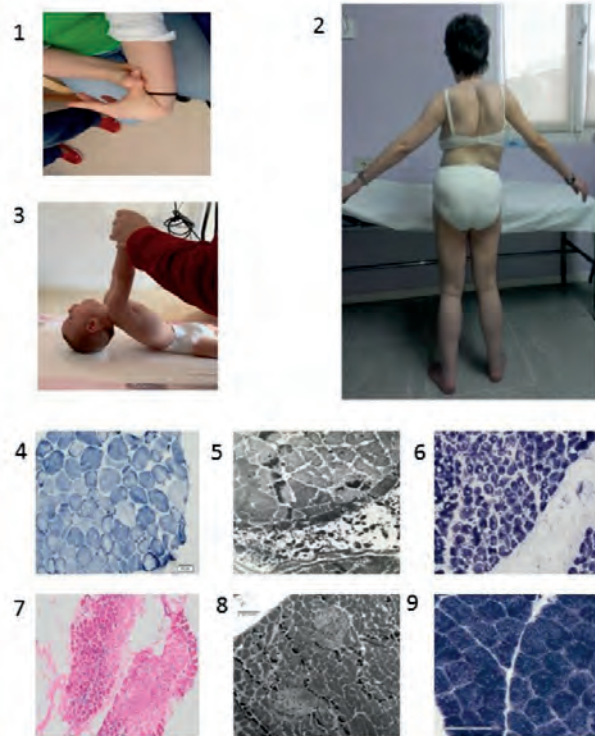
Clinical presentation and muscle biopsies
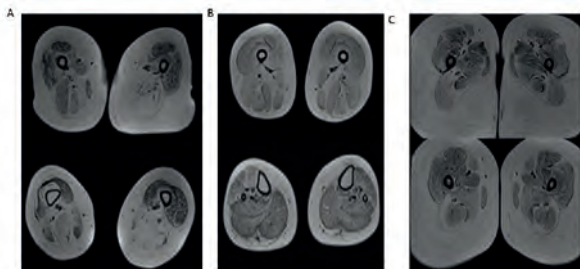
Muscle MRI of three patients

Conclusion: FXR1-related congenital myopathy is an emerging entity that is clinically recognizable. Phenotypic variability associated with variants in FXR1 can result from differences in variant location and type and is also observed between patients homozygous for the same variant, rendering specific genotype-phenotype correlations difficult. Molecular testing for FXR1 should be considered for patients with a clinical diagnosis of congenital myopathy, especially if cores are observed on muscle biopsy.

Disclosure: Two patients were diagnosed as part of the MYO-SEQ Project. Analysis was provided by the Broad Institute of MIT and Harvard Center for Mendelian Genomics (Broad CMG).

OPR-019

COMET: Efficacy and safety of avalglucosidase alfa in late-onset Pompe disease participants after 97 weeks of treatment

B. Schoser [1], P. Kishnani [2], J. Díaz-Manera [3], H. Kushlaf [4], S. Ladha [5], T. Mozaffar [6], V. Straub [3], A. Toscano [7], A. Van der Ploeg [8], K. Berger [9], P. Clemens [10], Y. Chien [11], J. Day [12], S. Ilarioshkin [13], M. Roberts [14], S. Attarian [15], G. Carvalho [16], Y. Choi [17], S. Erdem-Özdamar [18], O. Goker-Alpan [19], A. Kostera-Pruszczyk [20], K. An Haack [21], N. Thibault [22], T. Zhou [22], M. Dimachkie on behalf of the COMET Investigator Group [23]

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Background and aims: Avalglucosidase alfa (AVAL) is a recombinant human GAA enzyme replacement therapy with increased mannose-6-phosphate content for increased cellular uptake compared with alglucosidase alfa (ALGLU). Here we report efficacy and safety of AVAL in late-onset Pompe disease participants in the extended treatment period (ETP) of COMET (Phase 3; NCT02782741) after a 49-week primary analysis period (PAP).

Methods: At PAP enrollment, participants were treatment-naïve (n=100; age 16–78 years). All 51 participants receiving AVAL 20 mg/kg every other week (qow) in the PAP continued this in the ETP (AVAL arm). Of 49 participants receiving ALGLU 20 mg/kg qow in the PAP, 44 entered the ETP and received AVAL 20 mg/kg qow (switch arm).

Results: Trends for improvement or stabilisation from Baseline to Week 97 were observed for the primary and secondary outcomes of respiratory and motor function, muscle strength, and quality of life in AVAL-arm and switch-arm participants (Table 1). Treatment-emergent adverse events up to the last follow-up are summarised in Table 2 for the periods that participants were receiving AVAL. 17 AVAL-arm and 10 switch-arm participants had treatment-emergent serious AEs (SAEs); 4 and 2 of them, respectively, had treatment-related SAEs. Switch-arm participants showed no safety- or immunogenicity-related concerns.

	Avalglucosidase alfa arm PAP: Avalglucosidase alfa ETP: Avalglucosidase alfa (N=51)	Switch arm PAP: Alglucosidase alfa ETP: Avalglucosidase alfa (N=44)
Primary endpoint		
FVC % predicted (upright)	+2.65 (1.05)	+0.36 (1.12)
Secondary efficacy endpoints		
6MWT distance, m	+18.60 (12.01)	+4.56 (12.44)
MIP % predicted (upright)	+9.97 (1.86)	+5.32 (2.00)
MEP % predicted (upright)	+17.25 (3.26)	+13.90 (3.47)
HHD lower extremity composite score	+145.54 (50.92)	+195.06 (52.73)
QMFT total score	+3.83 (0.84)	+2.16 (0.91)
SF-12 PCS	+3.24 (0.98)	+2.13 (1.03)
SF-12 MCS	+1.62 (1.27)	+2.47 (1.32)

6MWT, 6-minute walk test; ETP, extended treatment period; HHD, hand-held dynamometry; LS, least squares; MCS, Mental Component Score; MEP, maximum expiratory pressure; MIP, maximum inspiratory pressure; PAP, primary analysis period; PCS, Physical Component Score; QMFT, quick motor function test; SE, standard error; SF-12, Short-Form-12.

Table 1: Least squares mean change (standard error) in primary and secondary outcome measures from Baseline (Week 0) to Week 97.

	Avalglucosidase alfa arm PAP + ETP (N=51)	Switch arm ETP* (N=44)
Any TEAEs, n (%)	50 (98)	42 (95)
TEAEs potentially related to treatment, n (%)	29 (57)	25 (57)
Serious TEAEs, n (%)	17 (33)	10 (23)
Serious TEAEs potentially related to treatment, n (%)	4 (8)	2 (5)
Severe TEAEs, n (%)	11 (22)	9 (20)
TEAEs leading to permanent treatment discontinuation, n (%)†	2 (4)	3 (7)
TEAEs leading to death, n (%)	0	1 (2)‡
Protocol-defined IARs, n (%)§	20 (39)	21 (48)

ETP, extended treatment period; IAR, infusion-associated reaction; PAP, primary analysis period; TEAE, treatment-emergent adverse event.

Numbers reported are the number (%) of participants with at least 1 TEAE in each category.

*Data for the switch arm are for the ETP only whilst participants were receiving avalglucosidase alfa; this group had received alglucosidase alfa during the PAP.

†5 participants discontinued treatment during the ETP by Week 97 for AEs (1 event each – treatment-related: ocular hyperaemia, erythema, urticaria, respiratory distress; non-treatment related: acute myocardial infarction, pancreatic adenocarcinoma).

‡Pancreatic adenocarcinoma considered not related to treatment.

§Defined as an adverse event that occurred during either the infusion or observation period following the infusion, related or possible related to the investigational treatment.

Table 2: Summary of treatment-emergent adverse events during avalglucosidase alfa treatment

Conclusion: The data show a sustained treatment effect and continued benefit with AVAL beyond the PAP, and stabilisation of treatment effect after switch from ALGLU to AVAL over 97 weeks, supporting long-term maintenance of clinically meaningful outcomes with AVAL.

Disclosure: Sanofi Genzyme funding. Editorial support was provided by Jane M Gilbert, BSc, CMPP of Elevate Medical Affairs, contracted by Sanofi Genzyme for publication support services. Some COMET 97-week data will be presented at WORLDSymposium 2022.

OPR-020

Ravulizumab Reduces Clinical Deteriorations in Patients with Generalised Myasthenia Gravis

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Background and aims: The efficacy and safety of the long-acting terminal complement C5 inhibitor ravulizumab in treating patients with anti-acetylcholine receptor antibody-positive (AChR Ab+) generalised myasthenia gravis (gMG) were demonstrated in the 26-week, phase 3, randomised, double-blind, placebo-controlled CHAMPION MG study (NCT03920293). This analysis of the study data assessed ravulizumab's efficacy in reducing acute clinical deterioration, including life-threatening myasthenic crisis.

Methods: Adults with AChR Ab+ gMG (Myasthenia Gravis Foundation of America Class II–IV and Myasthenia Gravis-Activities of Daily Living score ≥6) were randomised (1:1) to intravenous ravulizumab or placebo infusion every 8 weeks after the initial loading dose, for 26 weeks. Clinical deterioration was defined as an MG crisis (weakness severe enough to necessitate intubation or to delay extubation following surgery); significant symptomatic worsening; or administration of rescue therapy if the patient's health was in jeopardy.

Results: The analysis set comprised 175 patients (86 received ravulizumab; 89 received placebo). Fewer clinical-deterioration events occurred in the ravulizumab group (10 events in 8 patients [9.3 %]) than in the placebo group (26 events in 15 patients [16.9 %]) (Table). Rescue therapy was administered for 10 clinical-deterioration events in the ravulizumab group and 24 events in the placebo group (Table 1).

Outcome	Ravulizumab (n=86)		Placebo (n=89)	
	No. of events	No. of patients (%)	No. of events	No. of patients (%)
Clinical deterioration – total[b]	10	8 (9.3)	26	15 (16.9)
Clinical deterioration – by criterion				
MG crisis[c]	0	0 (0.0)	1	1 (1.1)
Significant symptomatic worsening[d]	1	1 (1.2)	6	5 (5.6)
Rescue therapy (health in jeopardy)[e]	9	7 (8.1)	19	12 (13.5)
Any use of rescue therapy[f]	10	8 (9.3)	24	14 (15.7)

[a] The full analysis set (n=175) comprised all randomised patients who received at least one dose of study drug.
[b] According to per-protocol criteria, a clinical deterioration event may have met more than one criterion, and patients may have experienced more than one event.
[c] Defined as weakness severe enough to necessitate intubation or to delay extubation following surgery; one patient in the placebo group received rescue therapy.
[d] Worsening to a score of 3, or a 2-point worsening from baseline, on any one of the individual Myasthenia Gravis-Activities of Daily Living questionnaire items other than double vision or eyelid droop, which in the investigator's assessment was associated with significant symptomatic worsening; one patient in the ravulizumab group and three patients (one patient on two occasions) in the placebo group received rescue therapy.
[e] Defined as administration of rescue therapy to a patient whose health, in the opinion of the investigator, would be in jeopardy if rescue therapy were not given.
[f] By patients experiencing clinical deterioration.

Table: Clinical deterioration during the 26-week CHAMPION MG study (full analysis set)[a]

Conclusion: Ravulizumab treatment was associated with numerically fewer clinical-deterioration events compared with placebo. These findings support the efficacy of ravulizumab in controlling acute worsening of symptoms in patients with AChR Ab+ gMG.

Disclosure: This study was funded by Alexion, AstraZeneca Rare Disease.

OPR-021

Long-term Safety and Efficacy of Efgartigimod in Patients With Generalised Myasthenia Gravis

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Background and aims: Efgartigimod is a human IgG1 antibody Fc-fragment that blocks neonatal Fc receptor. In the ADAPT study, treatment with efgartigimod resulted in clinically meaningful improvement (CMI) in generalised myasthenia gravis (gMG)-specific outcome measures. All patients completing ADAPT were eligible to enroll in its ongoing open-label, 3-year extension, ADAPT+. This study aimed to evaluate the safety, tolerability, and efficacy of efgartigimod in patients with gMG enrolled in ADAPT+.

Methods: Efgartigimod 10 mg/kg was administered intravenously in cycles of once-weekly infusions for 4 weeks, with subsequent cycles initiated based on clinical response. Efficacy was assessed during each cycle utilising MG-ADL and QMG scales, in addition to other secondary analyses.

Results: 90% of ADAPT patients (151/167) entered ADAPT+. As of February 2021, 106 AChR-Ab+/33 AChR-Ab- patients had received ≥1 dose of open-label efgartigimod (including 66 ADAPT placebo patients). The mean (SD) study duration was 363 (114) days, resulting in 138 patient-years of observation. The most common adverse events in the overall safety population (n=139) were headache (22.3%; n=31), nasopharyngitis (10.8%; n=15), and diarrhoea (8.6%; n=12), which were mostly mild or moderate. In cycle 1, CMI was observed in the overall population with a mean change (mean [SE]) of -5.1 (0.32) in MG-ADL and -4.8 (0.36) in QMG, and this magnitude of improvement occurred during each cycle for up to 10 cycles. Clinical improvements correlated with reductions in total IgG and AChR antibodies across all cycles. Additional analyses will be presented.

Conclusion: The results of these analyses suggest long-term treatment with efgartigimod was well tolerated and efficacious.

Disclosure: Multiple relationships financial and non-financial nature for authors AM, VB, CK, SP, JLdB, HM, SB, MP, AG, PU, CT, KU, JV, RM and JFH Jr. stated at point of presentation.

MS and related disorders: NMOSD and pediatric MS

OPR-022

Functional correlates of intelligence quotient and cognitive abilities in pediatric multiple sclerosis

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Background and aims: Clinical and cognitive features of pediatric MS differ from adult-onset disease. We evaluated the neuropsychological profile of pediatric MS patients and its association with resting-state functional connectivity (RS-FC) abnormalities in key cognitive and motor networks.

Methods: In this 3.0 T MRI study, 76 pediatric MS patients underwent a neuropsychological assessment of Wechsler-Intelligence-Scales for Intelligent Quotient [IQ], Semantic/Phonemic Verbal Fluency Test [SVFT/PVFT], Symbol Digit Modalities Test [SDMT], Coding subtest [CD], Block Design subtest [BD], Trial Making Test [TMT-A/B]. Test failure corresponded to a performance <5th percentile of normative values. Twenty-two matched healthy controls (HC) were also enrolled. Seed-based correlation analysis was used to reconstruct RS-FC within executive, language, motor, default-mode and basal ganglia networks. Age- and sex-adjusted between-group comparisons and correlations with cognitive scores were assessed in right-handed patients having good MRI quality (n=58).

Results: In patients, median IQ was 97.5; 18.4% scored below normatives (IQ<84). Patients most commonly failed CD (21.1%), TMT-B (15.8%), TMT-A (10.5%), SDMT (9.2%), PVFT (6.8%), and BD (3.9%). Compared to HC, patients exhibited reduced RS-FC within all explored networks, involving bilateral caudate nucleus and precentral gyrus. Basal ganglia and language networks also showed reduced RS-FC with anterior and posterior cingulate cortices and frontal regions. Decreased caudate RS-FC was associated with higher IQ and PVFT scores and worse performance in CD, while decreased RS-FC between basal ganglia and cingulate cortices was associated with worse SDMT and PVFT scores.

Conclusion: Reduced RS-FC of the caudate contributes to global cognitive efficiency but also to patients' fragility in different cognitive abilities.

Disclosure: Nothing to disclose.

OPR-023

Long-term eculizumab in AQP4+ NMOSD: relapse-risk reduction and safety in PREVENT and its completed open-label extension

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Background and aims: Eculizumab is well tolerated and significantly reduces relapse risk versus placebo in patients with aquaporin-4 immunoglobulin G-positive (AQP4+) neuromyelitis optica spectrum disorder (NMOSD). We report eculizumab's long term relapse-risk-reduction efficacy and safety in AQP4+ NMOSD during PREVENT (NCT01892345) and its completed open label extension (OLE; NCT02003144).

Methods: After receiving eculizumab or placebo during PREVENT, adults with AQP4+ NMOSD could enter the OLE (eculizumab maintenance dose, 1200 mg/2 weeks, with/without concomitant immunosuppressive therapy). Combined PREVENT and OLE (final data cut, 12 July 2021) data were analysed.

Results: During PREVENT and/or the OLE, 137 patients received eculizumab for a median (range) of 183.4 (0.1–342.0) weeks (3.5 years) and a total of 449.2 patient-years (Table 1). The estimated proportion of adjudicated relapse-free patients at week 216 (4.1 years) was 92.9% (95% CI: 85.9–96.5%; Figure). Nine patients experienced 10 adjudicated relapses (seven during the OLE, including one since the last interim analysis; Table 2). The adjudicated annualized relapse rate was 0.022 (95% CI: 0.012–0.041; Table 1). Rates of treatment-related adverse events and serious adverse events (SAEs)/100 patient-years were 165.3 and 7.0, respectively, versus 167.5 and 24.5 with placebo in PREVENT. The most common SAE was urinary tract infection (5.1% of patients). The serious infection rate was 10.5/100 patient-years with no meningococcal infections. No patients died during the OLE.

Table 1. Eculizumab treatment duration and adjudicated ARR during PREVENT and the OLE.

Variable	Statistic	OLE only			PREVENT + OLE combined
		Placebo/ eculizumab (n = 41)	Eculizumab/ eculizumab (n = 78)	Total eculizumab (n = 119)	Total eculizumab (N = 137)
Treatment duration (weeks)ᵃ	Mean (SD)	128.6 (75.5)	117.3 (52.9)	121.2 (61.5)	171.1 (87.1)
	Median	107.1	106.1	106.1	183.4
	Min., max.	0.1, 318.3	11.1, 295.1	0.1, 318.3	0.1, 342.0
Total number of PY in study period	Sum	101.0	175.4	276.4	449.2
Total number of PY in study period	Sum	101.8	176.0	277.8	451.3
Total number of adjudicated relapses	Sum	3	4	7	10
Number of patients with a total adjudicated relapse count of:					
0	n (%)	39 (95.1)	74 (94.9)	113 (95.0)	128 (93.4)
1	n (%)	1 (2.4)	4 (5.1)	5 (4.2)	8 (5.8)
2	n (%)	1 (2.4)	0 (0)	1 (0.8)	1 (0.7)
3	n (%)	0 (0)	0 (0)	0 (0)	0 (0)
Study-level adjudicated ARR	Rateᵇ	0.029	0.023	0.025	0.022
	95% CIᶜ	0.010–0.091	0.009–0.061	0.012–0.053	0.012–0.041

Accounting for COVID-19 disruption: for patients who missed two or more infusions consecutively in the OLE owing to COVID-19-related reasons, the time period for the calculation of eculizumab adjudicated ARR excludes the time period when the patient missed eculizumab infusions, to account for the impact of the pandemic. Any relapse occurring during this period was not included in the calculation of eculizumab adjudicated ARR.
ᵃTreatment duration = (Date of last study drug dose − Date of first study drug dose) + 1 day.
ᵇCalculated as the total number of relapses during the study period for all patients, divided by the total number of PY in the study period.
ᶜWald CI from Poisson regression.
ARR, annualized relapse rate; CI, confidence interval; OLE, open-label extension; max., maximum; min., minimum; PY, patient-years; SD, standard deviation.

Figure. Time to first adjudicated relapse during PREVENT and the OLE.
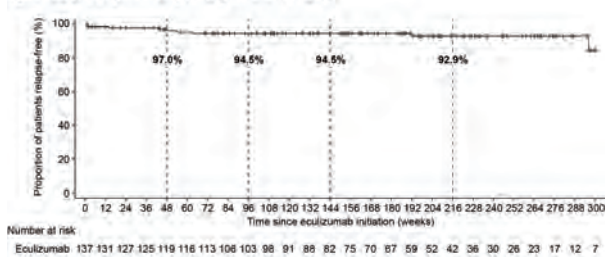
Patients who did not experience an adjudicated on-trial relapse were censored at the end of the study period. For patients who missed two or more consecutive doses owing to COVID-19-related reasons, the study period was truncated to the last dose date prior to the missed doses + 16 days (or + 9 days if in the induction phase), and patients who did not experience an adjudicated on-trial relapse were censored at this date. Tick marks indicate censoring of data. Proportions of patients who were adjudicated relapse-free at weeks 48, 96, 144 and 216 were estimated using the Kaplan–Meier product limit method.
OLE, open-label extension.

Table 2. Adjudicated relapses during PREVENT and the OLE.

Patient number	Study during which adjudicated relapse occurred	Eculizumab treatment day of adjudicated relapse onset	Type of adjudicated relapse (severityᵃ)
1	OLE (placebo in PREVENT)	15	ON unilateral left (major)
2	PREVENT	18	TM partial (minor)
3	PREVENT	98	ON unilateral right (minor)
1	OLE (placebo in PREVENT)	218	ON unilateral left (major)
4	OLE (eculizumab in PREVENT)	300	ON unilateral; TM partial (major)
5	PREVENT	338	ON bilateral (major)
6	OLE (placebo in PREVENT)	381	Brainstem; TM partial (major)
7	OLE (eculizumab in PREVENT)	433	ON unilateral left; TM partial (major)
8	OLE (eculizumab in PREVENT)	1336	Cerebral; ON bilateral (major)
9	OLE (eculizumab in PREVENT)	2065	ON unilateral left; TM partial (major)

Accounting for COVID-19 disruption: relapses with onset during a dose interruption due to COVID-19 were excluded.
ᵃSeverity was only determined for relapses of TM or ON.
OLE, open-label extension; ON, optic neuritis; TM, transverse myelitis.

Conclusion: The proportion of relapse-free patients remained high (92.9%) through 4.1 years' eculizumab treatment. Long-term eculizumab was well tolerated with no new safety signals. These long-term data confirm eculizumab's sustained benefit/risk profile in AQP4+ NMOSD.

Disclosure: Research funding for this study was provided Alexion, AstraZeneca Rare Disease.

OPR-024

Neuromyelitis optica as an in-vivo model of glymphatic system alterations

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Background and aims: Aquaporin-4 is involved in neuromyelitis optica spectrum disorder (NMOSD) autoimmunity and glymphatic functioning. We aimed to assess whether NMOSD patients have glymphatic impairment and its association with clinical disability.

Methods: 34 NMOSD patients and 46 age- and sex-matched healthy controls (HC) from two independent cohorts (exploratory- and validation-dataset) underwent a standardized 3.0 T MRI protocol (T2-, T1-weighted sequences and diffusion tensor imaging). Susceptibility-weighted imaging (SWI) was also acquired in the exploratory-dataset. We evaluated perivascular space (PVS) enlargement and glymphatic system function by calculating the diffusion along perivascular space (DTI-ALPS) index. In the exploration-dataset, SWI was used to draw the regions of interest for DTI-ALPS calculation in areas having veins perpendicular to lateral ventricles. Between-group comparisons, partial correlations and regression models were run to assess associations between DTI-ALPS index, PVS scores, clinical and MRI variables.

Results: The two datasets were similar for demographic and clinical features. In boths, NMOSD patients had reduced DTI-ALPS index (p-values: 0.004–0.038). Patients also showed a higher frequency of severe PVS enlargement in the centrum semiovale (29.4 vs. 8.7%, p=0.040). Lower DTI-ALPS index, deep grey matter and cortical volumes predicted NMOSD diagnosis (R2=0.62). Lower DTI-ALPS index, higher number of myelitis, and higher T2-lesion volume associated with worse disability (R2=0.55). Higher PVS scores correlated with global brain and deep grey matter atrophy (r-values: -0.44, -0.36; p-values=0.01–0.046).

Conclusion: We detected impaired glymphatic system functioning in two independent cohorts of NMOSD patients. It was associated with worse clinical disability, suggesting a correlation with disease pathogenetic mechanisms and their magnitude.

OPR-025

Teriflunomide in paediatric patients with relapsing multiple sclerosis: results from the open-label TERIKIDS extension

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Background and aims: In the 2-year, randomized, double-blind (DB), phase 3 TERIKIDS study (NCT02201108) of paediatric patients with relapsing MS, teriflunomide numerically reduced relapse risk and significantly reduced new/enlarging T2 and gadolinium-enhancing T1 lesion counts versus placebo (Chitnis T et al, Lancet Neurol 2021;20:1001-11). Here, we report final results from the TERIKIDS open-label extension (OLE).

Methods: Patients who completed DB treatment or qualified for early switch from DB treatment to open-label teriflunomide could continue in the OLE until 192 weeks after initial randomization. All patients in the OLE received teriflunomide at body weight-based dose (14 mg equivalence in adults).

Results: 152 patients from the DB period entered the OLE (teriflunomide, 100/109 [91.7%]; placebo, 52/57 [91.2%]) of which 104 (68.4%) completed the OLE. From DB randomization to the end of OLE, relapse risk was numerically lower for teriflunomide/teriflunomide versus placebo/teriflunomide (hazard ratio [95% CI]: 0.62 [0.39–0.98]; p=0.11), as was risk of disability progression sustained for 24 weeks (0.47 [0.23–0.96]). The teriflunomide/teriflunomide group showed reductions versus placebo/teriflunomide for new/enlarging T2 (5.7 vs 11.1; p=0.001) and gadolinium-enhancing T1 (1.5 vs 2.7; p=0.04) lesion counts per MRI scan. Proportion of patients with treatment-emergent adverse events (TEAEs) during the OLE was lower in the teriflunomide/teriflunomide group (81.0%) versus placebo/teriflunomide (90.4%), as was the proportion with serious TEAEs (teriflunomide/teriflunomide: 14.0%; placebo/teriflunomide: 28.8%). 12 patients discontinued open-label treatment due to TEAEs.

Conclusion: Continuous teriflunomide versus delayed teriflunomide initiation in paediatric patients numerically lowered relapse risk and disability progression, and significantly reduced MRI lesion counts with a manageable safety profile.

Ageing and dementia 1

OPR-026

Naturally occurring plasma tau autoantibodies and risk of systemic disease

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Background and aims: Microtubule-associated protein tau is highly expressed in neurons and is known to have a role in neurodegenerative diseases, including Alzheimer's disease. Most research efforts have focused on the function of tau in the nervous system and several clinical trials are exploring the use of tau immunization strategies to prevent progression of neurodegenerative diseases. However, tau protein is not only highly expressed in the brain but also in the kidney and skeletal muscle. A potential role of tau in systemic disease had not been previously explored and so that was the aim of our study.

Methods: Using a high-throughput ELISA (Enzyme-Linked Immunosorbent Assay) screening platform, we probed >20.000 plasma samples of patients visiting a university hospital for the presence of naturally occurring tau autoantibodies. Clinical conditions were classified using ICD-10 (International Classification of Disease and Related Health Problems, 10th revision) codes. Risk ratios and 95% confidence intervals for tau autoimmunity in different systemic disorders were estimated using multivariate log-binomial regression models (including age, sex).

Results: Using data from 21.995 patients, we identified cystitis (RR 1.59, 95% CI 1.14–2.16, p=0.004), other urinary disorders (RR 1.23, 95% CI 1.03–1.45, p=0.018), chronic kidney disease (RR 1.20, 95% CI 1.01–1.41, p=0.033), arterial embolism and thrombosis (RR 1.56, 95% CI 1.02–2.25, p=0.026) and atherosclerosis (RR 1.35, 95% CI 1.09–1.1.66, p=0.004) as independent predictors of naturally occurring tau autoantibodies.

Conclusion: Tau autoimmunity is associated with vascular, kidney and urinary disorders.

OPR-027

Effect of TREM2 on neurodegenerative diagnosis, cognitive profile and brain structure.

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Background and aims: Microglial genes are risk factors for neurodegenerative diseases, especially variant rs75932628 (p.R47H) TREM2. We investigated the association between different TREM2 variants and neurodegenerative disease and evaluated their association with brain structure and cognition.

Methods: Data was acquired from the UKBIOBANK study, including TREM2 variant carriers: p.R47H (n=1,863), p.T96K (n=665), p.R62H (n=7,988) and p.D87N (n=419), and noncarriers (n=392,373). Risk of Alzheimer's (AD; n=803) and Parkinson's (PD; n=1,687) disease was calculated using logistic regression. A subgroup of healthy older adults underwent brain volumetric MRI and cognitive profile. These were compared between carriers of each TREM2 variant and noncarriers.

Results: The p.R47H variant was associated with AD but not PD (Figure 1). Other variants were not associated with either disease. There was no difference in age of onset between p.R47H carriers and noncarriers (median 72 years). There were trend-level associations for reduced putamen (p=0.09), hippocampal (p=0.10) and total brain volumes (p=0.07) in healthy older p.R47H carriers. This was driven by under 65s for the putamen (p=0.09), hippocampal (p=0.10) and total brain volumes (p=0.07) in healthy older p.R47H carriers. This was driven by under 65s for the putamen (P<0.01) and total brain volume (p<0.01). Lower putamen volume (P=0.04) was found in p.D87N carriers. Lower memory scores were found in p.T96K carriers (p<0.01).
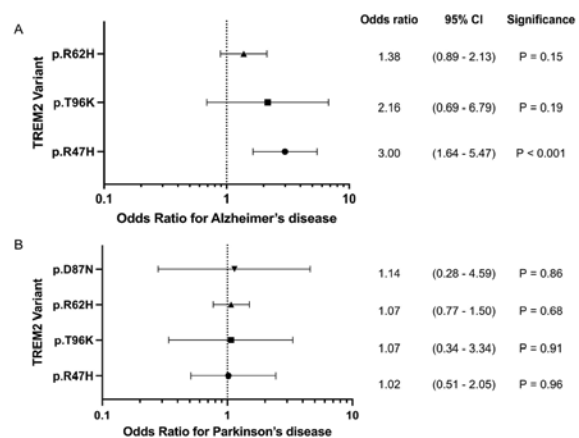
Conclusion: TREM2 p.R47H is a risk factor for AD but is not associated with younger age of onset or with PD. Lack of association between p.T96K, p.R62H or p.D87N and AD may relate to smaller effect sizes and cohort age (median 69 years). We found nominal brain volume reductions in healthy carriers of p.R47H and p.D87N. Therefore, TREM2 may influence brain structure prior to neurodegeneration onset.

Disclosure: Nothing to disclose.

OPR-028

DIAGNOSTIC VALIDITY OF CSF ALPHA-SYNUCLEIN TO PREDICT PSYCHOSIS IN PRODROMAL ALZHEIMER´S DISEASE

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Background and aims: The emergence of psychotic symptoms (PS) in Alzheimer´s disease (AD) involves a poor prognosis of the illness. To study the diagnostic validity of alpha-synuclein (AS) in CSF, to predict the emergence of PS in prodromal AD patients.

Methods: Mild cognitive impairment patients (according to Petersen 2006) from the out-patient consultation of Alicante University General Hospital (Spain) were recruited between 2010–2018. All the patients followed NIA-AA 2018 criteria for AD biomarkers. At inclusion, all of them had MMSE higher than 22, Neuropsychiatric Inventory lower than 10 and a follow-up higher than 2 years. The Pittsburgh sleep quality index and the Cummings criteria for psychosis (2020) were applied. Core AD biomarkers and AS were measured in CSF obtained in the prodromal phase of the illness.

Results: 130 prodromal AD were included. 50 of them (38.4%) accomplished the PS criteria into the 8 years follow-up. In every comparison made between groups and subgroups, AS was the best CSF biomarker to differentiate psychotic versus non psychotic groups. The level of AS 1.257 pg/mL reached at least 80% of sensitivity to differentiate between both groups. A negative predictive value of 80% was found to differentiate between groups.

Conclusion: The measurement of AS in CSF is the most valid biomarker used in this study to predict the emergence of PS during the 8 years after the prodromal phase of AD. In our knowledge, is the first time that a CSF biomarker shows a diagnostic validity to predict PS in prodromal AD.

Disclosure: Funded by ISABIAL.

OPR-029

Belgian Carriers of Rare ABCA7 Mutations Present with Pronounced Cerebral Amyloid Angiopathy and Alzheimer's Disease

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Background and aims: ABCA7 is a major risk gene for Alzheimer's disease (AD), and rare premature termination codon (PTC) and missense mutations are enriched in AD patients. In preliminary studies, we obtained that ABCA7 PTC and missense mutation carriers present with a classical AD phenotype, but severe levels of cerebral amyloid angiopathy (CAA) were also observed at neuropathological examination. We aim to delineate the clinicopathological phenotype of rare ABCA7 mutation carriers in Belgian CAA patients.

Methods: Genetic screening of ABCA7 in Belgian CAA cohort (n=83), with genotype-phenotype comparison of the ABCA7 carriers using demographic and clinicopathology data.

Results: In 20.5% of CAA patients a rare ABCA7 mutation was identified. Six patients carried a PTC mutation, 10 a missense mutation and in one patient we found a deletion. Mean onset age was 66.4±12.8 (range 47-84) years, while mean age at death was 68.0±10.3 (range 48-92) years. Cognitive decline was present in 52.9% (9/17). Nine patients were diagnosed as probable CAA, and four as possible CAA. In six patients postmortem examination showed moderate-to-severe levels of CAA in all but one patient (83.3%, 5/6) and AD neuropathological hallmarks (100%, 6/6). Extensive levels of CAA were present in both the meningeal and capillary blood vessels, and moderate to high levels of CAA in the parenchymal blood vessels.

Figure 1. Neuropathology of *ABCA7* PTC mutation carrier
A. Frontal cortex. 4G stain. Cortical micro infarction. In the region of infarction, there is abundant CAA. B. Frontal cortex. 4G stain. Capillary CAA. C. Frontal cortex. 4G stain. Focus on capillary CAA(*). D. Hippocampus. 4G8 stain. Presence of diffuse plaques and capillary amyloid angiopathy (*). E. Hippocampus. AT8 stain. Presence of neurofibrillary tangles (*) and dystrophic neurites (arrow). F. Cerebellum. 4G8 stain. Extensive meningeal CAA.
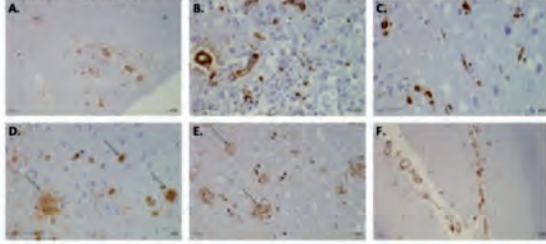
Conclusion: Our data suggest that rare ABCA7 mutations are frequently present in CAA patients. Carriers show signs of severe levels of CAA, as well as AD neuropathological hallmarks. The findings of this study have important implications for future research and clinical practice.
Disclosure: Nothing to disclose.

OPR-030

Huntingtin as a presymptomatic regulator of Alzheimer's disease

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Background and aims: The identification of pathological elements that regulate disease progression, so called regulators, are essential when studying progressive diseases. When Alzheimer disease (AD) presents with symptoms, irreversible nerve damage has already occurred. Targetable intervention and therapy need to address presymptomatic processes and regulators of disease progression. Due to the multi-factorial pathology of AD, a multi-modal approach is needed in order to identify disease regulators.

Methods: Proteomics and subsequent ingenuity pathway analysis was performed on human and the App NL-F/NL-F mouse model brain. The App NL-F/NL-F mouse is a knock-in model, which specifically produces increased levels of highly neurotoxic Aβ42, making it suitable for the study of Aβ42-driven pathology. The levels of huntingtin in human and mice brain were quantified using immunohistochemistry and the location was determined by fluorescence-microscopy.

Results: Huntingtin was identified as a presymptomatic regulator of disease progression in AD. Microscopic studies showed increased levels of huntingtin in pyramidal neurons in the hippocampus and frontal cortex of AD patients compared to nondemented controls. In contrast to Huntington's disease, huntingtin did not colocalize with reactive astrocytes in AD brain. Huntingtin increased in a time-dependent manner and preceded amyloid deposition in App NL-F/NL-F mice.
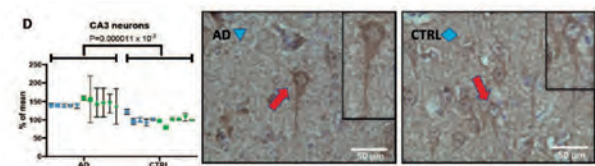
Huntingtin levels in Alzheimer's disease brain(red arrows) show increased accumulation in pyramidal neurons. Huntingtin were found in particularly high levels in hippocampal subareas such as CA3.
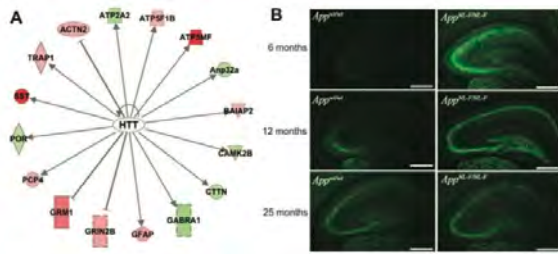
Ingenuity pathway analysis (A) show huntingtin as a regulator of disease progression. APP NL-F/NL-F mice brain show a time-dependent increase in huntingtin (B) which predates accumulation of other pathological elements typical of Alzheimer's disease.

Conclusion: Huntingtin accumulates in the AD brain and is distinct from the huntingtin accumulation seen in Huntington's disease. These findings implicate huntingtin in the pathology of AD and warrant further studies. Huntingtin could possibly be a target for therapeutical intervention. Mechanistic studies in neuronal cell cultures will shed light on the relationship between huntingtin and AD pathogenesis.

Disclosure: Nothing to disclose.

OPR-031

Huntingtin intermediate alleles influence the progression from Subjective Cognitive Decline to Mild Cognitive Impairment

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Background and aims: Huntingtin (HTT) is a gene containing a key region of CAG repeats. HTT alleles containing from 27 to 35 CAG repeats are termed as intermediate alleles (IAs). We aim to assess the effect of IAs on progression of cognitive impairment in patients with subjective cognitive decline (SCD).

Methods: We included 106 patients with SCD. All the patients underwent neuropsychological assessments and blood sample collections at baseline. Patients were followed-up for a median time of 13.75 (IQR=8.17). We genotyped APOE and HTT at the end of the follow-up.

Results: Eleven out of 106 patients (10.38% [95% CI=4.57–16.18]) were carriers of IA (IA+). During the follow-up, 44 patients (41.51% [95% CI=32.13–50.89]) progressed to MCI (p-SCD), while 62 patients (58.49% [95% CI=49.11-67.87]) did not (np-SCD). Rate of progression to MCI was associated with IAs (Fig.1), age at baseline, and APOE ε4. We dichotomized age at baseline (<60 = younger patients [YP], >60 = older patients [OP]) and classified patients into four groups: YP/IAs–, YP/IAs+, OP/IAs– and OP/IAs+. OP/IAs+ had a higher proportion of progression from SCD to MCI (85.71% [95%C.I.=59.79-100]) as compared to YP/IAs– (28.57% [95%C.I.=13.60-43.54], $\chi2$=15.25, p<0.001) and OP/IAs– (45.00% [95%C.I.=32.41-57.59], $\chi2$=7.903, p=0.005) (Fig.2). We classified patients according to APOE and IA as: ε4–/IA–, ε4–/IA+, ε4+/IA–, ε4+/IA+. Proportion of progression in ε4+/IA+ group (100%) was higher as compared to ε4–/IA– (33.33% [95% C.I.=21.96–44.71], χ^2=14.43, p<0.001) and ε4+/IA– (55.56% [95% C.I.=36.81–74.30], χ^2=4.60, p=0.032) (Fig.3).
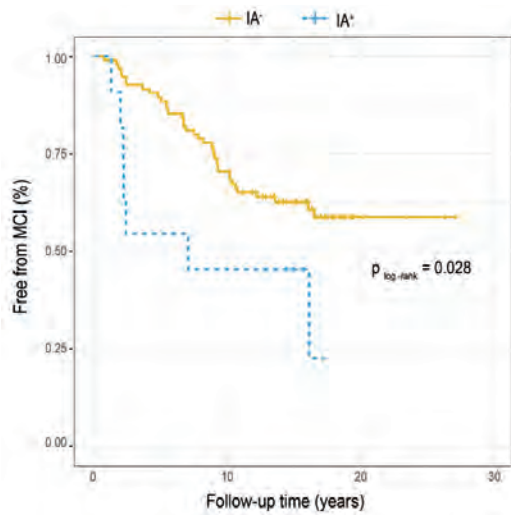
Kaplan-Meier survival analysis for comparison of distributions of progression from SCD to MCI between IA– (n=95) and IA+ (n=1).
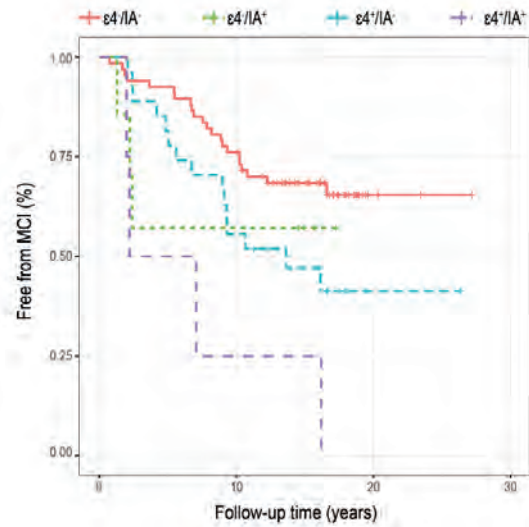
Kaplan-Meier survival analysis for comparisons of distributions of progression from SCD to MCI among groups defined according to APOE status and IA: ε4–/IA– (n = 67), ε4–/IA+ (n = 7), ε4+/IA– (n = 27) and ε4+/IA+ (n = 4).
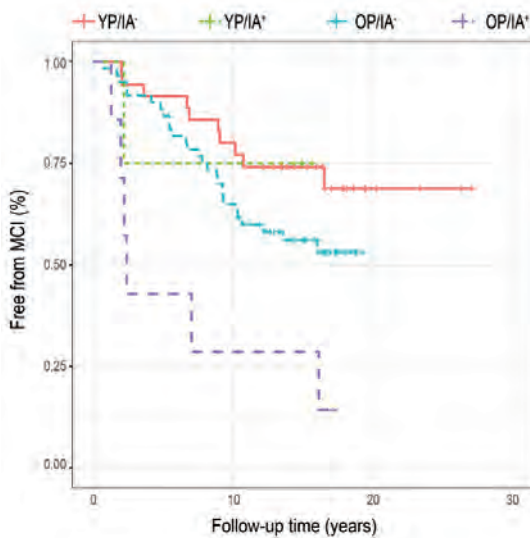
Conclusion: IAs interact with age and APOE ε4 increasing the risk of progression to MCI in SCD patients.
Disclosure: No authors report any conflicts of interest for this study.

Kaplan-Meier survival analysis for comparisons of distributions of progression from SCD to MCI among groups classified according to age at baseline and IA: YP/IA– (n=35), YP/IA+ (n=4), OP/IA– (=60) and OP/IA+ (n=7).

COVID-19

OPR-032

Persistent olfactory dysfunction in COVID-19: a seed-based resting-state fMRI study

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Background and aims: Olfactory dysfunction (OD) is a frequent manifestation of COVID-19 and, in a minority of patients, may persist for several months. The pathogenesis is still debated and may involve disruption of the olfactory system at different levels. We aimed to explore the integrity of the olfactory network in a cohort of patients with COVID-19-related persistent OD, through resting-state functional magnetic resonance imaging (rs-fMRI).

Methods: We included 23 patients (mean age 37±14 years, 12 females) with persistent (11±5 months) COVID-19-related OD confirmed by Sniffin' Sticks Test (mean score 24±5/48, hyposmia cut-off: 30) and 28 sex- and age-matched healthy controls. Participants underwent a neuropsychological assessment and a standardized brain MR acquisition protocol (3 T), including rs-fMRI. Seed-based correlation analysis was performed on pre-processed rs-fMRI data to localize each subject's olfactory network, using spherical seeds in the bilateral anterior insula, piriform cortex and orbitofrontal cortex (Figure 1). Whole-brain functional connectivity (FC) with the seeds was compared between patients and controls (statistical significance: p-value<0.05).

Location of the ROI used as seeds for the seed-based correlation analysis

Results: The olfactory network was successfully identified in seven patients, and significantly lower FC was found, compared to healthy controls, between the right anterior insula and a wide spread area of the bilateral superior temporal, middle frontal and inferior parietal areas (Figure 2). Additionally, the FC between the left piriform cortex and the right frontal pole was significantly higher in the patients' group compared to controls.

Clusters of altered functional connectivity with the right superior insula

Conclusion: Patients with persistent COVID-19-related OD showed altered olfactory network connectivity (i.e. anterior insula and the piriform cortex).
Disclosure: Nothing to disclose.

OPR-033

The risk of neurological diseases after COVID-19, influenza A/B or community-acquired pneumonia infection

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Background and aims: Two years after onset of the pandemic, the precise nature and temporal evolution of the effects of COVID-19 on neurologic disorders remain uncharacterized. Studies have established an association with neurological syndromes, including anosmia, encephalopathy, and ischemic stroke, but it is unknown whether COVID-19 also influences the incidence of specific neurologic diseases and whether it differs from other respiratory infections.

Methods: Using population-based electronic health records we investigated the association between COVID-19 and specific central and peripheral neurologic diseases. We compared patients with COVID-19 to individuals without, and to patients with influenza A/B and community-acquired bacterial pneumonia. We assessed the incidence of neurologic disease one, three, six, and twelve months after positive test results.

Results: We identified 42,535 people with COVID-19, 8,329 with influenza, 1,566 with pneumonia, and 2,392,400 without COVID-19. Compared to individuals without COVID-19, patients with COVID-19 had increased relative risk (RR) of developing Guillain Barré syndrome (RR=3.1; 95% CI=1.5–6.7), multiple sclerosis (RR=1.4; 95% CI=1.2–1.7), narcolepsy (RR=3.2; 95% CI=1.6–6.2), Parkinson's disease (RR=2.8; 95% CI=2.4–3.2), Alzheimer's disease (RR=4.9; 95% CI=4.0–6.0), dementia of any type (RR=5.2; 95% CI=4.5–6.1), and ischemic stroke (RR=2.3; 95% CI=2.1–2.5). However, compared to patients hospitalized with influenza, patients hospitalized with COVID-19 only had an increased risk of ischemic stroke at one (RR=1.9; 95% CI=1.3–2.8), three (RR=1.8; 95% CI=1.3–2.5) and six months (RR=1.9, 95% CI=1.3–2.7). Compared to patients hospitalized with pneumonia, the risk of neurologic diseases was not increased.

Conclusion: COVID-19 increases the risk of a broad range of neurological disorders. However, except for ischemic stroke, there is no excess risk compared to influenza A/B and community-acquired pneumonia.

Disclosure: The authors have none to declare.

OPR-034

Neuronal and glial damage during acute COVID infection in absence of clinical neurological manifestations

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Background and aims: SARS-Cov 2 has a particular tropism for the nervous system and can infect neurons and glia. Serum neurofilament light chain (sNfL) and serum glial fibrillary acidic protein (sGFAP) represent two promising markers of neuronal and glial degeneration. The aim of this study is to evaluate sNfL and sGFAP levels in COVID hospitalized patients without neurological symptoms and previous neurological co-morbidities.

Methods: 68 COVID patients, 72 healthy subjects (HSs) and 21 non-COVID patients with interstitial pneumonia were enrolled in the study. Blood samples were collected within 24–48 h of hospitalization and sNfL and sGFAP levels were assessed in each serum sample of patients and controls. We used the commercially available immunoassay kits for GFAP and NfL run on the ultrasensitive SR-X™ Biomarker Detection System (Quanterix) following manufacturer instructions. Non parametric statistical analysis was performed to assess difference between the three groups.

Results: In this ongoing study, COVID patients showed higher levels of sNfL (COVID: 38.02+57.87 pg/mL) than in non-COVID pneumonia (13.63+6.82, p 0.02) and HSs (6.65+2.85 pg/mL, p<0.0001). COVID patients showed also higher levels of sGFAP (COVID: 232.98+223.06 pg/mL) in comparison to non-COVID pneumonia (145.32+77.26, p=0.05) and HSs (84.12+33.70 pg/mL, p=0.006). No significant differences were found between non-COVID patients and HSs for both biomarkers. In COVID patients, no significant correlation was found between blood levels of sNfL or sGFAP and disease severity.

Conclusion: The preliminary results of this ongoing study suggest inflammatory-related neuronal and glial degeneration in patients with COVID infection independently of presence of clinical neurological manifestations.

Disclosure: R. Cortese was awarded a MAGNIMS-ECTRIMS fellowship in 2019. N. De Stefano received honoraria from Biogen-Idec, Bristol Myers Squibb, Celgene, Genzyme, Immunic, Merck Serono, Novartis, Roche and Teva.

OPR-035

Does gender influences outcome of stroke in COVID+ and COVID- patients: a large collaborative study in Northern Italy

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Background and aims: The impact of the COVID-19 pandemic during the first wave in Italy caused a decrease of hospital admissions, delays in reperfusion treatments and an overall worse outcome in COVID+ patients with stroke. However, few data are available on outcome of stroke stratified by gender.

Methods: A multi-center observational study on neurological complications in COVID-19 patients was conducted in 19 Neurology Units by the Italian society of Hospital Neuroscience (SNO). Adult patients admitted to Neurological units between March–April 2020 with ischaemic stroke were recruited. Demographic, clinical, treatment and outcome data were compared in patients with (COVID19+) and without COVID-19 (COVID19-), as well as in male and female patients.

Results: 812 patients with ischemic stroke were enrolled (682 COVID-, 129 COVID+); males were 54.1% and 52.7%. Intra-hospital mortality was 31.9% in COVID+ patients (38.6% in male and 27.8% in female) and 7.2% in COVID- (8.4% in males and 6% in females). Male patients with COVID+ were more likely to have cPAP (30.9% vs 14.8%; $p=0.03$) or being intubated (14.9% vs 3.3%; $p=0.02$) than females. Reperfusion treatment was administered more frequently in women if COVID- (34.5% vs 29.8%), while less frequently if COVID+ (11.5% vs 29.4%; $p=0.01$). COVID+ patients had a higher frequency of ESUS than COVID- (31.8% vs 22.3%; $p=0.02$), with a higher frequency in COVID+ females compared to males (36.1% vs 27.9%).

Conclusion: Our study detected some differences due to gender in ischaemic stroke with and without COVID-19. Multivariate analyses is ongoing to define predictors of mortality across gender categories.

Disclosure: Nothing to disclose.

OPR-036

The COVID-19 pandemic has caused large disruptions to dementia mortality, care, and diagnosis in Sweden during 2020

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Background and aims: Covid-19 might cause indirect deaths and reduction in diagnoses amongst vulnerable patient populations such as dementia patients. Quantifying the effect of Covid-19 on dementia patient population in the form of deaths and diagnosis amongst the group is essential to understand the full scope of the pandemic impact and formulate future response.

Methods: Registry based national data from 2015–2019 was collected in the form of periodic mortality, years of potential life lost, dementia diagnosis coding, and Covid-19 incidence in Sweden and its 21 regions. Multivariable regression analysis and moving averages was used to predict values for each parameter during 2020. Pearson correlation analysis was used to confirm correlation between Covid-19 incidence and mortality, years of potential life lost, or dementia diagnosis coding.

Results: During 2020, Covid-19 caused a seasonal increase in mortality amongst dementia patients that coincided with pandemic waves. Dementia diagnosis coding was severely impacted in all regions and correlated to Covid-19 incidence but not mortality. All dementia diagnoses decreased significantly. Elderly women were particularly affected. Unspecified dementia was found to be increased. Preliminary data from first half of 2021 showed similar results.
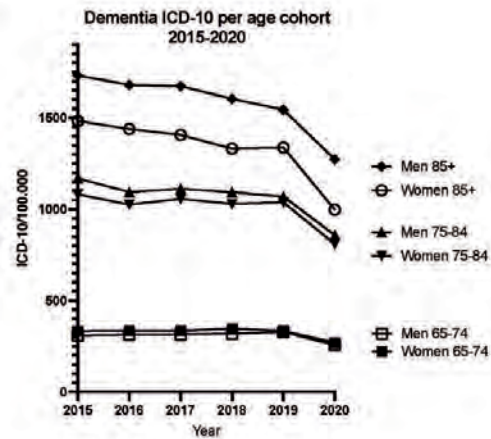
Dementia associated ICD-10 coding of age cohorts in Sweden during 2015–2020 showing a marked decrease in dementia coding during 2020.
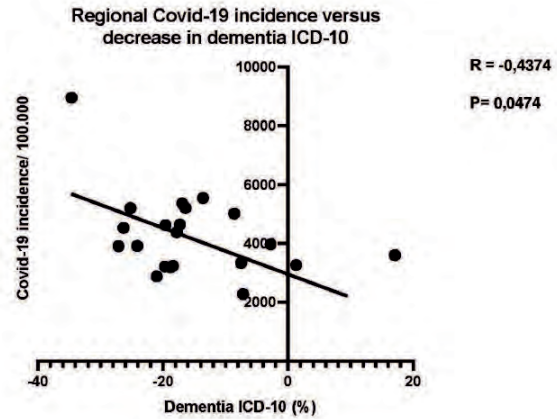
Dementia ICD-10 associated coding correlate to Covid-19 incidence in the 21 regions of Sweden.

Conclusion: Covid-19 is linked to increase in mortality amongst dementia patients. Covid-19 has also caused large impacts to dementia diagnosis and care. These findings might have severe long-term consequences in the form of underdiagnosis and undertreatment of dementia, particularly amongst elderly women. Increased percentage of unspecified dementia making up dementia diagnoses might be indicative of decreased quality in dementia diagnosis. Healthcare reforms are necessary to address these shortcomings.

Disclosure: Nothing to disclose.

OPR-037

Safety of vaccines against SARS-CoV-2 among patients with multiple sclerosis treated with disease modifying therapies

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Background and aims: The aim of the study was to report side effects after vaccination against coronavirus disease 2019 (COVID-19) among individuals with multiple sclerosis (MS) treated with disease-modifying therapies (DMTs) in Poland.

Methods: The study included 2,203 patients with MS treated with DMTs and vaccinated against COVID-19 in 17 Polish MS centers. The data was collected through 15 December 2021. The information included demographics, specific MS characteristics, current DMTs, type of vaccine, side effects after vaccination, time of side effect symptoms onset and resolution, applied treatment, relapse occurrence, and incidence of COVID-19 after vaccination. The results were obtained using maximum likelihood estimates for the odds ratio and logistic regression.

Results: The majority (1,782/2,203; 80.89%) of included patients were vaccinated with nucleoside-modified messenger RNA (mRNA) vaccines. Mild symptoms after immunization, more often after the first dose, were reported by 70.04% of individuals. Most common were: arm pain (47,34% after the first and 34,59% after the second dose), fever (18.11% after the first and 19.38% after the second dose), and fatigue (10.67% after the first and 10.94% after the second dose). Only one individual presented severe side effects (pro-thrombotic complications). None of the DMTs predisposed to the development of particular side effects. Relapse after vaccination occurred in 99 individuals, in 16 ones less than 21 days after the first or second dose of immunization. 7 patients had confirmed SARS-CoV-2 infection despite vaccination

Conclusion: Serious side effects after vaccination against COVID-19 in patients with MS are very rare and are not related to particular DMT.

Disclosure: Authors have nothing to disclose.

Cerebrovascular diseases: Small vessel disease and ICH

OPR-038

Clinical characteristics of Cortical Superficial Siderosis – a 10 years (2009-2021) single centre experience

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Background and aims: Cortical Superficial Siderosis (cSS) is caused by supratentorial hemosiderin deposits limited to the cortical sulci, supposedly due to acute non-traumatic convexity subarachnoid haemorrhage (cSAH) in subarachnoid space. cSS is a neuroimaging biomarker for cerebral amyloid angiopathy (CAA) and a common cause of transient focal neurological deficits (TFNEs).

Methods: This is a descriptive retrospective study of symptomatic patients with cSS and TFNEs who presented in the Christian-Doppler-University Hospital, between 2009 and 2021. We analysed demographic, semiological, and MRI data of 37 patients older than 55 years, with cSS/cSAH and neuroimaging features of probable/possible CAA in conformity with the Boston-Criteria.

Results: We identified 37 patients (35% male) with probable (n=24; 65%) or possible (n=13; 35%) CAA with a median age of 70 years (IQR 68–77). 65% (n=26) of them showed cardiovascular risk factors, and 56% were presented in our clinic with at least one transient focal neurological episode, mostly in the form of non-motor sensory symptoms (n=19) with a median duration of symptoms up to 15 minutes (IQR 10–30). The patients with only TFNEs were significantly older (median 81 vs. 70 years of age, p=0.005) than patients with symptoms due to stroke (infarction or haemorrhagic) ±TFNEs. In the MRI, the most frequent localization of cSS was in the frontal (n=54) followed by parietal (n=38) and occipital (n=28) region.

Conclusion: In the population with established cSS, those presenting only with TFNEs tend to be older than their counterparts presenting with additional stroke symptoms.

Disclosure: Nothing to disclose.

OPR-039

MRI small vessel disease classification of intracerebral haemorrhage and risk of recurrent cerebrovascular events

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Background and aims: We present a novel MRI-based small vessel disease (SVD)-phaenotype classification of intracerebral haemorrhage (ICH) and investigate associations with outcomes.

Methods: We included all consecutive patients with non-traumatic, small vessel disease-related ICH from the multi-center, prospective Swiss Stroke Registry who underwent MRI. Patients were classified according to a novel MRI-based classification using haemorrhagic (microbleeds, cortical siderosis) and non-haemorrhagic (white matter hyperintensities, lacunes) markers and haematoma location as cerebral amyloid angiopathy (CAA), deep perforator arteriopathy (DPA), mixed SVD or undetermined SVD. Primary outcome was recurrent ICH or ischaemic strokes within 3 months.
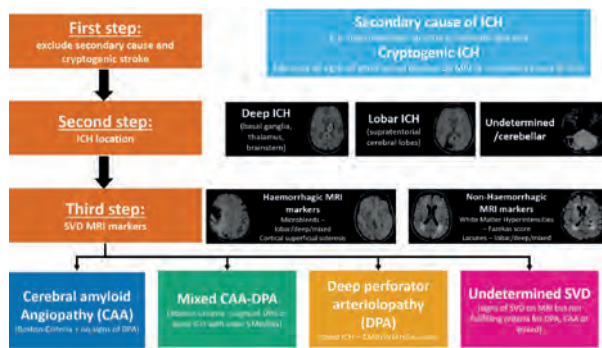
MRI-based small vessel disease phaenotype classification: Flowchart

Results: We enrolled 858 patients (median age 73 years, IQR 62–79; 44.4% female, admission NIHSS 8). The distribution of MRI-phenotypes was 22.6% DPA (194 patients), 10.8% CAA (93 patients), 51.0% mixed SVD (438 patients) and 15.5% undetermined SVD (133 patients). During follow-up, 8.4% (58 patients) suffered ≥1 recurrent event (27 ischaemic strokes, 32 ICH). Rates of recurrent ICH and ischaemic stroke were 3.1%/3.1% respectively in patients with DPA, 3.9%/0% in CAA, 4.6%/6.1% in mixed SVD and 7.9%/1.0% in patients with undetermined SVD. After adjusting for confounders (incl. atrial fibrillation for ischaemic stroke and history of ICH for recurrent ICH), we did not observe a significant association of events with MRI phaenotype.

Conclusion: This new MRI-based SVD-ICH phaenotype classification is feasible and reproducible. Larger studies with longer follow-up are needed to determine distinct risk profiles for recurrent ICH and ischaemic stroke beyond established risk factors.

Disclosure: Dr. Goeldlin: Grants from Swiss Academy of Medical Sciences/Bangerter-Rhyner-Foundation (for the submitted work), Mittelbauvereinigung der Universität Bern and Pfizer congress grant (outside the submitted work).

OPR-040

Tranexamic Acid Administration for Patients with Aneurysmal Subarachnoid Hemorrhage

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Background and aims: Antifibrinolytics as ε-aminocaproic acid and tranexamic acid (TXA), have been widely used for decades to reduce the risks of rebleeding. Here, we aim to synthesize evidence from published clinical trials on the efficacy and safety of the administration of tranexamic acid (TXA) in patients with aneurysmal subarachnoid hemorrhage (aSAH).

Methods: We followed the standard methods of Cochrane Handbook of Systematic Reviews for interventions and the PRISMA statement guidelines 2020 when conducting and reporting this study. A computer literature search of PubMed, Scopus, Web of Science, and Cochrane Central Register of Controlled Trials was conducted from inception until 1 January 2022. We selected observational studies and clinical trials comparing TXA versus no TXA in aSAH patients. Data of all outcomes were pooled as the risk ratio (RR) with the corresponding 95% confidence intervals in the meta-analysis models.

Results: 13 studies with a total of 2,991 patients were included in the analysis. TXA could significantly cut the risk of rebleeding (RR 0.56, 95% CI 0.44 to 0.72) and mortality from rebleeding (RR 0.60, 95% CI 0.39 to 0.92, p=0.02). However, TXA did not significantly improve the overall mortality, neurological outcome, delayed cerebral ischemia, or hydrocephalus (all p>0.05). In terms of safety, no significant adverse events were reported. No statistical heterogeneity or publication bias were found in all outcomes.

Conclusion: In patients with aSAH, TXA significantly reduces the incidence of rebleeding and mortality from rebleeding. However, current evidence does not support any benefits in overall mortality, neurological outcome, delayed cerebral ischemia, or hydrocephalus.

Disclosure: Nothing to disclose.

OPR-041

Inter-method reliability and validity of the modified Rankin Scale in patients with aneurysmal subarachnoid hemorrhage

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Background and aims: The aims of this study are to assess: 1) inter-method reliability of different assessment methods of the mRS 2) convergent validity and 3) responsiveness of the mRS; and 4) the distribution of mRS scores across patient reported outcome measures (PROMs).

Methods: This is a prospective, randomized, multicenter study. Patients were seen by a physician who assigned an mRS score, followed depending on randomization by either the structured interview or the self-assessment. All patients completed different PROMs. Inter-method reliability was assessed with the quadratic weighted kappa score and percentage of agreement. Convergent validity and responsiveness were assessed by testing hypotheses.

Results: The quadratic weighted kappa was 0.60 between the assessment of the physician and structured interview and 0.56 between assessment of the physician and self-assessment. Percentage agreement was respectively 50.8% and 19.6%. The assessment of the mRS through a structured interview and self-assessment resulted in systematically higher mRS scores than by the physician. The correlation of the mRS with PROMs was moderate. Three out of four hypotheses for convergent validity were met. Improvement on GPE was indicated by 83% of patients; the mean change score on the mRS was -0.08 (SD 0.915). None of the hypotheses for responsiveness were met.

Conclusion: The mRS scores obtained with different assessment methods differ significantly. The agreement between the scores is low, although the reliability between the assessment methods is good. The mRS generally correlates with other instruments as expected, but it lacks responsiveness.

Disclosure: Nothing to disclose.

OPR-042

Clinical manifestations of deep perforator small vessel disease in intracerebral haemorrhages versus lacunar stroke

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Background and aims: Deep perforator arteriolopathy is the leading etiology of intracerebral haemorrhage (ICH) and lacunar strokes (LS) located in deep, non-lobar brain regions. We compared clinical and MRI characteristics and outcomes in patients with deep ICH and LS.

Methods: We included patients with MRI-confirmed LS or ICH in the basal ganglia, thalamus, internal capsule or brainstem from the Bernese Stroke Registry (2013–2019). We assessed MRI markers of small vessel disease (SVD), calculating overall burden. Co-primary outcomes were modified Rankin Scale (mRS) and new ischaemic stroke or ICH at 3-months.

Results: We included 711 patients, 112 patients (15.8%) with deep ICH (mean age (SD) 65 (±15.1) years, 36.8% female) and 599 patients (84.2%) with LS (mean age (SD) 69.7 (±13.6) years, 39.9% female). Deep ICH was independently associated with higher SVD burden score (aOR 3.2, 95% CI 2.2–4.7). At 3 months, deep ICH was associated with higher mRS (ordinal shift: aOR 2.2, 95% CI 1.2–4.0). Risk of ischaemic strokes was numerically higher in deep ICH (8.6%) compared to LS (2.9%; p=0.046), but attenuated after adjustment for confounders (e.g. atrial fibrillation; aOR 2.9, 95% CI 0.96–8.7). Recurrent ICH within 3 months occurred in only two patients with ICH, but none with LS.

Conclusion: Deep perforator arteriolopathy manifesting as ICH is less frequent but characterized by more severe disease burden on MRI and worse outcome compared to LS. The risk of subsequent ischaemic stroke seems at least as high in deep ICH as in LS, advocating for shared pathomechanisms with potential consequences for future secondary prevention strategies.

Disclosure: Disclosures Dr. Goeldlin: Grants from Swiss Academy of Medical Sciences/Bangerter-Rhyner-Foundation (for the submitted work), Mittelbauvereinigung der Universität Bern and Pfizer congress grant (outside the submitted work).

OPR-043

Cerebral white matter hyperintensities indicate severity and progression of coronary artery calcification

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Background and aims: Cerebral white matter hyperintensities (WMH) are an important brain imaging feature of cerebral small vessel disease and have been associated with subclinical atherosclerosis including coronary artery calcification (CAC). However, previous studies on this association are limited by only cross-sectional analysis. We here aimed to explore the relationship between WMH and CAC in elderly individuals both cross-sectionally and longitudinally.

Methods: The study population consisted of elderly participants without stroke and dementia from the community-based Austrian Stroke Prevention Family Study (ASPS-Fam). Baseline and follow-up assessment comprised brain MRI, coronary artery computed tomography and clinical/laboratory examination of vascular risk factors. WMH load (via semi-automated volumetric assessment) and CAC levels (via the Agatston Score) were analyzed quantitatively at baseline and after a median follow-up period of 6 years.

Results: Of 331 study participants (mean age: 65.1 ± 10.5 years; female: 59.8%), 105 underwent follow-up. Baseline WMH load (mean: 7.9 ± 13.7cm³) correlated with baseline CAC levels (mean Agatston Score: 149 ± 329) in univariable ($r=0.253$, $p=0.007$) and multivariable analysis (adjusted for age, sex and hypertension; $p<0.001$). While baseline CAC levels were not predictive for WMH progression (mean: 1.1 ± 2.6cm³, $p>0.1$), baseline WMH load was associated with increase of CAC (mean: 149 ± 289) during the follow-up period in multivariable analysis ($ß=0.321$, $p<0.001$).

Conclusion: In this community-based cohort of elderly individuals, WMH were associated with CAC at baseline and predictive of its progression over a 6-year follow-up after adjustment for important co-variables.

Disclosure: Nothing to disclose.

Neuroimaging 1

OPR-044

Normative charts for brain volume development: Use and interpretation

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Background and aims: Child growth standards (e.g. height, weight) defined by the World Health Organization are used worldwide. However, brain volume charts (i.e. quantitative models of brain development) are rarely used and occasionally misinterpreted as abnormal even though within normal limits. In this study, we investigate the reliability of percentiles provided by normative charts for pediatric MRI data and propose a suitable interpretation.

Methods: In 2,114 healthy subjects aged 5 to 96, gray matter (GM) and white matter (WM) volumes scaled for head size were computed using the automatic software icobrain. Afterwards, volumetric percentile trajectories were modeled as a function of age. An independent multicenter test-retest pediatric MRI dataset composed of 211 subjects aged 6 to 20 was then employed to evaluate the reproducibility of percentiles on these normative brain volume charts.

Results: Percentile variability was higher for test-retest means close to the percentile 50 (see Figure 1). As most of the controls were distributed around this value, slight volumetric differences led to high differences in percentile values (see Figure 2). On the contrary, test-retest errors were smaller when the test-retest mean was below percentile 10 or above percentile 90, providing higher confidence about the atypical volumes.
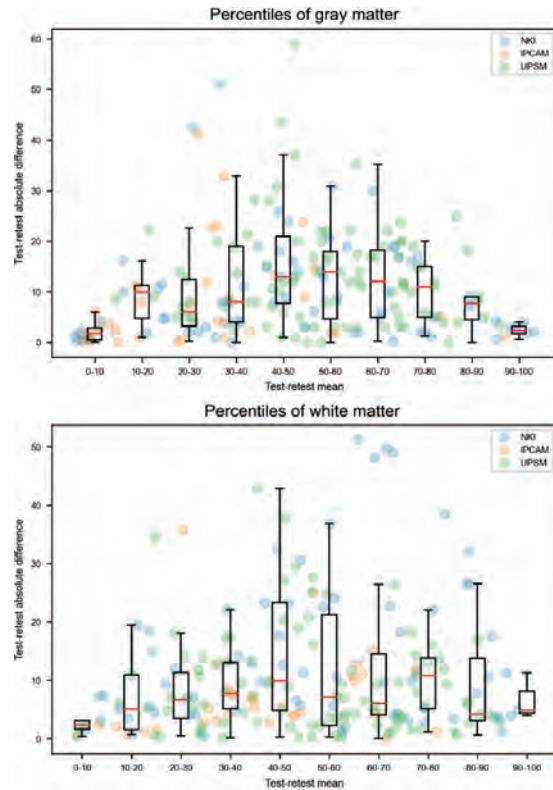
Fig 1: Absolute version of Bland-Altman plot of the test-retest percentiles of gray matter (top) and white matter (bottom). In these box plots, each independent dataset is color-coded.
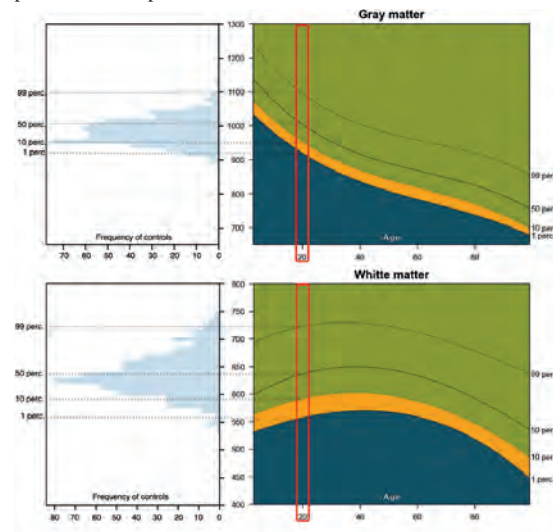
Fig 2: Control subjects distribution and quantitative models of brain development for gray matter (top) and white matter (bottom). The distribution represents the controls subjects used to compute the percentiles for 20 years old.

Conclusion: Given the high variability of percentiles close to the percentile 50, individual changes in a patient's brain volume should be assessed as within or out of the normal range. In contrast, abnormal brain development can reliably be assessed by extreme percentiles.

OPR-045

Brain age estimation by machine learning outperforms brain parenchymal fraction as imaging marker in multiple sclerosis

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Background and aims: The brain age paradigm applies patterns of normal aging from large brain imaging data repositories, allowing us to estimate an individual's brain age. Our objectives were to apply an established brain age estimation model on longitudinal brain magnetic resonance imaging (MRI) data from people with multiple sclerosis (pwMS) and healthy controls (HC) and to compare clinical and demographic associations with brain age and brain parenchymal fraction (BPF).

Methods: PwMS (n=1.515, mean age 38.9 years) and HC (n=876, mean age 45.9 years) were included from Oslo and Karolinska University Hospitals. Structural 3D T1-weighted MRI data were processed using a harmonized pipeline to extract 1.118 cerebellar, cortical and subcortical features per subject. We estimated brain age using our published training set (n=35,474, age 3–89 years), residualizing for age, age^2, sex and scanner. We used linear mixed models to test for clinical and demographic associations with brain age and BPF, respectively.

Results: The average estimated brain age of pwMS was 6.5 years older than HC (CI=5.4–7.5, p=2.6×10^{-34}). PwMS had an accelerated annual increase in brain age of 22% (CI=0.15–0.29, p=8.0×10^{-11}), not evident for HC. Brain age performed better than BPF for clinical associations (expanded disability status scale; t=4.5, p=7.0×10^{-6} vs. t=2.6, p=0.01 and disease duration; t=4.3, p=2.5×10^{-5} vs. t=1.8, p=0.07).

Table 1 Overview of the demographic and clinical features of the multiple sclerosis cohort at the first scan

Table 1. Overview of the demographic and clinical features of the multiple sclerosis cohort at the first scan

Figure 1. An overview of the multiple sclerosis cohort.

Conclusion: In our large-scale study, pwMS displayed older brain age and accelerated brain aging compared to HC. The brain age paradigm outperformed standard BPF analyses in terms of mapping clinical associations and can potentially serve as an individual global imaging marker of neurodegeneration in MS.

MS Phenotype	RRMS	SPMS	RRMS	SPMS
Disease duration (years)	11.2	8.2	9.3	12.1
EDSS score	0.0	7.5	8.0	9.0
Gender	Female	Female	Female	Female
Age (years)	33	38	33	28
Brain age gap (years)	+0.1	+1.5	+21.0	+34.0
DMT	No treatment	Rituximab	No treatment	Natalizumab

Figure 2 A visualisation of four people with multiple sclerosis. All people in the same age group, but with different disability, brain age, treatment, and disease duration.

Disclosure: EAH, SB, PBH, MKB, PS, AM, TO, EGC, JH, HFH, FP and TG received honoraria from different pharmaceutical companies and grants. All other authors report no relevant disclosures.

OPR-046

The subcortical and neurochemical organisation of the ventral and dorsal attention networks

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Background and aims: The cortical mapping of attentional systems identified two segregated networks that mediate stimulus-driven and goal-driven processes, the Ventral and the Dorsal Attention Networks. Deep brain electrophysiological recordings, behavioural data from phylogenetic distant species and observations from human brain pathologies suggest that purely corticocentric models might not fully express the neural background of attention. Here, we aimed to map the subcortical architecture of attention networks, using advanced methods of functional alignment applied to resting-state functional connectivity.

Methods: First, we seeded functional network maps of the Ventral and the Dorsal Attention Networks from 110 7T resting-state functional MRIs. Network maps were functionally aligned in a functional space through iterative diffeomorphic transformations. Then, we examined the structural, functional and graph centrality properties of the identified subcortical structures. Finally, we computed the spatial correlation between the projections of the brainstem nuclei and the distribution maps of the neurotransmitter systems.

Results: Functionally aligned maps of both networks overlapped the pulvinar, the superior colliculi, the head of caudate nuclei, and a cluster of brainstem nuclei (Fig. 1). Structurally, these nuclei were densely connected network hubs, integrating projection fibers, namely fronto-pulvinar, parieto-pulvinar and tecto-pulvinar tracts. The structural projections of the brainstem nuclei were spatially correlated with the distribution of the nicotinic acetylcholine receptors and the dopamine transporters (Fig. 2).
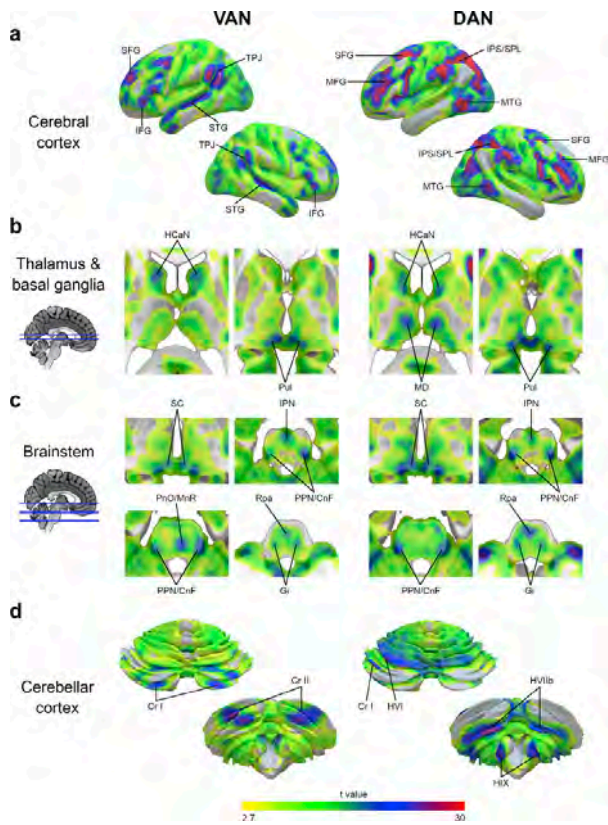
Figure 1: VAN (left) and DAN (right) maps after functional alignment, at different anatomical levels, namely cerebral cortical surface (a), thalamus and basal ganglia (b), brainstem (c) and cerebellar cortical surface (d).
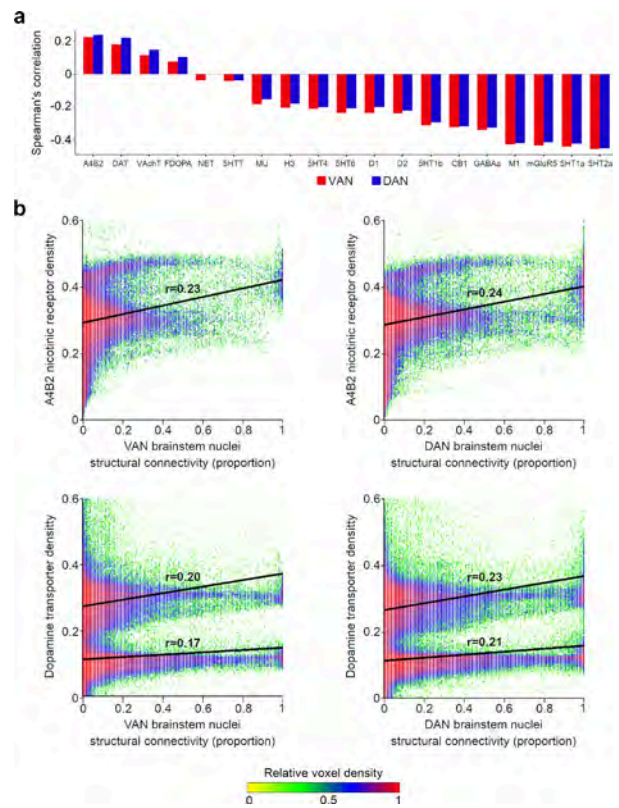
Figure 2: Correlation between the structural projections of the brainstem nuclei and the neurotransmitter systems. (a) Spearman's correlation with the maps of receptors and transporters; (b) Graphical representation of the highest correlations.

Conclusion: The convergence of functional, structural and neurochemical evidence provides a novel framework to comprehensively understand the neural basis of attention across different species and the pathophysiology of attention disorders that may arise from lesions of deep brain nuclei, such as subcortical neglect.

Disclosure: Nothing to disclose.

OPR-047

Brain network centrality abnormalities associated with multiple sclerosis disease course

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Background and aims: Voxel-wise degree centrality (DC) captures brain network topography from resting-state functional MRI (RS fMRI). We aimed at assessing DC abnormalities in multiple sclerosis (MS) patients and to evaluate their association with disease course.

Methods: 971 MS patients (47 clinically isolated syndrome [CIS]; 704 relapsing-remitting MS [RRMS]; 145 secondary progressive MS [SPMS] and 75 primary progressive MS [PPMS]) and 330 healthy controls (HCs) performed RS fMRI and clinical assessment. SPM12 age-, sex-, centre- and gray matter volume adjusted ANOVA and multivariable regressions were employed. All p were <0.05 family wise error corrected.

Results: MS patients showed reduced DC in the bilateral insula and somatosensory areas and increased DC in the bilateral precuneus and middle occipital gyri vs HCs. These DC abnormalities were mostly observed in RRMS and SPMS. We reported on increased DC in frontal and temporal regions in RRMS vs CIS, which became more widespread in PPMS vs CIS and also involved the precunei and the hippocampus in SPMS vs RRMS patients. Cognitively impaired patients showed reduced DC in somatosensory areas and increased DC in the default mode network (DMN) vs both HCs and cognitively preserved patients. Finally, in MS, more severe disability correlated with increased DC in the right precuneus.

Conclusion: MS patients showed progressive DC reduction in the salience and primary sensory networks and a DC increase in the DMN over the disease course mirroring disability accrual. MS pathology may produce a sensorimotor network collapse, with a possible attempt of the DMN to counteract for this damage.

Disclosure: Antonio Carotenuto was supported by a MAGNIMS/ECTRIMS research fellowship.

Headache

OPR-048

Resting state fMRI to assess the Pain Connectome integrity during nitroglycerin-induced migraine attacks

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Background and aims: Resting state functional MRI (rs-fMRI) has been widely used to study the brain functional connectivity (FC) changes occurring in migraine, to better understand the underlying cyclical mechanisms. In this pilot study, we focused on the pain connectome (PC) and we used rs-fMRI to address its functional integrity during a nitroglycerin-induced migraine-like attack.

Methods: Ten episodic migraineurs (EM, 4 female, 29.4 yo, 4 MMD) underwent 3T MRI examination consisting in four rs-fMRI repetitions during the subsequent phases of a nitroglycerin-induced migraine attack (baseline, prodrome, full-blown attack, recovery, Fig.1). Nine healthy controls (HC, 3 female, 26.7 yo) were enrolled for reference. Subjects' scans were processed to identify the PC (Fig. 2). A non-parametric permutation test was run to detect significant FC changes inside PC between EM and HC subjects in the different attack phases.
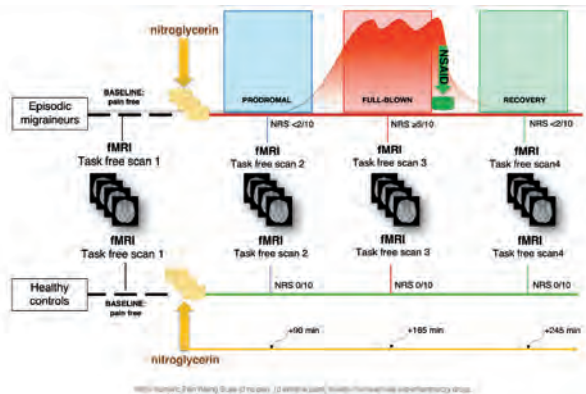
All subject underwent four rs-fMRI scans temporally-matched with a nitroglycerin-induced migraine attack: pain-free baseline, prodromal, full-blown attack, recovery. None of the HCs developed a migraine attack following the nitroglycerin challenge.
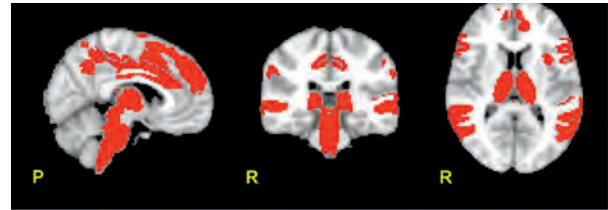
Brain areas of the pain connectome (PC) used for the present study. The PC mainly includes: inferior, middle and superior Frontal gyri, bilateral insula, inferior, middle and superior Temporal gyri, precuneus, bilateral thalami, pons and posterior cerebel.

Results: At baseline EM subjects showed a significantly reduced FC within PC in right temporal lobe and superior frontal gyrus when compared to HCs. This difference was progressively lost during the full-blown phase and the recovery. During the full-blown phase, EM subjects showed increased FC in prefrontal cortex and cerebellar crux of the PC, which persisted over the recovery (Fig. 3).
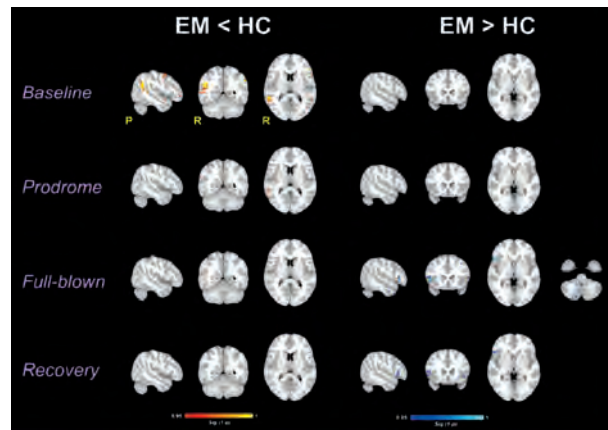
Altered areas of FC within the pain connectome in EM subjects compared to HCs. On the left: in red-yellow, areas of reduced FC in EM vs HC (EM < HC). On the right: in blue-light blue, areas of increased FC in EM (EM > HC).

Conclusion: The findings observed suggest a baseline alteration in descending modulation pain processing in migraine. Migraine-like pain induction caused a profound PC alteration, which persisted over recovery. Our findings also point to the involvement of the cerebellum - a multiple effector system integrator and a ruler of pain perception modulation - possibly in the resolution of pain.

Disclosure: RDI has received speaker honoraria for oral presentations from Eli-Lilly. CT has received fees for advisory boards or scientific lecturing from Allergan/AbbVie, Eli Lilly, Lundbeck, Novartis, and TEVA; and institutional payments for clinical trials from Allergan/AbbVie, Eli Lilly, Novartis Lundbeck, and TEVA. SG received honoraria for the participation in advisory board or for oral presentation from: Eli-Lilly and Novartis. MA SG received honoraria for the participation in advisory board or for oral presentation from: Eli-Lilly and Teva. All other Authors have no conflicts of interest to declare.

OPR-049

CGRP plasma levels in migraine patients before and after CGRP monoclonal antibodies therapy

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Background and aims: Monoclonal antibodies against calcitonin gene-related peptide (CGRP) or its receptor are the first targeted preventive migraine treatment. Erenumab - one of these medications - is well studied in clinical trials; however, the data on its use in real-world practice are still insufficient. To date, there is no knowledge of whether it has any effect on plasma CGRP levels.

Methods: We included 58 patients (50 women, average age 44,6±11,4) with migraine on the preventive therapy with CGRP monoclonal antibody erenumab. We evaluated previous prophylactic medications, headache days per month, adverse events. To assess CGRP levels, we obtained blood samples from the antecubital vein outside a migraine attack before and after 6 months of therapy. CGRP levels were measured by enzyme-linked immunosorbent assay (ELISA).

Results: 49 patients had chronic migraine, 15 patients had resistant migraine and 2 patients – refractory migraine. During the study, two patients dropped out due to adverse events (constipation). 42 patients continued taking erenumab 70 mg for at least six months. The average number of headache days per month before treatment was 21.6, decreasing to 6.8 after therapy. In the preliminary analysis, we assessed plasma samples from 18 patients. Before treatment, the mean plasma CGRP level was 23.1±26.5 pg/ml and 59.1±29.6 pg/ml after treatment. Thus, plasma CGRP level in peripheral blood after 6 months of therapy with erenumab increased on average more than twice the baseline level.

Conclusion: CGRP levels increase significantly after the therapy. Further studies with more participants are needed to confirm these data.

Disclosure: Nothing to disclose.

OPR-050

Late response to anti-CGRP (calcitonin gene-related peptide) monoclonal antibodies: implication for clinical practice

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Background and aims: Monoclonal antibodies (mAbs) targeting the Calcitonin Gene-Related Peptide (CGRP) are characterized by an early onset of efficacy, but late response (>12 weeks) may occur in some patients. Aims: To assess the prevalence of late responders (≥50% response after >12 weeks) to antiCGRP mAbs in patients affected by high-frequency episodic (HFEM: 8-14 days/month) or chronic migraine (CM).

Methods: In this multicenter (n=16), cohort, real life study, we evaluated the ≥50% response rate in all consecutive patients affected HFEM or CM treated with erenumab, galcanezumab or fremanezumab for ≥12 months from 20/12/2018 to 01/12/2021. Primary endpoint was the proportion of late-responders (≥50% response >12 weeks); the secondary endpoint was the estimation of median week of response in these patients.

Results: 912 migraine patients (HFEM/CM: 222/690) were treated with mAbs (erenumab: 789 pts; fremanezumab: 65 pts; galcanezumab: 58 pts) for at least 12 months. Overall, 352 patients (38.6%) were non-responders at week 12 (erenumab: 344, 43.6%; fremanezumab: 14, 21.5%; galcanezumab: 14, 24.1%). Among non-responders, 128 patients (36.4%) were indeed late responders (erenumab: 114, 33.1%; fremanezumab: 5, 35.7%); galcanezumab: 9, 64.2%), showing on average a $\geq$50% response after median 20 (IQR 4–24) weeks of treatment (erenumab median weeks: 20, IQR 16–24; fremanezumab: 16, IQR 16–24; galcanezumab: 20, IQR 16–21).

Conclusion: Late response to antiCGRP mAbs may occur in more than one third of migraine patients considered not responders at 12 weeks. Our findings suggest extending the efficacy treatment evaluation for antiCGRP mAbs to 6 months, also in terms of reimbursement policies.

Disclosure: Nothing to disclose.

OPR-051

Functional connectivity changes in complex migraine aura: beyond the visual network

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Background and aims: Although the majority of migraine with aura (MwA) patients experiences simple visual aura, a discrete percentage also reports somatosensory, dysphasic or motor symptoms (the so-called complex auras). The wide aura clinical spectrum led to investigate whether the heterogeneity of aura phenomenon could be subtended by different neural correlates, suggesting an increased visual cortical excitability in complex MwA. We aimed to explore whether complex MwA patients are characterized by more pronounced connectivity changes of the visual network and whether functional abnormalities may extend beyond the visual network encompassing also the sensorimotor network in complex MwA patients when compared to simple visual MwA patients.

Methods: By using a resting state-fMRI approach, we compared the resting state functional connectivity (RS-Fc) of both visual and sensorimotor networks in 20 complex MwA patients in comparison with 20 simple visual MwA patients and 20 migraine without aura (MwoA) patients.

Results: Complex MwA patients showed a significantly higher RS-Fc of the left lingual gyrus, within the visual network, and of the right anterior insula, within the sensorimotor network, when compared to both simple visual MwA and MwoA patients (p<0.001). The abnormal right anterior insula RS-Fc was able to discriminate complex MwA patients from simple aura MwA patients as demonstrated by logistic regression analysis (AUC: 0.83).
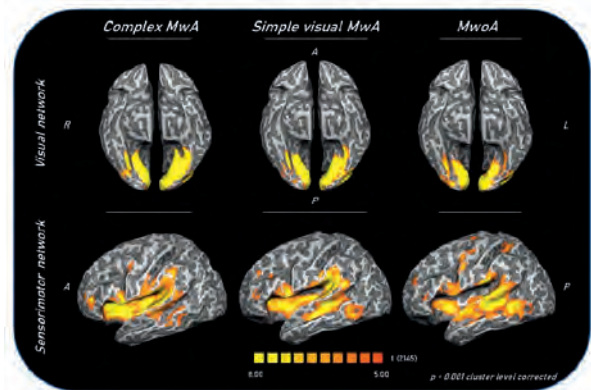
Group-level (main effects) functional connectivity of visual and sensorimotor networks in complex MwA, simple visual MwA and MwoA patients
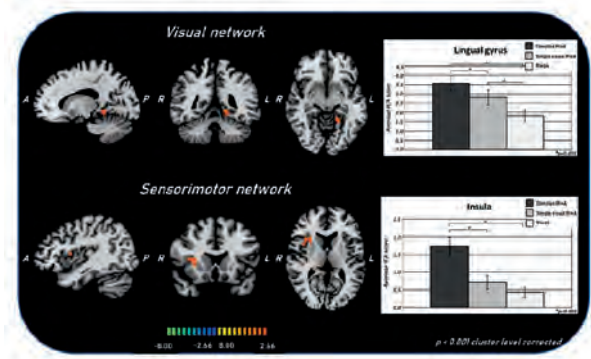
T-map of statistically significant differences within the visual and sensorimotor networks between complex MwA and simple visual MwA

Conclusion: Our findings suggest that higher extrastriate RS-Fc might promote the CSD onset representing the neural correlate of simple visual aura that can propagate to sensorimotor regions, if an increased insula RS-Fc coexists, leading to complex aura phenotypes.

Disclosure: Nothing to disclose.

Motor neurone diseases

OPR-052

Electrodiagnostic Findings in Facial Onset Sensory Motor Neuronopathy (FOSMN)

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[2] Brain and Nerve Research Centre, Concord Clinical School, Sydney Medical School, The University of Sydney, Sydney, Australia, [3] Department of Neurophysiology, Royal Victoria Infirmary, Newcastle upon Tyne, United Kingdom,
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Background and aims: FOSMN is a rare clinical syndrome initially described in a seminal case series of five patients who presented with facial sensory deficits, followed by motor deficits, evolving rostro-caudally. Clinical, genetic and neuropathological data strongly suggest that FOSMN is a rare phenotype of amyotrophic lateral sclerosis (ALS). Herein, we review the published electrodiagnostic data for FOSMN and report detailed electrophysiological data from two cohorts (n=10) with this syndrome, proposing a specific approach to electrodiagnostic testing in patients who present with facial sensory symptoms.

Methods: Blink Reflexes, Electromyography, Nerve Conduction Studies, Somatosensory Evoked Potentials, Threshold Tracking Transcranial Magnetic Stimulation.

Results: Findings on standard electrophysiological assessment were in broad agreement with those published: blink reflexes were abnormal in all but one patient (Figure 1); SNAPs were reduced but CMAPs preserved; mixed acute and chronic neurogenic change was identified on needle EMG in bulbar and cervicothoracic muscles in approximately 50% of patients. In addition, upper limb SEP central conduction times were increased (n=4) and progressed on repeat testing (n=3) (Figure 2), and upper motor neuron dysfunction was revealed by several measures [ipsilateral MEPs (n=1); reduced short interval intra-cortical inhibition on threshold-tracking TMS (n=2); absent beta-band intermuscular coherence (n=3)].
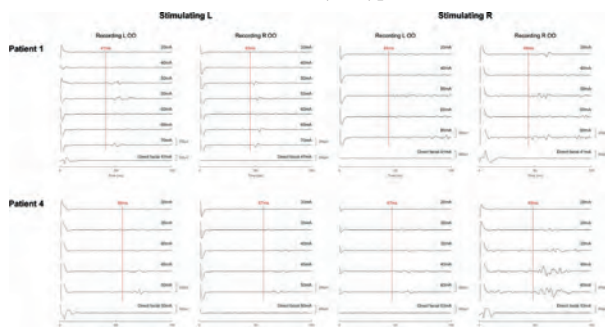
Figure 1. Blink reflexes. Illustrative examples of blink reflex responses acquired from patients 1 and 4. Responses were recorded from left (L) and right (R) orbicularis oculi (OO) following stimulation of the supraorbital nerve at a range of intensities.
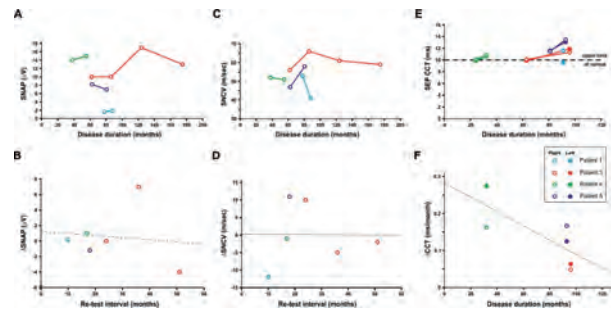
Figure 2. Changes in SNAP amplitudes, SNCVs and upper limb SEPs. In a subset of FOSMN patients (n=4) nerve conduction studies were repeated more than once. Only median digit III SNAP/SNCV data are presented (NB. There was no evidence of carpal tunnel syndrome.
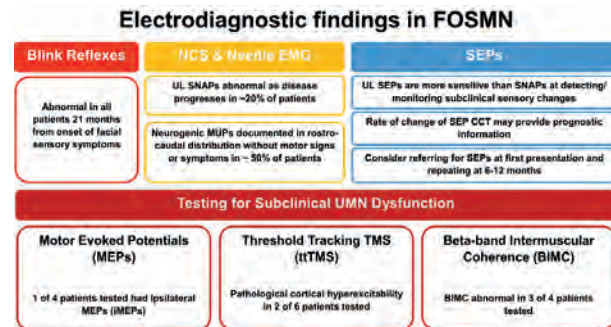
Figure 3. Summary of electrodiagnostic findings in FOSMN. The neurophysiological examination is useful in identifying pathognomonic signs of FOSMN such as abnormal blink reflexes, in addition to identifying subclinical lower and upper motor neurons.

Conclusion: Electrodiagnostic investigation of FOSMN should include blink reflex testing, SEPs and tests of upper motor neuron function (Figure 3). The combination of progressive lower motor neuron disease and upper motor neuron disease on neurophysiological investigation provides further support for the contention that FOSMN is a rare phenotypic variant of ALS.

Disclosure: Nothing to disclose.

OPR-053

Directionality of disease spread is associated with clinical phenotype in amyotrophic lateral sclerosis

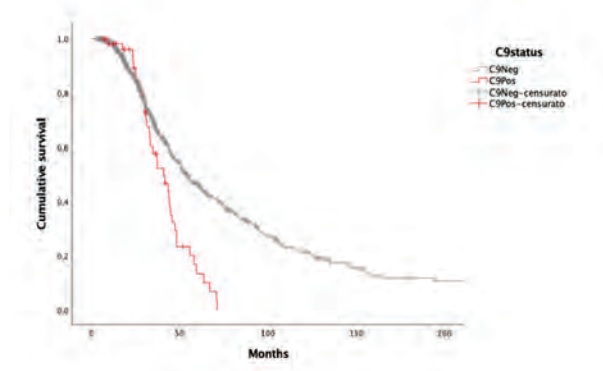A. Maranzano [1], E. Colombo [1], B. Poletti [1], S. Torre [1], F. Verde [2], C. Morelli [1], V. Silani [2], N. Ticozzi [2]
[1] Department of Neurology, Istituto Auxologico Italiano IRCCS, Milan, Italy, [2] Department of Pathophysiology and Transplantation, "Dino Ferrari" Center, Università degli Studi di Milano, Milan, Italy

Background and aims: increasing evidence shows that disease spread in amyotrophic lateral sclerosis (ALS) follows a preferential pattern rather than a random model with more frequent involvement of contiguous regions from the site of symptoms onset. Aim of our study is to assess if specific pattern of disease progression may influence the clinical phenotype.

Methods: A single center retrospective cohort of 854 Italian ALS patients has been evaluated to assess correlations between directionality of the disease process after symptoms onset and motor/neuropsychological phenotype. Order of affected regions was established from medical history. Penn Upper Motor Neuron Score (PUMNS) and MRC scale for muscle strenght were used to assess motor phenotype. The Italian version of the Edinburgh Cognitive and Behavioural ALS Screen (ECAS) was administered to evaluate cognitive and behavioural profiles.

Results: The most frequent directionality of initial spread included adjacent horizontal regions (41%) and it was observed in patients with lower MRC (p=0.049) while vertical diffusion (17%) was associated with higher PUMNS (p<0.0001) and with reduced survival (p=0.001). Noncontiguous disease spread was more frequently observed in older individuals with the same motor profile of patients with vertical diffusion and with impairment of ALS specific and non-specific domains at ECAS.
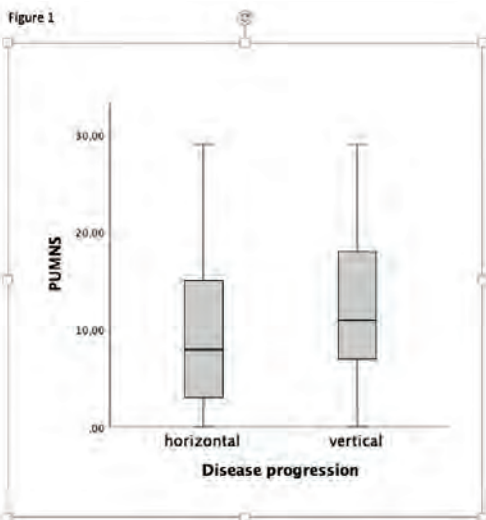
Distribution of UMN involvement using the Penn Upper Motor Neuron Score (PUMNS) in ALS patients with horizontal and vertical disease spread. Kruskal-Wallis test for independent samples.
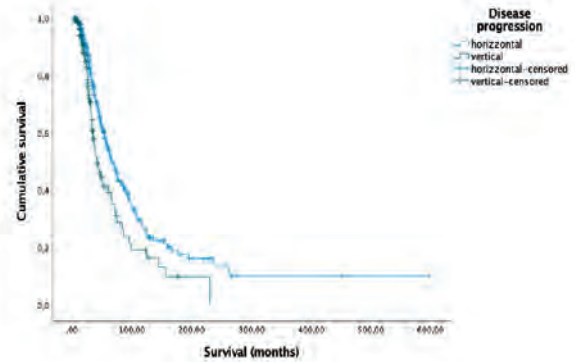
Kaplan-Meyer plots of survival probabilities: patients with horizontal disease progression (green line) had significantly prolonged survival when compared to patients with vertical spread (light blue line) (Log Rank: $\chi2$=10,438; p= 0,001)
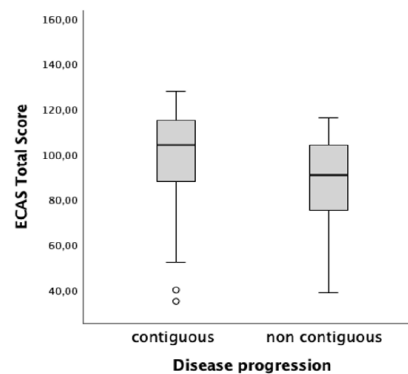
Distribution of ECAS Total score in ALS patients with contiguous and noncontiguous disease spread. Kruskal-Wallis test for independent samples.

Conclusion: our study supports the hypothesis of a preferential pattern of disease spread according to prevalent involvement of upper or lower motor neuron. Furthermore, our results indicate that disease extension from site of onset may influence the clinical phenotype.

Disclosure: Nothing to disclose.

OPR-054

Motor, cognitive and behavioral features of C9ORF72-associated amyotrophic lateral sclerosis

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Background and aims: In several reports, ALS individuals carrying the hexanucleotide repeat expansion (HRE) in the c9orf72 gene (C9Pos) have been described as presenting distinct features compared to the general population (C9Neg). Here we aim to identify the phenotypic traits more closely associated with the HRE and analyze the role of the repeat length as a modifier factor.

Methods: We studied a cohort of 960 ALS patients. Motor phenotype was determined using the MRC scale, the lower motor neuron score (LMNS) and the Penn upper motor neuron score (PUMNS). Neuropsychological profile was studied using the Italian version of the Edinburgh Cognitive and Behavioral ALS Screen (ECAS), the Frontal Behavioral Inventory (FBI), the Beck Depression Inventory-II (BDI-II) and the State-Trait Anxiety Inventory (STAI). A two-step PCR protocol and a Southern blotting were performed to determine respectively the presence and the size of HRE.

Results: HRE was detected in 55/960 (5.7%) patients. C9pos patients showed a younger onset, higher odds of bulbar onset, increased burden of UMN signs and, reduced survival, and higher frequency of concurrent dementia. Concerning cognitive phenotype, we found an inverse correlation between the HRE length and the performance at ECAS ALS-specific tasks (p=0.031). C9pos patients also showed higher burden of behavioral disinhibition (p=1.6x10-4) and lower degrees of depression (p=0.015) and anxiety (p=0.008) when compared to C9Neg cases.

Simple dispersion with adjustment curve of hexanucleotide repeat expansion (HRE) length for for Edinburgh Cognitive and Behavioural ALS Screen (ECAS) ALS-specific
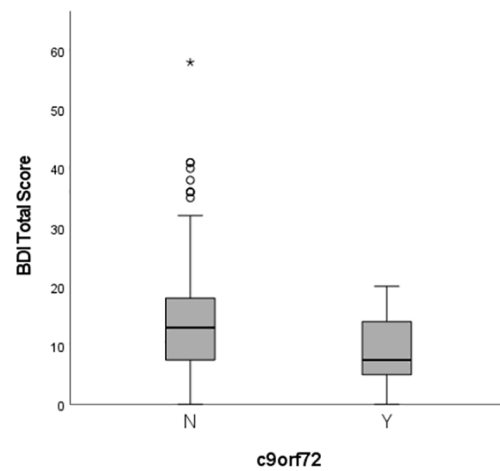
Distribution of BDI -II total scores in C9Pos and C9Neg patients. Kruskal-Wallis for independent samples.

Conclusion: Our study provides an extensive characterization of motor, cognitive and behavioral features of c9orf72-associated ALS. Furthermore, our results indicate that the c9orf72 HRE size may represent a modifier of cognitive phenotype along the ALS-FTD spectrum.

Disclosure: Nothing to disclose.

Kaplan-Meier plots of survival probabilities: the patients carrying the pathogenic C9orf72 repeat expansion (C9Pos, red line) display shorter survival time than the patients without genetic mutations (C9Neg, grey line); +: censored cases.

OPR-055

The heterogeneity of respiratory failure occurrence in Amyotrophic Lateral Sclerosis: a two-step cluster analysis.

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Background and aims: Recognizing early respiratory impairment in Amyotrophic Lateral Sclerosis (ALS) can be demanding. We aimed at identifying ALS patients' clusters, based on clinical features, pulmonary function tests, and arterial blood gas analysis (ABG) parameters, to improve patients' prognostic stratification and respiratory management.

Methods: We included 488 ALS patients. A two-step cluster analysis was performed by using the following model variables: respiratory symptoms derived from ALSFRS-r scale, disease progression rate (ΔALSFRS), severe bulbar involvement, FVC, pCO_2 and HCO_3^- arterial blood levels. We compared the survival analysing the differences among clusters. Regression analysis was used to identify the variables that better predict the occurrence of respiratory symptoms.

Results: Five clusters were identified: Cluster 1, patients without respiratory failure ("normal" patients, NP); Cluster 2, patients with nocturnal hypoventilation (NH); Cluster 3, fast progressors (FP); Cluster 4, patients with severe bulbar impairment (SB); Cluster 5, patients with respiratory failure (RF). NH, FP, SB and RF clusters showed a shorter survival when compared to NP (21.6 months, 95% CI 19.7–23.4, p<0.001), without any significant difference among them (p>0.05 for all comparisons). After NIV adaptation FP had the longest prolongation of survival (about 10 months, p<0.001), while SB patients did not show any benefit (p=0.675). Respiratory symptoms can be predicted by a combination of variables (FVC%, pCO_2, ALSFRS-r score, ΔALSFRS), showing only a moderate correlation to them (R=0.490, p<0.001).
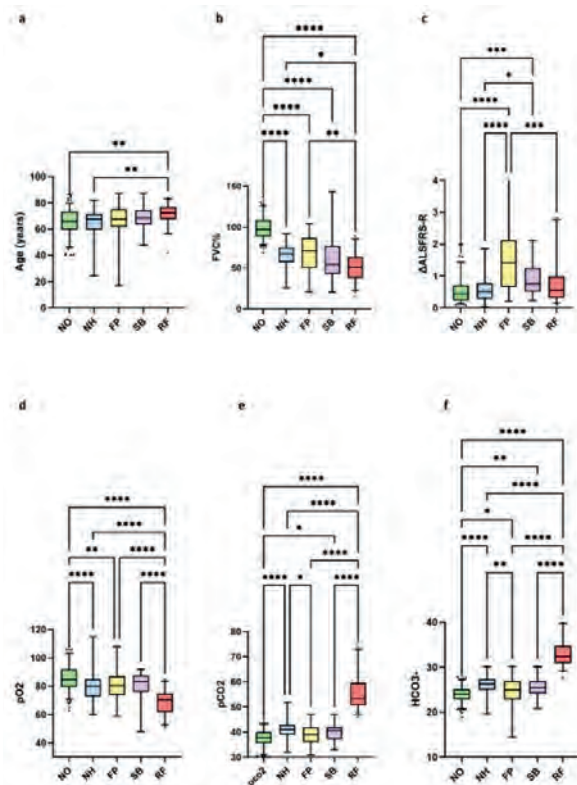
Figure 1. Box-plots: significant differences among clusters.
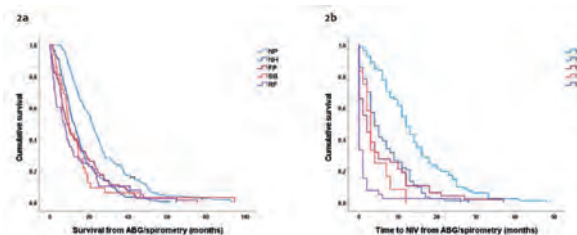
Figure 2. Kaplan-Meier curves. Fig. 2a: Survival from ABG/spirometry in all clusters. Fig. 2b: time from ABG/PFT to NIV initiation in all clusters.
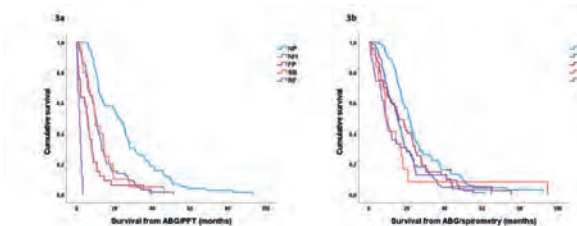
Figure 3. Kaplan-Meier curves: survival from ABG/spirometry in all clusters depending on NIV adaptation (Fig 3a patients who did not undergo NIV; Fig 3b patients who underwent NIV).

Conclusion: ALS patients show different pulmonary dysfunction presentations, independently from respiratory symptoms, that can be grouped in homogeneous clusters, to predict prognosis and plan respiratory management properly.

OPR-056

Phenotype analysis of FUS mutations in ALS

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[1] ALS Centre, "Rita Levi Montalcini" Department of Neuroscience, University of Turin, Italy, [2] Neuromuscular Diseases Research Section, Laboratory of Neurogenetics, National Institute on Aging, NIH, Bethesda, MD, United States of America

Background and aims: Mutations in Fused in Sarcoma (FUS) are among the most common genetic causes of ALS worldwide. They are supposedly characterized by a homogeneous pure motor phenotype with early-onset and short disease duration. However, a few FUS-mutated cases with a very late disease onset and slow progression have been reported. Therefore, here we analyzed genotype-phenotype correlations and identify the prognostic factors in FUS-ALS cases.

Methods: We identified and cross-sectionally analyzed 22 FUS-ALS patient histories from a single-center cohort of 2615 genetically tested patients and reviewed 289 previously published FUS-ALS cases.

Results: Survival of FUS-ALS is age-dependent: in our cohort only, early-onset FUS ALS patients had a rapid disease progression and short survival (p=0.000003). Meta-analysis of literature data confirmed this trend (p=0.00003). This survival pattern is not observed in other ALS-related genes in our series. We clustered FUS-ALS patients in three phenotypes: (a) axial ALS, with upper cervical and dropped-head onset in mid-to-late adulthood; (b) benign ALS, usually with a late-onset and slow disease progression, (c) juvenile ALS, often with bulbar onset and preceded by learning disability or mild mental retardation. Those phenotypes arise from different mutations.
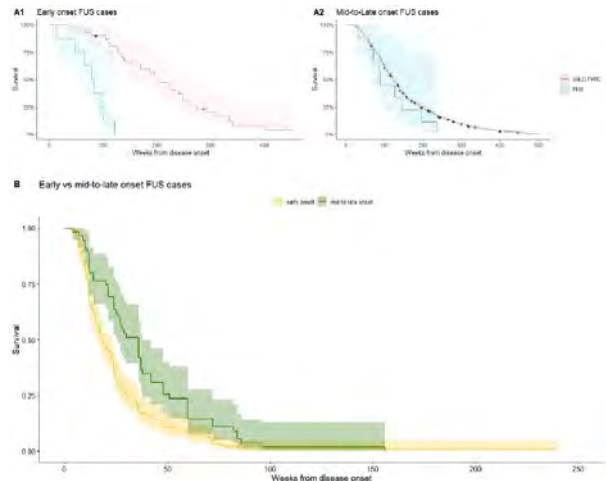
(A) Survival analysis of early onset FUS carriers (age at onset < 46 ys, A1) and mid-to-late onset FUS (> 46 ys, A2) vs non-mutated ALS cases. (B) Survival analysis of early onset FUS carriers (age at onset < 46 ys) vs mid-to-late onset FUS (> 46 ys)

Conclusion: We observed specific genotype-phenotype correlations of FUS-ALS and identified age at onset as the most critical prognostic factor. Our results demonstrated that FUS mutations underlie a specific subtype of ALS and enable a careful stratification of newly diagnosed FUS-ALS cases in terms of clinical course and potential therapeutic windows. This will be crucial in the light of incoming gene-specific therapy.
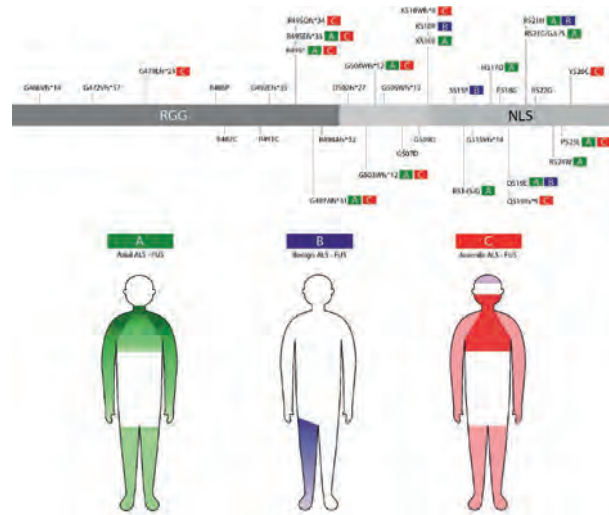
Patterns of motor and non-motor involvement in FUS-ALS and genotype-phenotype correlation of FUS mutations

Disclosure: All authors report no disclosures relevant to the study.

Sunday, June 26, 2022
Movement disorders 1

OPR-057

3D visualization of Lewy Bodies: Insight into Parkinsonian's subtantia nigra using Synchrotron Phase-Contrast Imaging

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Background and aims: Parkinson disease (PD) is histologically characterized by alpha-synuclein aggregates forming the Lewy Bodies (LB), mostly found in the substantia nigra (SN). Conventional imaging techniques such as MRI or TDM lack of spatial resolution. Histology and electronic microscopy do not allow 3D analysis, require staining and are limited in the size of sample (µm). Synchrotron Phase contrast X-ray imaging (S-PCI) is an emerging modality that exploits the differing refractive indices of materials to create additional contrast, especially in soft tissues. The aim of this study was to assess the ability of multiscale S-PCI to visualize the morphologic abnormalities present in human SN affected by PD.

Methods: Five samples of SN from four deceased-donors affected by PD and one age-matched control were imaged at the European Synchrotron Radiation Facility (ESRF, Grenoble, France). The whole SN was acquired at a resolution of 3 and 0.6 microns. Then, targeted regions were imaged at a resolution of 50 nanometers. No contrast agent was used in this study.

Results: Targeting of neuromelanin neurons was easy, and few artefacts were observed. Neuromelanin neurons, were individualizable in the SN (Fig. 1). Some Parkinsonian neuromelanin neurons contained dense spheric structures repelling the neuromelanine granulations, recognized as LB (Fig. 2 and Fig. 3). Pale bodies were identified too.
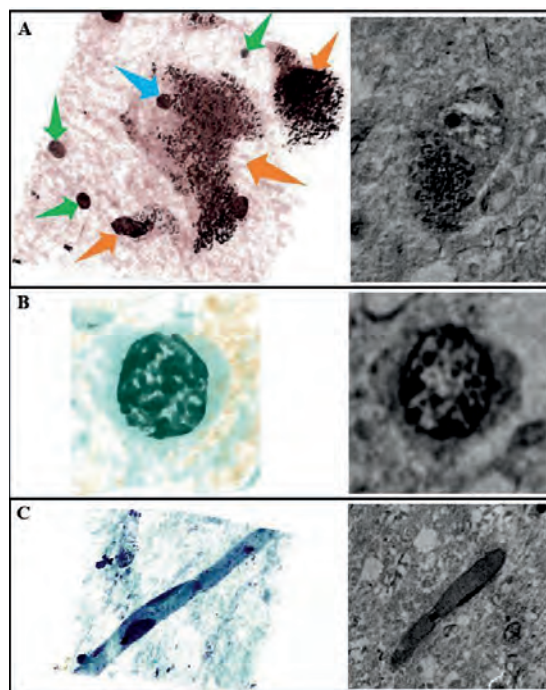
Figure 1. SN components at 50nm resolution: A. Neuromelanin neurons (purple = Neuromelanin; Green = Glial cells; Blue= nucleus; Orange = neurons) ; B. Glial cell ; C. Blood vessel.
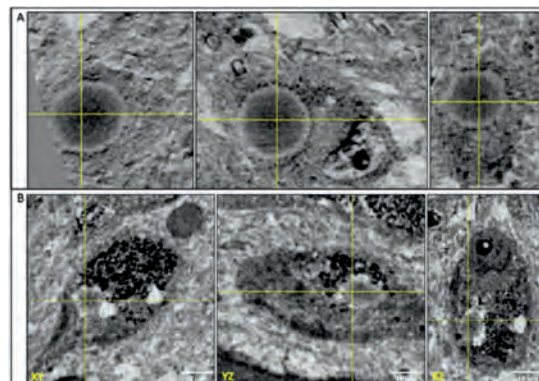
Figure 2. Lewy Body in SN in of two different donnors (A and B) at 50nm resolution. Yellow crosses indicate the position of the LB in the different views and planes (XY, YZ, XZ)
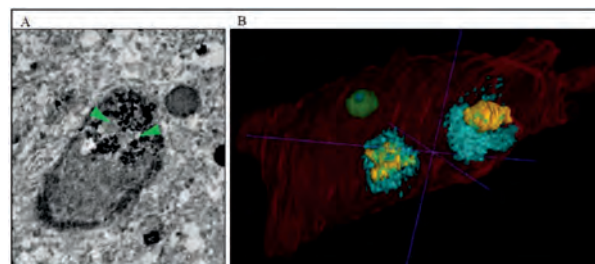
Figure 3. (A) 2D representation of a cell containing two misshapen LB at 50nm (Green arrows = LB). (B) matching 3D representation (Red = Cell membrane; Green = nucleolus; Yellow = LB; blue = Neuromelanin)

Conclusion: In this study we proved non-inferiority of multiscale S-PCI for visualizing LB in PD compared with conventional histological technique, and the capacity to study them in 3D for the first time. A deeper understanding of LB 3D structure with the S-PCI technology could allow new therapeutic targets.

Disclosure: The authors declare that they have no relevant or material financial interests that relate to the research described in this manuscript.

OPR-058

Neuroimaging evidence for a body schema disorder in Pisa syndrome of Parkinson's disease

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Background and aims: The pathogenesis of Pisa syndrome (PS) in Parkinson's disease (PD) is still uncertain and both 'central' and 'peripheral' mechanisms have been claimed. We explored nigrostriatal function and grey matter metabolism to unveil possible central dysregulation.

Methods: We retrospectively selected 34 mostly de novo PD patients (18 females, mean age:69+/-8) undergoing Dopamine Transporter (DaT)-SPECT (30 pts) and/or FDG-PET (22 pts) and who developed PS 56+/-53 months later. We divided both DaT (right 14 pts, left 16 pts) and FDG-PET (right 9 pts, left 13 pts) groups according to body leaning side. 'Right' and 'left' subgroups were compared each other with both techniques. Then, 30 DaT-SPECT PS patients were compared with 60 de novo PD patients without PS, and 22 FDG-PET PS patients were compared with 42 healthy controls. 'Right' and 'left' subgroups were also compared with controls in both modalities.

Results: There were no significant DaT-SPECT or FDG-PET differences between 'right' and 'left' subgroups, and in DaT-SPECT between PS patients and PD controls. Conversely, PS patients as a whole (Fig. 1) but also the 'left' and the 'right' subgroups showed significant relative hypometabolism in a right hemispheric cluster (Brodmann area 39).
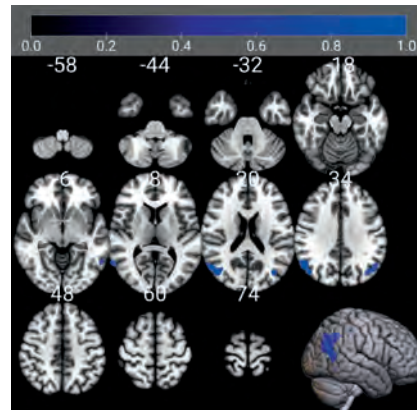
Figure 1 shows clusters of relative hypometabolism (FWE-corrected p

Conclusion: We showed that right angular gyrus metabolism is impaired since the time of diagnosis in PD patients who will later develop PS, irrespective of body leaning side. This finding suggests that a disorder of body schema representation is involved in the PS pathogenesis.

Disclosure: The authors do not have disclosures related to this manuscript.

OPR-059

Intestinal histomorphological and molecular alterations in patients with Parkinson's disease: results from a pilot study

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Background and aims: Parkinson's disease (PD) is characterized by alpha-synuclein accumulation, changes in gut microbiota composition, impairment of intestinal epithelial barrier (IEB) and enteric neurogenic/immune/inflammatory responses, which could all play a role in the pathogenesis of the disease. The aim of the study was to investigate in PD patients 1) changes of inflammatory markers in plasma and stool, 2) morpho-functional alterations of colonic mucosal barrier and 3) changes in faecal microbiota composition.

Methods: 19 PD patients and 19 healthy controls were enrolled. Plasma lipopolysaccharide binding protein (LBP; marker of altered intestinal permeability) and interleukin-1 beta (IL-1beta), as well as stool IL-1beta and tumour necrosis factor (TNF) were assessed. Gut microbiota analysis was also performed. Colonic biopsies collected during colonoscopy were processed for the evaluation of epithelial mucins, collagen fibres, Claudin-1 and S-100 positive glial cells.

Results: Compared with controls, PD patients showed a significant increase in plasma LBP, faecal TNF and IL-1beta levels. Histological analysis of tissues from PD patients identified elevated expression of acidic mucins, collagen fibres and S-100 positive glial cells, and a decrease in neutral mucins and Claudin-1 expression, compared with controls. Faecal microbiota analysis revealed a significant difference in the alpha-diversity between PD patients and controls, whereas no differences were found in the beta-diversity.
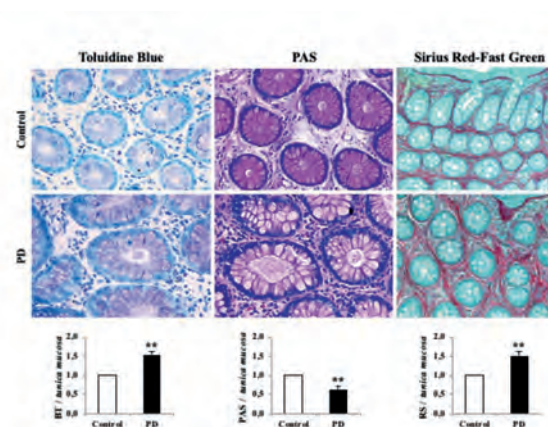
Representative photomicrographs of toluidine blue (BT)-stained acidic mucins, PAS-stained neutral mucins, Sirius Red (SR)-stained collagen fibres and Fast Green (FG)-stained non-collagen proteins in colonic mucosal biopsies from controls and PD patients.
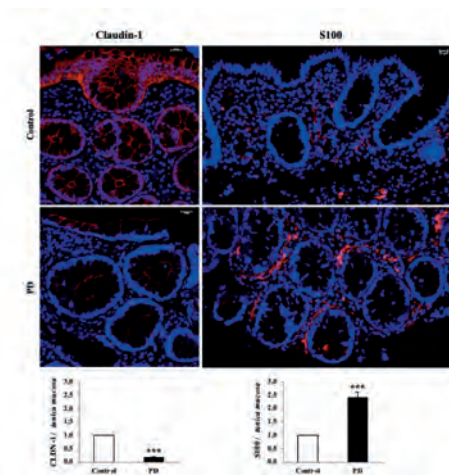
Representative photomicrographs of claudin-1 and S100 immunostaining in colonic mucosal biopsies from controls or PD patients. Original magnification 40× and 63×, respectively. Column graphs display the fold changes of the respective immunostaining ± SEM.
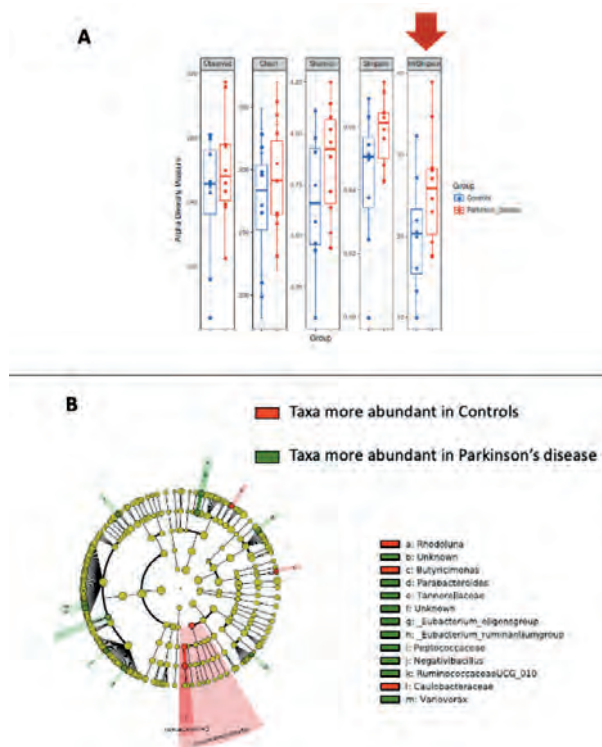
(A) Significant difference in the alpha-diversity in PD patients in comparison with control subjects; (B) Significant difference in Bacterial Taxa abundance between PD patients in comparison with control subjects.

Conclusion: PD patients exhibited increased permeability of the gut barrier and colonic mucosal barrier remodelling, associated with changes in gut microbiota composition. Further studies are needed to establish whether such alterations are relevant in PD pathogenesis or represent only a consequence of the disease.

Disclosure: The authors declare that there are no additional disclosures to report.

OPR-060

MRI and genetic correlates of apathy and impulsive-compulsive behavior in Parkinson's disease

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Background and aims: Many Parkinson's disease (PD) patients concomitantly suffer from impulsive-compulsive behavior (ICB) and apathy. We investigated whether ICB and apathy share similar neural underpinnings in form of functional connectivity and structural brain alterations and evaluated the influence of D2/D3 receptors status in a group of PD patients.

Methods: 54 PD patients underwent resting-state fMRI and T1-weighted MRI. They completed the QUIP-RS (ICB quantification) and the AES (Apathy Evaluation Scale). Taq1A (D2) and Ser9Gly nucleotide (D3) polymorphism were determined. We examined resting-state connectivity patterns and structural volume. SPM12 was used for voxel-wise correlation analyses (ICB, Apathy).

Results: ICB and Apathy were positively correlated (R=0.51, p<0.001). D3 polymorphism was associated with more ICB. An interaction analysis revealed that ICB severity was influenced by apathy and D3 receptor status (Figure 1). Apathy was associated with smaller anterior cingulate cortex volume (Figure 2A). When controlling for ICB, we found a negative correlation between Apathy and volume of the ventral striatum and putamen (p<0.001 uncorrected) (Figure 2B). The connectivity analysis with a seed in the left putamen led to a connectivity network similar to the salience network (Figure 3). In apathetic PD, connectivity between putamen and superior frontal gyrus was stronger than in non-apathetic (p<0.05 FWE-corrected).
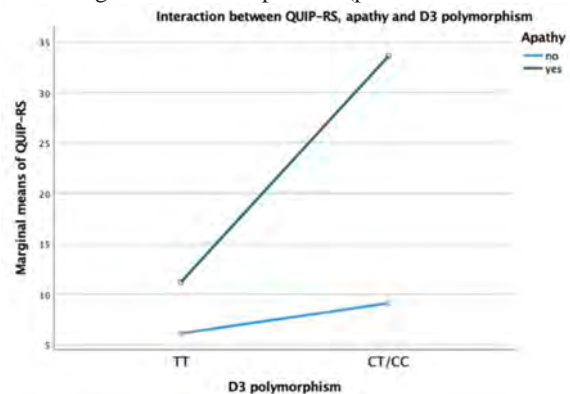
Figure 1: Univariate two-way ANOVA with bootstrap. D3, F=10.882, p<0.002. Apathy, F=14.770, p<0.001. D3*Apathy, F=6.365, p=0.015
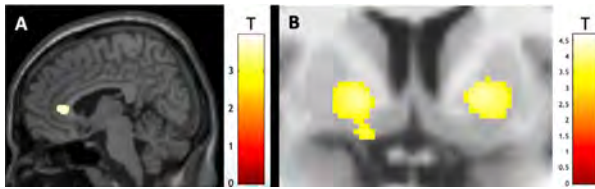
Figure 2: A Significant negative correlation between AES and volume of the anterior cingulate cortex. B Significant negative correlation between AES and volume of the striatum controlled for QUIP-RS. (Illustratory threshold p<0.001 uncorrected.)
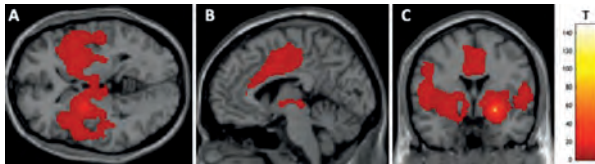
Figure 3: A (axial view), B (sagittal view), C (coronal view): Average functional connectivity map with seed in the left putamen. (Illustratory threshold: p<0.05 FWE-corrected.)

Conclusion: Apathy and ICB were strongly correlated, but underlying neural underpinnings were different, since apathy was associated with atrophy and connectivity changes in the salience network. Interestingly, there were no imaging changes associated with ICB. Together, apathy in combination with D3 status elevates the risk for ICB severity in PD.

Disclosure: Nothing to disclose.

OPR-061

Visual Sequencing Search Strategy in Parkinson's Disease

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Background and aims: Patients with Parkinson's disease (PD) have prominent visual and oculomotor dysfunctions. In early stages, disturbances in visual acuity, pupil reactivity, saccadic and pursuit eye movements, motion perception, peripheral visual fields and visual processing speeds are reported. It has been demonstrated that patients with Parkinson's disease have greater difficulty discriminating details of peripheral images and perceive these images less strongly than healthy volunteers.

Methods: To further investigate the pattern of visual exploration in PD patients, we examined the distribution of fixation during the execution of a high cognitive demanding task of visual sequential search (TOP-DOWN Search) in 46 PD patients compared to controls. In the Visual Sequential Search Test (VSST) the subjects are asked to connect by gaze a logical sequence of numbers and letters. Visual search can be quantified in terms of the analysis of the scan-path, which is a sequence of saccades and fixations.

Results: The distribution of fixation in PD patients was lower in the peripheral ROIs, being concentered mostly over central ROIs. Overall, these results might indicate the need for resampling the element's position because of a deficit in spatial map, working memory or attention or difficulties in encoding the sequential string of letters and numbers. Moreover, the profile of fixation distribution may indicate a neglected attraction to peripheral target or deficit in peripheral vision.

Conclusion: We detected a score of Visual Search Strategy (VSS) performance that was significantly lower in PD patients than controls, indicating a significant deficit of sequencing ability in PD patients.

Disclosure: All authors declare no conflict of interest.

OPR-062

Abstract withdrawn

Epilepsy 1

OPR-063

Analysing clinical text from electronic health records to diagnose anti-NMDAR encephalitis, a proof-of-concept study

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Background and aims: Anti-NMDAR encephalitis typically presents with psychiatric symptoms resembling a primary psychiatric disorder, which can lead to delays in diagnosis and treatment. We aim to investigae whether the clinical notes in electronic health records (EHR) could serve to discriminate between diseases.

Methods: We analysed all patients diagnosed with anti-NMDAR encephalitis (n=35) and compared it with other psychosis (n=70), from a large mental health provider from the NHS (UK). Text analysed comprised clinician-recalled quoted speech (QS) and the mental state examination (MSE). We used a bag of word representation, latent dirichlet allocation for topic modelling, and support vector machines -SVM-, multinomial naive bayes and logistic regression for binary classification. Performance was measured in the test set with accuracy and F1 scores by 5-fold cross-validation.

Results: We obtained two raw corpora of 5.898 or 275 instances (14% or 8% for encephalitis) in 105 or 44/105 patients for QS or MSE corpus respectively. Topic modelling found a different distribution in QS corpus (chi2 p-value=0.03); features like "paediatric", "bladder", "shakes" only appeared in encephalitis. The best accuracy, F1-encephalitis metrics were respectively 88%, 23% for QS corpus, and 95%, 44% for the MSE corpus, with a precision of 100% for encephalitis in MSE corpus using SVM.

Conclusion: Textual features in EHR could serve as diagnostic biomarkers in autoimmune encephalitis. Although a distinct psychopathological pattern is not evident, prediction of encephalitis with machine learning using the mental state examination corpus can reach a precision (or positive predictive value) of 100%.

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OPR-064

Abnormal sensorimotor cortex and thalamo-cortical networks in FAME2: pathophysiology and diagnostic implications

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Background and aims: To systematically study with an extensive electrophysiological battery the sensory-motor hyperexcitability in Familial Adult Myoclonic Epilepsy type2 (FAME2) patients and to establish reliable neurophysiological biomarkers for the diagnosis.

Methods: We evaluated the facilitatory and inhibitory circuits within the primary motor cortex (M1) using single and paired-pulse transcranial magnetic stimulation (TMS) paradigms. We also probed the excitability of the somatosensory (S1) cortex as well as the thalamo-S1 connection by using ad hoc somatosensory evoked potential (SEP) protocols in a cohort of genetically confirmed Italian FAME2 patients, a group of patients with Juvenile Myoclonic Epilepsy (JME) and a subset of healthy control subjects. The sensitivity, and specificity of TMS and SEP metrics were derived from receiver operating curve analysis.
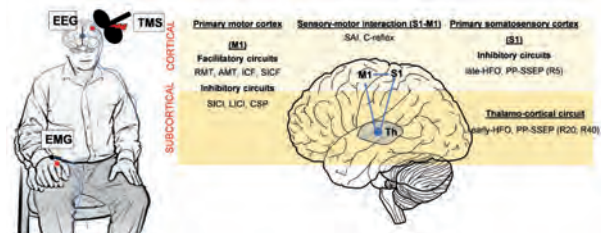
Overview of Neurophysiological protocols to evaluate cortical and subcortical circuits. During the experiment patients and healthy controls underwent an extensive neurophysiological battery aimed to evaluate the excitability of cortical circuits.

Results: 26 FAME2 subjects, 17 JME patients and 22 healthy controls (HC), were evaluated. Overall, FAME2 patients displayed increased facilitation and decreased inhibition within the sensory-motor cortex compared with JME patients (all p<0.05) and HC (all p<0.05). SEP protocols also displayed a significant reduction of early high-frequency oscillations and less inhibition at paired-pulse protocol, suggesting a concomitant failure of thalamo-S1 circuits. Disease duration, age and myoclonus severity, and surface EMG did not correlate with sensory-motor hyperexcitability (all p>0.05). Finally, FAME2 condition was reliably diagnosed using TMS, demonstrating its superiority as a diagnostic factor compared to SEP measures.
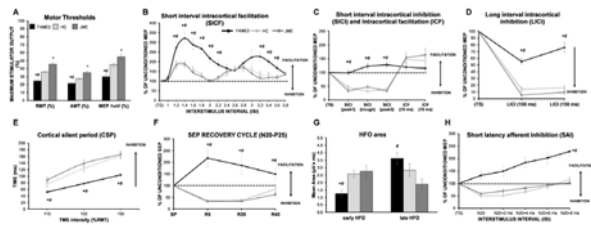
Assessment of facilitatory and inhibitory circuits in the primary motor cortex (M1), in the somatosensory cortex (S1) and evaluation of thalamo-cortical connectivity. Group average of stimulation intensity to produce motor thresholds (RMT, AMT).
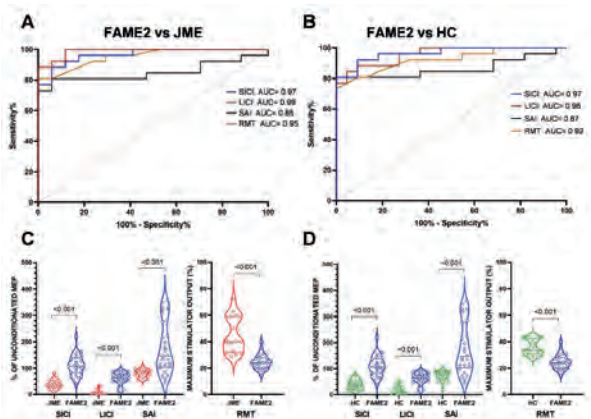
Diagnostic accuracy of TMS measures Receiver operating characteristic (ROC) and area under the curve (AUC) values for TMS parameters, namely RMT, SICI, LICI and SAI in differentiating patients with FAME2 from those with JME (A) and HC (B).

Conclusion: Sensory-motor cortical and thalamo-cortical circuits are involved in the pathophysiology of FAME2. In addition, TMS displays an overall higher accuracy than SEP to reliably distinguish FAME2 from JME and HC.
Disclosure: Nothing to disclose.

OPR-065

GAD-antibody associated temporal lobe epilepsy: T cells kill neurons, plasma cells and antibodies are bystanders

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Background and aims: GAD-antibody associated temporal lobe epilepsy is a chronic condition. Response to immunotherapy is mostly unsatisfying. A better understanding of the pathophysiology may help improving the timing of immunotherapy.
Methods: We collected formalin-fixed paraffin-embedded mediotemporal brain samples of 15 patients and compared them to a control cohort (n=8) by performing histopathology and whole-genome transcriptomics. We assessed MRI courses and CSF-serum pairs.
Results: After shorter disease duration, CD3+CD8+GranzymeB+ cytotoxic T-cells were elevated in the brain parenchyma. T cell numbers decreased with longer disease duration. Transcriptomics showed upregulated T cell genes in patients with high T cell counts. In such cases, also B cell- and complement-associated pathways were overrepresented. This was paralleled by high numbers of plasma cells in the perivascular space of blood-vessels as well as in the parenchyma. These cases, however, showed no neural IgG deposition or complement activation. In cases with short disease duration, loss of hippocampal neurons and APP+ axonal bulbs indicated acute neural damage. Patients showed mediotemporal volume and signal increase on MRI and intrathecal IgG- or GAD antibody-synthesis in temporal proximity to active brain inflammation. This resulted in hippocampal sclerosis.

Conclusion: Early in the disease course, cytotoxic T cells damage neurons. Subsequently, plasma cells enter the brain but there are no signs of antibody-mediated pathology. This early encephalitic period can be recognized by MRI scans showing mediotemporal swelling with signal increase and CSF studies revealing intrathecal antibody synthesis. The early irreversible neural destruction may explain incomplete responses to delayed immunosuppressive therapy and calls for early immunotherapy.

Disclosure: Nothing to disclose.

OPR-066

DNA methylation profiling of cfDNA in epilepsy patients demonstrates potential cerebral origin

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Background and aims: Cell-free DNA (cfDNA) consist of highly degraded DNA fragments shed into peripheral blood circulation. Its origin is predominantly associated with cell deat. DNA methylation patterns are strongly preserved in specific tissues and cell types. Screening of cfDNA methylation has been used to track cell type-specific cell-death. Mesial Temporal Lobe Epilepsy with Hippocampal Sclerosis (MTLE-HS) is characterized by severe neuronal death in the mesial regions.

Methods: We performed cfDNA methylation profiling, using EPIC BeachChips, in serum of 12 MTLE-HS patients (2M, 9F; 44.8±11.4 years of age) and 11 non-epileptic controls (4M, 8F; 38.9±8.4 years of age). Cell-of-origin deconvolution was performed with the meth_atlas algorithm. Differential methylation was performed with the minfi and limma R packages.

Results: No significant differences in the proportion of "cortical neuron"-derived cfDNA was observed between MTLE-HS patients and controls. We identified 235 differentially methylated CpG positions between patients and controls. Gene ontology analysis of the hypomethylated cluster (151 CpGs) revealed enrichment of terms associated with cerebral function, such as chemical synaptic transmission, positive regulation of oligodendrocyte progenitor proliferation and glutamate receptor activity.

Conclusion: The use of a deconvolution tool could not detect significant differences in the proportions of neuron-derived cfDNA in MTLE-HS. However, direct differential comparison of methylation between patients and controls demonstrated enrichment of pathways associated with CNS function. We consider relevant to enhance the detection of brain-derived cfDNA through more precise deconvolution tools. The detection of brain-derived cfDNA in serum of MTLE-HS patients may constitute a promising new biomarker for early detection of occurring neuronal death.

Disclosure: No conflicts of interest disclosed.

Sleep-wake disorders

OPR-067

Derivation and validation of a conversion pattern in idiopathic REM sleep Behavior Disorder

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Background and aims: Idiopathic REM-Sleep Behaviour disorder (iRBD) is considered an early-stage alpha-synucleinopathy. We aimed to identify an iRBD brain glucose metabolism phenoconversion-related pattern (RBDconvRP), which could potentially be used to predict phenoconversion of iRBD patients to Parkinson's disease (PD) or Dementia with Lewy bodies (DLB).

Methods: 76 (70±6 years, 15 females) iRBD patients were enrolled in Genoa and Rome and prospectively evaluated for 28±18 months. 30 patients (Table 1) phenoconverted to overt alpha-synucleinopathy (14 PD and 16 DLB). Patients underwent baseline brain 18F-FDG-PET. A RBDconvRP was identified using Scaled-Subprofile-Model Principal-Component-Analysis (SSM-PCA), and cross-validated by a leave-one-out procedure. Survival-analysis and Cox-regression were used to explore prediction power, using age, site, and sex as covariates.

Table 1: Demographic and clinical characteristics of RBD patients. Values are shown as mean ± standard deviation, median [minimum-maximum] for continuous variables, as absolute numbers for categorial variables.

Results: SSM-PCA was first applied in a derivation set (Genoa patients) of 16 converter and 27 non-converter patients. The pattern was applied to a validation set (Roma) of 14 converter and 19 non-converter patients. Another SSM-PCA was performed using Roma patients to derive a pattern and Genoa patients as the validation set. The two patterns were comparable, thus SSM-PCA was applied to the whole set, identifying the RBDconvRP (figure 1). Receiver operating characteristic analysis showed an area under the curve of 0.87 (sensitivity 80%, specificity 78%) in differentiating converters from non-converters. At Cox-regression analysis, RBDconvRP showed high prediction power in identifying converters patients, surviving adjustment for site, age, and sex (figure 2, HR: 9.87, CI 95%: 3.8–25.9).
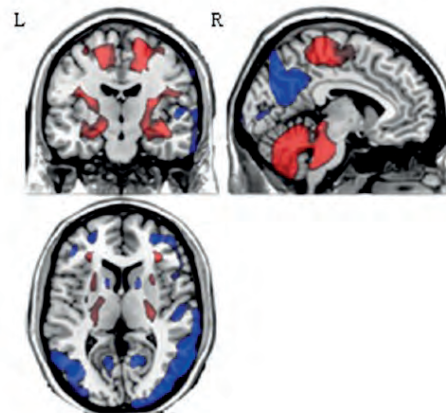
Figure 1: Results of the SSM-PCA. Stable voxels of the RBDconvRP, determined after bootstrap resampling 95% confidence interval not straddling zero are shown. Red indicates positive voxel weights and blue indicates negative voxel weights.
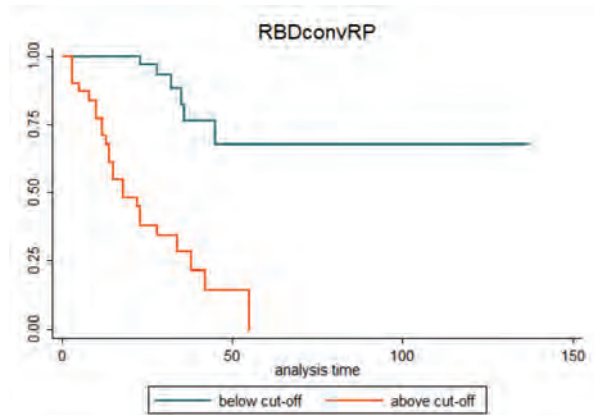
Figure 2. Survival analysis of RBDconvRP expression. On the x axis, survival time is reported in months, on the y axis percentage of patients. The green line represents patients expressing RBDconvRP below the empirical optimal cut-point (1.05 ds)

Conclusion: We identified and validated a stable RBDconvRP, able to discriminate converter from non-converter iRBD patients and possibly useful in future studies to predict phenoconversion.

Disclosure: I have nothing to disclose.

OPR-068

Unsupervised clustering of central hypersomnolence disorders enables data-driven phenotyping

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Background and aims: Recent studies fueled doubts as to whether the currently defined central disorders of hypersomnolence are stable entities, especially narcolepsy type 2 (NT2) and idiopathic hypersomnia (IH). The main aim of this data-driven observational study on neurological sleep disorders was to see if data-driven algorithms would segregate narcolepsy type 1 (NT1), and identify more reliable subgrouping of individuals without cataplexy.

Methods: We used the newly developed agglomerative hierarchical clustering package Bowerbird, an unsupervised machine learning algorithm, to identify distinct hypersomnolence clusters in the large-scale European Narcolepsy Network database. We included 1,078 unmedicated patients and 97 variables, covering all aspects of central hypersomnolence disorders (e.g, symptoms, demographics, sleep measures, laboratory biomarkers).

Results: Seven clusters were identified, of which clusters 1–4 included predominantly individuals with cataplexy (Figure 1). The two most distinct clusters (5 and 6) were dominated by those without cataplexy and, amongst other variables, significantly differed in presence of sleep drunkenness, subjective difficulty awakening and weekend-week sleep length difference. Patients formally diagnosed as NT2 and IH were evenly mixed in these two clusters.
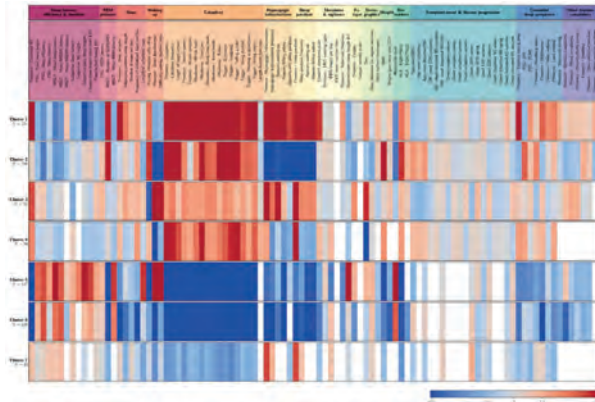
Each column represents 1 variable and each row represents 1 of 7 clusters. The difference between the mean value of the individual cluster with the entire EU-NN database is displayed for each variable in standard deviations in blue-to-red (lower-higher).

Conclusion: In the largest study on central disorders of hypersomnolence to date, we identified distinct data-driven subgroups within the central disorders of hypersomnolence population. Our results confirm NT1 diagnosis with multiple subtypes, contest inclusion of sleep-onset rapid eye moment periods (SOREMPs) in diagnostic criteria for people without cataplexy, and provide promising new variables for reliable diagnostic categories. Data-driven classification will result in a more solid hypersomnolence classification system with less vulnerability to single, instable features.

Disclosure: The EU-NN database is internally financed, but financial support from UCB Pharma Brussels was provided for database development.

OPR-069

Sleep disordered breathing and atrial fibrillation in acute stroke and their impact on long-term outcome

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Background and aims: Despite the evidence of a complex and bidirectional relationship between sleep disordered breathing (SDB) and atrial fibrillation (AF) on cerebro-cardiovascular events, studies investigating the long-term effects of this association in stroke patients are still rare.

Methods: We prospectively studied 353 patients with acute ischemic stroke with a follow-up of three years. The apnea-hypopnea index (AHI) was determined acutely after stroke with respiratory polygraphy. 7-days long-term electrocardiograms (7d-ECG) were performed up to three times during the first year.

Results: During the acute phase after stroke, 89 patients (25%) had moderate-severe SDB (AHI ≥20/h). AF was diagnosed in 56 patients (16%) and 23 patients (7%) had both AF and SDB (AHI ≥20/h). Over the follow-up period, 95 new cerebro-cardiovascular events were recorded, including 17 fatal casualties. Patients with comorbid SDB (AHI ≥20/h) and AF have a significantly increased risk (Hazard Ratio, 2.30) of an incident cerebro-cardiovascular or fatal event compared with either AF (Hazard Ratio, 1.77) or SDB (Hazard Ratio, 1.39) after adjusting for age, sex, body mass index, hypertension, diabetes mellitus and dyslipidemia. Moreover, stroke patients with comorbid SDB and AF are more likely to have cardioembolism.

Table 1: Baseline Characteristics according to AF

	No (N=297)	AF (N=56)	Total (N=353)	P value
Age, Mean (SD)	63.659 (13.155)	70.327 (9.896)	64.717 (12.914)	< 0.0011
Sex				0.0452
Male	181 (60.9%)	42 (75.0%)	223 (63.2%)	
Female	116 (39.1%)	14 (25.0%)	130 (36.8%)	
AHI	13.534 (15.902)	18.614 (16.064)	14.340 (16.013)	0.0291
SDB severity				0.0032
AHI < 20	231 (77.8%)	33 (58.9%)	264 (74.8%)	
AHI >= 20	66 (22.2%)	23 (41.1%)	89 (25.2%)	
NIHSS at admission	3.192 (3.814)	4.446 (6.093)	3.391 (4.271)	0.0441
NIHSS at discharge	1.347 (2.214)	0.839 (1.233)	1.266 (2.096)	0.0971
TOAST				< 0.0012
CE	81 (27.3%)	31 (55.4%)	112 (31.7%)	
LAA	77 (25.9%)	10 (17.9%)	87 (24.6%)	
Other	20 (6.7%)	0 (0.0%)	20 (5.7%)	
SVO	22 (7.4%)	5 (8.9%)	27 (7.6%)	
Unknown	97 (32.7%)	10 (17.9%)	107 (30.3%)	
Hypertension				0.0472
Yes	170 (57.2%)	40 (71.4%)	210 (59.5%)	
No and undiagnosed	127 (42.8%)	16 (28.6%)	143 (40.5%)	
Diabetes mellitus				0.5662
Yes	46 (15.5%)	7 (12.5%)	53 (15.0%)	
No and undiagnosed	251 (84.5%)	49 (87.5%)	300 (85.0%)	
Dyslipidemia				0.2522
Yes	161 (54.2%)	35 (62.5%)	196 (55.5%)	
No and undiagnosed	136 (45.8%)	21 (37.5%)	157 (44.5%)	

*Abbreviations: CE, Cardioembolic; SVO, Small vessel occlusion; LAA, Large artery atherosclerosis; NIHSS, National Institutes of Health Stroke Scale
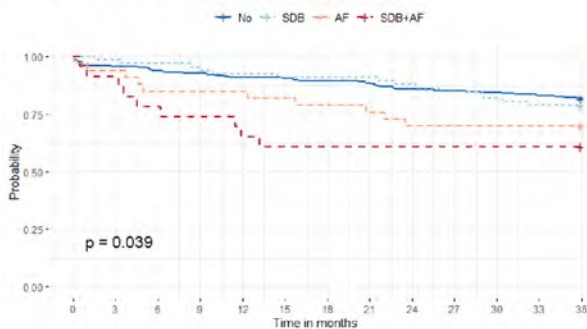
Figure 1. Time to events probability in No, SDB, AF, and SDB+AF groups. No: No AF with AHI=20; AF: AF with AHI=20.
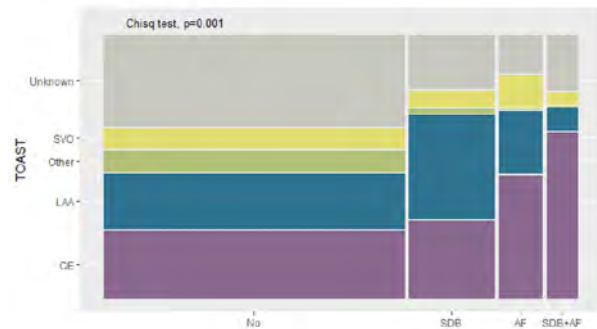
Figure 2. Distribution of TOAST stroke subtype classification in No, SDB, AF, and SDB+AF groups.

Conclusion: Stroke patients with both SDB and AF have a significantly higher risk of long-term cardiovascular morbidity and mortality compared to SDB or AF alone. Further studies are needed to clarify the pathomechanisms underlying this observation and lead to specific diagnostic and treatment recommendations.

OPR-070
Abstract withdrawn

Peripheral nerve disorders

OPR-071

RFC1-neuropathy cases frequently convert to full-blown CANVAS: a cohort-sequential study

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Background and aims: Cerebellar Ataxia with Neuropathy and Vestibular Areflexia Syndrome (CANVAS), a multisystem neurological disease often characterized by sensory disturbances at onset, has recently been associated to a biallelic Replication Factor C subunit 1 AAGGG intronic repeat expansion mutation (RFC1exp). Penetrance of the full phenotype and predictors of clinical progression are currently unknown. We investigated RFC1exp in a Chronic Idiopathic Axonal Polyneuropathy (CIAP) population to assess its prevalence, characteristics and long-term disease progression.

Methods: We identified 286 CIAP cases among patients referred to our Center for sural nerve biopsy. We reported clinical features at the time of biopsy (T1) and pathology results. RFC1exp patients were longitudinally reevaluated (T2) to assess disease progression.
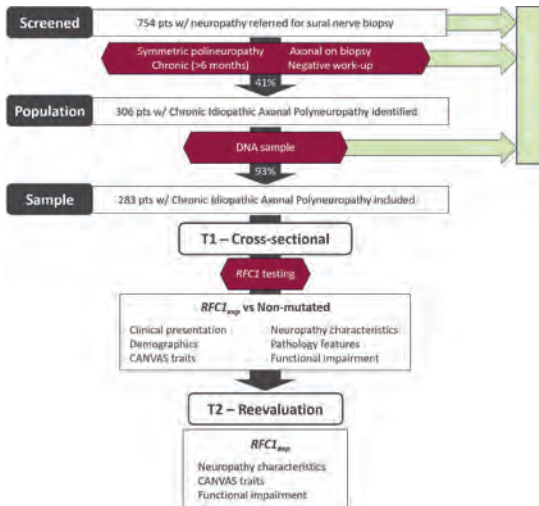
Study flowchart

Results: RFC1exp cases were common in pure sensory (31/58, 53%) and predominantly sensory neuropathies (13/73, 18%) compared to sensorimotor cases (3/155, 2%) and characterized by frank signs of sensory ataxia and mild autonomic disturbances. Apart from retention of deep tendon reflexes, other peculiar CANVAS features at T1 were exceptional. Pathology revealed a severe involvement of all nerve fibers but scant regenerative changes. At T2 (median disease duration 13 years IQR 9–16) most patients exhibited at least mild features of cerebellar (19/23, 83%) and vestibular involvement (16/22, 73%). Chronic cough was universally reported. Intriguingly, age at visit was a stronger predictor of overall functional impairment than disease duration.
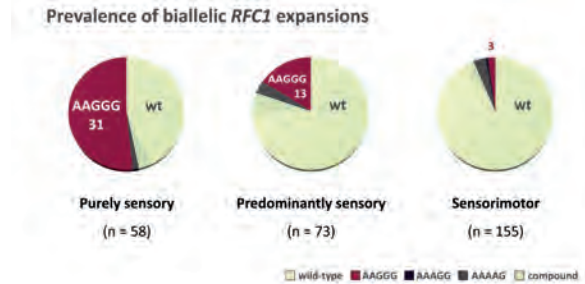
Prevalence of RFC1 expansion mutations according to clinical presentation
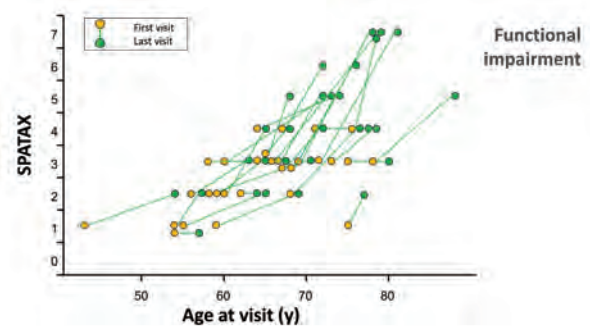
Grade of functional impairment according to SPATAX scale and age at first (yellow) and last (green) visit in RFC1-neuropathy

Conclusion: Emergence of the full-blown CANVAS phenotype is a frequent but late event in RFC1exp patients presenting with an isolate sensory neuropathy. Aging but not age at onset is a major determinant of disease progression.

Disclosure: Nothing to disclose.

OPR-072

Kinesin-5 inhibition enhances functional recovery in experimental autoimmune neuritis

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Background and aims: Kinesin-5 is a motor protein that interacts with microtubules and is highly expressed in postmitotic neurons. Inhibition of kinesin-5 accelerates the growth rates of cultured neurons. We examined the influence of kinesin-5 inhibition on functional recovery in experimental autoimmune neuritis (EAN) in female Lewis rats.

Methods: EAN was induced using myelin 53-78 P2 protein. The clinical disease severity score was assessed daily until day 30 post-immunization (p.i.). At the peak of EAN, at days 18, 22, and 26 p.i, rats were treated with either sham or 1 mg/kg body weight of the kinesin-5 inhibitor monastrol intraperitoneally. Nerve conductions studies and histological analysis of the sciatic nerve and the tibialis anterior muscle were performed. Non-parametric Mann-Whitney t-test was used for statistical analysis.

Results: Treatment with 1 mg/kg body weight monastrol ameliorated significantly clinical signs in the recovery phase of EAN (p-value for the area under curve: 0.0288). Motor nerve conduction velocity (mNCV) reached near pre-immunization values (p-value for days 0 and 30: 0.1819). Immunohistochemical analysis of the macrophage marker IbA1 showed no differences (p-value: 0.0564), while a significant reduction of CD3+ T-cells was observed (p-value: 0.0012). An increase of partially or fully innervated neuromuscular junctions (NMJs) was observed (76.49% to 65.05%).
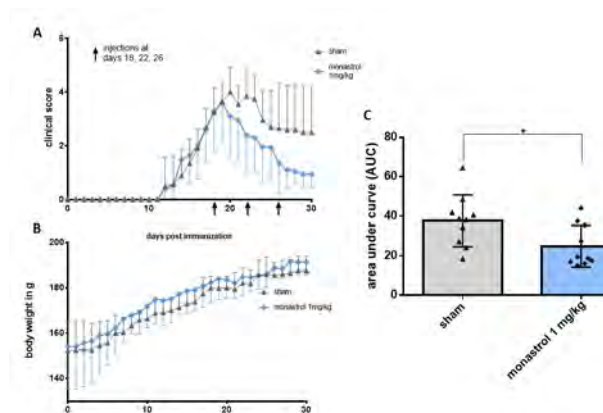
Treatment with 1 mg/kg of the kinesin-5 inhibitor monastrol enhances functional recovery after EAN.
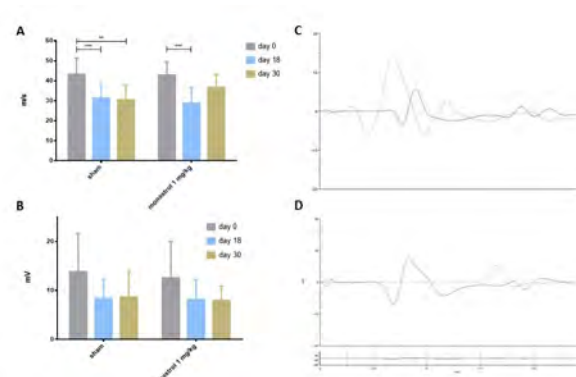
Kinesin-5 inhibition accelerates mNCV recovery.

Conclusion: Kinesin-5 inhibition accelerates functional and histological recovery in EAN. Our preliminary results suggest an effect on infiltratory T-cells and reinnervation of disrupted NMJs. Further studies are warranted to investigate the potential of kinesin-5 inhibition in patients suffering from autoimmune neuropathy.
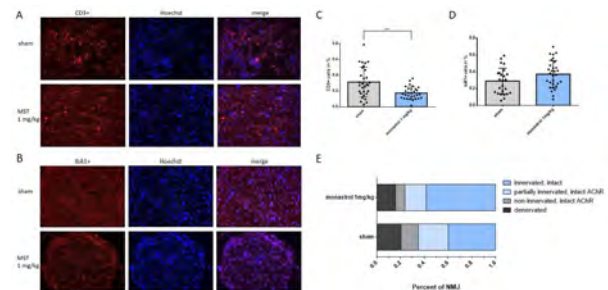
Immunohistochemical analysis of the sciatic nerve shows a significant reduction of CD3+ T-cell infiltration and enhanced recovery of NMJ-innervation.

OPR-073

A software platform to identify diagnostic and prognostic parameters in neuromuscular diseases towards trials readiness

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Background and aims: We are working on an integrated, multiparametric approach in diagnosis and management of neuromuscular diseases (NMDs) by using a single support software platform, potentially useful in implementing diagnosis and taking care towards trials readiness. Promising preliminary results have been obtained to date with the Health360 platform under the umbrella of the InGene 2.0 project.

Participants and aims of the InGene2.0 Project

Methods: Health360, a platform developed under the Software-as-a-Service (SaaS) principles, merges all that, with sections dedicated to the collection of personal data (under the premises of the EU 2016/679 GDPR Regulation), as well as modules devoted to biomedical images storage and interpretation.

Modules of the software platform and integration with wearable devices

Results: In particular, further modules, including neurological examination and functional motor tests, mta, muscle biopsies, are under development and optimization.
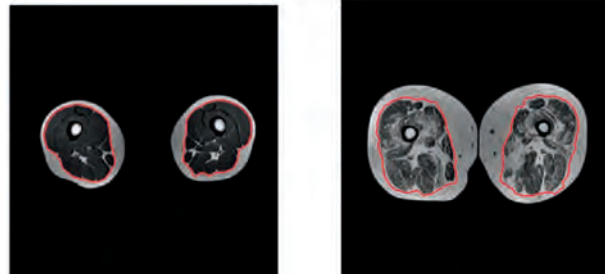
Development of and AI algorithm for muscle MRI analysis

Conclusion: The possibility to upload such images in a common, user-friendly software platform, where data and image storage, as well as the analysis of images and loops can be performed in an intelligent manner, would be of extreme aid to the clinician. If confirmed on larger cohorts and with robust statistical approach, such results could drive the present tool to be used for diagnostic aims, phenotypic characterization and clinical follow-up.

Disclosure: The project is funded by the Progetto Toscana Salute 2018.

OPR-074

Cancer-related neuropathic pain in Europe: differences in diagnosis and treatment in 13 countries-patient´s perspective

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Background and aims: With effective treatments available, people with cancer live longer but often with sequelae such as neuropathic pain. Cancer patients from 13 European countries shared their experiences with the diagnosis and management of CRNP.

Methods: An online survey, prepared, conducted and analysed with a team of experts including physicians, nurses and patients, was completed in June 2021. Adults consenting to participate and diagnosed with cancer were screened for symptoms of CRNP. Respondents who met three or more of the DN4 (Douleur Neuropathique 4) criteria were enrolled and provided detailed information about diagnosis and management of their pain.

Results: 549 persons living with CRNP participated in the survey (24–103 respondents per country). Of those recruited, 32% experienced severe pain daily (21–49%). Although neuropathic pain symptoms were present, only 60% of respondents received a formal diagnosis of CRNP varying from 40% in France to 87% in Switzerland. Pharmaceutical treatment by a healthcare professional (HCP) varied from 32% in Norway to 79% in Switzerland where also the highest treatment satisfaction was reported with 91% of responses. On average 60% of patients have been warned by a HCP to develop CRNP (thereof 45% by their oncologist) with the highest rate in Switzerland (83%) and the lowest in the UK (42%).

Conclusion: Major differences have been identified between European countries regarding diagnosis and treatment of CRNP. Highest patient satisfaction was reported in countries where HCPs spent enough time with their patients, which demonstrates the relevance of HCP-patient communication in CRNP care.

Disclosure: Grünenthal GmbH has financially supported this survey.

OPR-075

The diagnostic value of the rise slope of the compound sensory nerve action potential in human nerves

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Background and aims: The average rise slope of the sensory nerve action potential (SNAP) appreciates the steepness of the initial negative deflection of the waveform, which might be a useful metric for the first part of the potential.

Methods: Sural nerve sensory neurography was performed in patients with various axonal neuropathies and median nerve sensory studies were carried out in patients suffering from carpal tunnel syndrome. Age matched healthy individuals served as controls. The rise slope was compared to conventional SNAP parameters such as conduction velocity, latency, duration and rise time.

Results: 537 sensory studies were prospectively analyzed. The rise slope of the sural SNAP demonstrated superior classification performance in terms of sensitivity (92.5%), specificity (97%) and area under the receiver operating characteristic curve (0.986), as compared to conventional SNAP parameters. Its diagnostic power was similarly excellent in median nerve studies, whereas here a slightly better classification performance was obtained by SNAP latency and conduction velocity.

Conclusion: The average rise slope appears to do justice to the tight interplay between amplitude and rise time of the initial negative spike deflection, outperforming many conventional measures. This composite metric proved high diagnostic potency in particular with regard to axonal sensory nerve dysfunction.

Disclosure: None of the authors has any conflict of interest to disclose.

OPR-076

Super-resolution imaging provides new insights into nerve pathologies in patients with peripheral neuropathies

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Background and aims: With today's super-resolution fluorescence microscopy methods, it is possible to study the molecular organization of the Node of Ranvier. Previous studies have revealed a 190nm periodic arrangement of nodal, paranodal and internodal structural proteins of murine myelinated axons. However, the ultrastructural anatomy of the paranodal region of peripheral human myelinated axons under physiological and pathophysiological conditions has not been explored yet.

Methods: We use dual color dStorm microscopy and high content confocal imaging in combination with colocalization analysis to examine the structure of the paranodal complex and its cytoskeletal anchor molecules in nerve biopsies of n=16 patients with peripheral neuropathies.

Results: We show an increase in the periodic distance of the proteins of the paranodal axoglial complex of Neurofascin-155 and Caspr-1 in patients with polyneuropathy. Double immunofluorescence colocalization analysis shows that both proteins are not detached even if the periodic arrangement is pathologically altered. However, colocalization of Caspr-1 to its anchor protein ß2-Spectrin is disrupted in patients with axonal neuropathy. In comparison to chronic axonal (n=5) and demyelinating (n=5) forms, patients with acute axonal polyneuropathies (n=6) show a paranodal elongation and a significant reduction of nodes per tissue volume in teased fiber preparations correlating to the cross-sectional fiber density.

Conclusion: Our data provide new insights into the histopathologic changes in polyneuropathy and objectively quantify alterations between different forms of neuropathy. In the future, dStorm and high content confocal microscopy could serve as sophisticated tools for a better understanding and discrimination of subtypes and stages of polyneuropathies.

Disclosure: The authors declare no competing financial interests.

Epilepsy 2

OPR-077

Cenobamate: preliminary results of efficacy and safety in a real-life setting

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Background and aims: The percentage of patients with drug-resistant epilepsy has not changed despite the increasing available anti-seizure medications (ASMs). Cenobamate (CNB) has been recently approved as adjunctive treatment of uncontrolled focal-onset seizures (FOS). So far, evidence about CNB use in clinical practice is limited.

Methods: Starting from December 2020, 20 patients aged ≥18 years, diagnosed with uncontrolled FOS and without other potential treatment alternatives, were enrolled in an Italian Expanded Access Program (EAP). Clinical data to assess CNB efficacy and safety were collected at 3, 6, and 12 months after CNB administration, along with plasma concentrations of concomitant ASMs. Therapeutic adjustment of concomitant ASMs was allowed. Primary efficacy outcomes were median percentage change in monthly seizure frequency compared to baseline and responder rate (patients with ≥50% monthly seizure frequency reduction from baseline). Adverse events (AEs) were reported considering their severity and duration.

Results: Patients taking CNB reported significant reductions in monthly seizure frequency compared to baseline at 3 months (– 63%) with 11/20 (58%) presenting ≥50% seizure frequency reduction. Sustained decrease in seizure frequency was registered at 6 and 12 months. 16/20 (80%) patients experienced AEs, which were mainly mild and transient and generally disappeared after reducing the posology of concomitant ASMs.

Conclusion: Despite the small number of patients and the short follow-up, to our knowledge, this is one of the first real-world study on CNB use in clinical practice.

Disclosure: Nothing to disclose.

OPR-078

Seizure forecasting with non-invasive and minimally-invasive mobile devices – Epilepsy Foundation My Seizure Gauge study

P. Viana [1], M. Nasseri [2], E. Nurse [3], P. Karoly [3], T. Pal Attia [2], N. Gregg [2], B. Joseph [2], C. Grzeskowiak [5], M. Dümpelmann [6], M. Cook [3], G. Worrell [2], A. Schulze-Bonhage [6], D. Freestone [4], M. Richardson [1], B. Brinkmann [2]
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Background and aims: Seizure forecasting has been established using continuous intracranial EEG, however invasive devices are not appropriate for all patients. Non-invasive and minimally invasive devices may facilitate seizure forecasting, and they may provide accurate seizure records to support clinical decision making.

Methods: Patients with drug-resistant epilepsy were enrolled for ultra long-term (>8 months) monitoring with an electronic diary, a wearable device (Empatica E4, Fitbit Charge 4/HR, or Fitbit Inspire) and ambulatory EEG monitoring (UNEEG SubQ, EpiMinder Subscalp, NeuroPace RNS) at three sites. Recorded data were analyzed to identify circadian and multi-day seizure cycles which, together with machine learning methods, were used to forecast seizures.

Results: 40 enrolled subjects have recorded over 11,400 days (31.2 years) of ambulatory data, including over 1,600 seizures. Nine patients left the study prematurely due to device malfunctions, complications, poor adherence, poor data quality or unanticipated seizure freedom. 20 patients continue recording data and eleven have completed the study. Analyses in this cohort has established the following:
• Heart rate circadian and multi-day cycles are significantly phase-locked with self-reported seizure likelihood
• Electrodermal activity, heart rate, and actigraphy were significantly correlated with electrographic seizures in 11 patients • Seizure forecasting significantly better than chance in 5 of 6 patients using a wrist-worn device and long-short term memory (LSTM) neural networks • Circadian and multi-day seizure cycles are detectable in subcutaneous EEG recordings • Seizure forecasting significantly greater than chance in 5 of 6 patients using subcutaneous EEG

Conclusion: This project has established the feasibility of forecasting seizures using seizure cycles, wearable devices and subcutaneous EEG.

Disclosure: This work is supported by the Epilepsy Foundation of America.

OPR-079

Epilepsy in School-aged Children and academic performance in standardized tests: A Danish nation-wide cohort study

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Background and aims: We evaluated whether epilepsy is associated with performance in standardized tests among Danish school-aged children.

Methods: We performed a register-based, nation-wide, matched cohort study of children born in Denmark during 1997–2009 who participated in the Danish National School Test Program between 2010–2019. Population and health registers were used to identify CWE along with randomly sampled sex- and age-matched reference children without epilepsy (ratio 1:10). Academic performance was assessed in language (2nd, 4th, 6th, 8th grade) and mathematics (3rd, 6th, 8th grade). Differences in mean standardized scores (scale, 1–100) between children with and without epilepsy were estimated using linear regression models while adjusting for relevant confounders.

Results: Of 582,475 eligible children, we studied 4,322 (0.74%) CWE and sampled 43,220 matched reference children. The median (IQR) age at epilepsy onset was 6.9 (3.5–10.2) years. Having epilepsy was significantly associated with poorer performance in language (mean score CWE=48.8 and reference=56.4; adjusted difference=-6.0, 95% CI: -6.8 to -5.2), and mathematics (mean score CWE=47.7 and reference=57.3; adjusted difference =-7.7, 95% CI: -8.6 to -6.8). Worse performance was found in all epilepsy subgroups, including in the 3,015 CWE considered neurotypical (i.e. with no pre-existing neurologic or intellectual disabilities or an identified underlying cause for the epilepsy), (adjusted difference=-6.0, 95% CI: -6.8 to -5.1).

Conclusion: CWE are at increased risk of poor academic outcomes, with average score differences of -10.6% in language and -13.4% in mathematics. Our findings highlight the need for educational support of CWE, even among those who are otherwise neurotypical.

Disclosure: This work was supported by the Independent Research Fund Denmark, the Novo Nordisk Foundation (NNF16OC0019126), the Central Denmark Region, and the Danish Epilepsy Association. Dr. Christensen reports personal fees from Eisai AB, personal fees from UCB Nordic, during the conduct of the study. The other authors report no conflicts of interests.

OPR-080

The European Study on the Burden and Care of Epilepsy

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Background and aims: The European Study on the Burden and Care of Epilepsy (ESBACE) provides data on the burden and care of epilepsy in Europe.

Methods: This study had three main goals: 1) to estimate prevalence of epilepsy in four European countries based on information from medical record, 2) to use a "top-down," register-based approach in more than 5 million people in Denmark to study prevalence and cost of epilepsy, and 3) to study stigma and quality of life in persons with epilepsy.

Results: The retrospective chart review found a prevalence of 0.67% (0.61–0.72), but a precise prevalence estimate could not be generated because of limited information and access to hospital records. In the "top-down" study, the prevalence of epilepsy was 0.67% (0.69% males; 0.65% females), (Figure 1), and the cost of epilepsy was €30,683/person/year. Epilepsy was associated with stigma and lover quality of life compared to matched controls.
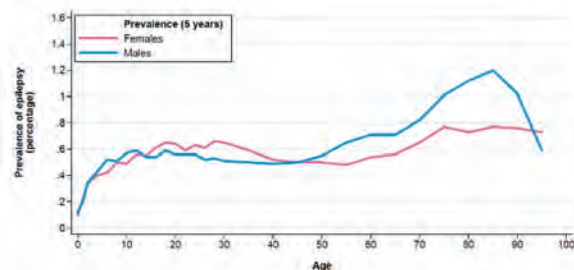
Figure 1. Age- and sex-specific prevalence of epilepsy in Denmark on December 31, 2016

Conclusion: This European study provides important insight into burden and care in persons with epilepsy:
• Chart review faced a number of challenges largely due to data protection legislation, and poor documentation of epilepsy diagnoses in medical records. • It was possible to use a "top-down" approach to estimate epilepsy prevalence, and establish the very high costs associated with epilepsy. • A significant proportion of people with epilepsy are still affected by the stigma and report lower quality of lives compared with those without the condition – a circumstance that has not improved in recent decades.

Disclosure: The European Union (no. 2014//199564).

OPR-081

The Scottish Epilepsy Deaths Study Score (SEDS Score): a risk prediction model for epilepsy-related deaths

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Background and aims: This study uses routine clinical information to develop a risk-prediction model for epilepsy-related deaths.

Methods: In this age/sex-matched case-control study, we compared adults (aged ≥16 years) suffering epilepsy-related death between 2009–2016 to living adults with epilepsy in Scotland. Cases were captured from national mortality records, and controls from a research database or epilepsy clinics. Medical record data were used in univariable and multivariable conditional logistic regression to develop a risk prediction model consisting of four variables chosen a priori. A sum of the factors present was taken to create a risk index – the SEDS Score. Odds ratios (OR) with 95% CIs were estimated.

Results: 224 cases and 224 controls were compared (mean age 48 years). Univariables predicting epilepsy-related death were recent epilepsy-related A&E attendance (OR 5.1, CI 3.2–8.3), living in deprived areas (OR 2.5, CI 1.6–4.0), developmental epilepsy (OR 3.1, CI 1.7–5.7), alcohol abuse (OR 4.4, CI 2.2–9.2), absent recent neurology review (OR 3.8, CI 2.4–6.1), generalised epilepsy (OR 1.9, CI 1.2–3.0), and mental health problems (OR 1.6, CI 1.0–2.6). SEDS Score model variables consisted of the first three listed above, alongside the number of comorbidities (adjusting variable). Compared to having a SEDS Score of 0, those with a SEDS Score of 1, 2, and 3, had 3.6x (CI 1.9–6.8), 17.2x (CI 7.4–39.6), and 19.8x (CI 5.1–76.6) increased odds of death, respectively.

Conclusion: SEDS Scoring may help predict epilepsy-related death and requires external validation. Figure 1 illustrates a prototype SEDS Scoring card for clinical use.

Figure 1: Prototype SEDS Scoring card

Disclosure: Nothing to disclose.

OPR-082

Short term efficacy and safety of adjunctive cenobamate in patients with super-refractory focal epilepsy

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Background and aims: To assess safety and efficacy of cenobamate (CNB) as adjunctive therapy in adult patients with focal onset seizures participating in an early access program.

Methods: We performed a multicenter prospective longitudinal study including adult patients with drug-resistant focal epilepsy who were treated with at least a single dose of CNB as adjunctive therapy in the early access program. We analyzed adverse effects (AE) at 3 and 6 months and responder, seizure free and retention rates at 6 months. Baseline seizure frequency was measured during a 3-month period prior to CNB initiation.

Results: 58 patients were included (mean age 40, range: 19–70; 53.4% women). Median number of previous and concomitant antiseizure medications (ASM) were 9 and 3, respectively. Median dose at 6 months was 200 mg/day (range: 75–400 mg/day). Median seizure frequency per month decreased significantly at 6 months (4 vs 8; p<0.001). 67.5% of patients (25/37) were responders (reduction of >50% seizure frequency) and 8.1% (3/37) were seizure-free at 6 months. Retention rate at 6 months was 85% (34/40). 36/58 patients experienced AE during the titration period at 3 months, and 21/39 at 6 months, the most common being somnolence, unsteadiness and dizziness. 8/58 patients discontinued CNB (3 due to AE, 2 due to lack of efficacy and 3 due to both).

Conclusion: In our series, cenobamate showed a high efficacy as adjunctive therapy in patients with super-refractory focal epilepsy. AE were the typical of other ASM and led to CNB withdrawal in 10% of the patients.

Disclosure: Nothing to disclose.

Movement disorders 2

OPR-083

Scoring Algorithm-Based Genomic Testing in Dystonia: real-life data from the outpatient clinic

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Background and aims: A recent multicentric study defined a scoring algorithm to guide the choice of whole exome sequencing (WES) in patients with dystonia. Positive predictors consisted of an age at onset <20 (2 points), segmental/generalized involvement (1 point) and presence of further neurological symptoms (1–2 points). This scoring algorithm has been validated in a second prospectively recruited multicentric cohort. Real-life data from dystonia outpatient clinics are lacking.

Methods: We screened the patients regularly attending the dystonia outpatient clinic of the Innsbruck Medical University, excluding acquired forms (e.g. history of trauma, neuroleptic intakes) and secondary dystonia forms (e.g. oromandibular dystonia or blepharospasms due to atypical parkinsonism). WES studies were performed within a cooperation with the Technical University and the Helmholtz Center, Munich.

Results: We regularly follow 372 patients with primary dystonia. WES was performed in 4/4 patients with score=5, 27/29 patients with score=3–4 and 140/338 patients with score ≤2 (total=171). WES yielded a genetic diagnosis in 3 out of 4 patients with a score of 5 (75%), in 16 out of 27 patients with a score=3–4 (59%) and in 12 out of 140 patients with a score ≤2 (9%).

Conclusion: The diagnostic yield of WES in our dystonia cohort correlated with a higher predictive score. Furthermore, our positivity rates were overall higher than previously described in a unselected prospective cohort (51%, 25% and 2% with a score of 5, 3 to 4 and ≤2 respectively). Our real-life date outline the even greater diagnostic rate of WES in the setting of a clinically well-defined dystonia population.

Disclosure: No disclosures related to the present abstract.

OPR-084

Abstract withdrawn

OPR-085

Survival in monogenic forms of Parkinson's disease: results of a large retrospective study

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Background and aims: Parkinson's Disease (PD) is a neurodegenerative disorder with environmental and genetic determinants. The most common mutations causing PD are in the SNCA, LRRK2, and PRKN genes, while variants in GBA are considered as risk factors. This is the first study comparing mortality in PD patients carrying SNCA, LRRK2, PRKN, or GBA variants.

Methods: Data were retrieved from a large multicentric cohort of PD patients. Multivariable Cox proportional hazards model with time since first visit as the time scale were adjusted for age, sex, time from symptom onset to first visit, and included a random effect to account for intra-familial correlations (shared frailty). Patients were censored at time of death or end of study. The reference group were PD patients without any mutation.

Results: A total of 2,037 patients were included in this analysis, of whom had 890 died during follow up. In the multivariable model, patients with LRRK2 (Hazard ratio of death [HR]=0.5, p=0.028) or PRKN (HR=0.42 p=0.001) mutations had a longer survival than PD patients without mutations, while those with SNCA (HR=10.20, p <0.001) or GBA (HR=1.36, p=0.048) mutations had a shorter survival.
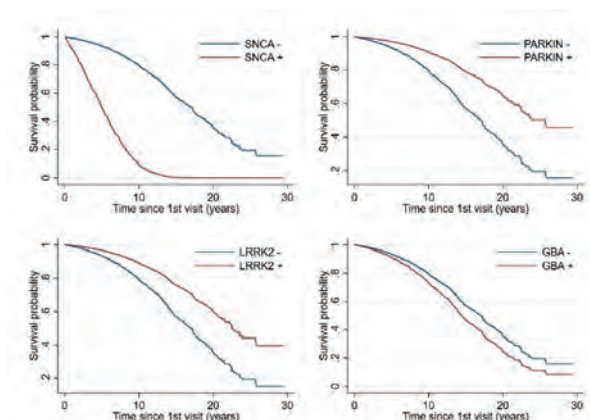
Survival predicted by Cox models according to mutation

Conclusion: Survival from the first visit is increased in LRRK2 and PRKN mutated patients while it is decreased in SNCA and GBA mutated patients compared to PD patients without mutations. The later mortality of LRRK2- and PRKN-mutated patients may be related to slower progression, while the earlier mortality of SNCA- and GBA-mutated patients could be due to faster progression and early development of cognitive impairment.

Disclosure: Nothing to disclose.

OPR-086

Differentiation of Essential and Parkinson´s Disease Tremor using time series feature extraction and machine learning

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Background and aims: Tremor is a frequent symptom, causing a relevant disease burden in individual patients. In the absence of a bio-marker, diagnostic differentiation between even the most prevalent tremor disorders Essential Tremor (ET) and Parkinson's Disease (PD) is non-trivial. Massive time series feature extraction and machine learning approaches are novel tools to analyse oscillating biological signals. This study aims to explore the utility of combining these two methods to facilitate tremor disorder diagnosis.

Methods: Accelerometer recordings from n=340 patients suffering from ET and PD from four centres have been collated in a single data set. Clinical diagnosis was based on current, recognized diagnostic criteria. After quality control and pre-processing, massive higher-order feature extraction is applied to same length segments of recordings from the more affected hand. Supervised learning is performed using different machine learning algorithms according to clinical diagnosis in order to identify disease-specific features.

Results: Based on the combination of recordings taken at rest and posture, statistical learning based on >7000 extracted features correctly classified up to 86.2% of patients correctly, depending on centre and number of features combined. We evaluate the effects of different machine learning algorithms to further optimize stratification.

Conclusion: This study provides evidence for the usefulness of unbiased tremor signal analysis to differentiate ET and PD tremor. Feature-based tremor analysis has the potential to improve patient care beyond differential diagnostic accuracy, e.g. as a tool to predict treatment response or guide therapeutic interventions.

Disclosure: Authors report no conflict of interest.

OPR-087

Neural correlates of motor and non-motor manifestations in cervical dystonia, revealed by fixel-based analysis

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Background and aims: Cervical dystonia (CD) is a form of isolated focal dystonia, characterized by abnormal head posture. It is often accompanied by psychiatric symptoms, such as depression, and its pathophysiology has been linked to large-scale brain networks abnormalities. However, the specific neural correlates of motor and psychiatric manifestations, respectively, are still unknown. We analyzed patterns of white matter fibers in CD, and investigated the brain networks associated with abnormal head posture and psychiatric symptoms.

Methods: 18 CD patients and 21 healthy controls had diffusion weighted imaging (DWI). We applied fixel-based analysis, a novel method able to extract multiple populations of fibers within the same voxel, and thus account for fiber orientation across voxels. We compared white matter fibers between CD patients and controls, and correlated them with the severity of dystonia (Toronto Western Spasmodic Torticollis Rating Scale - TWSTRS), and depression (Beck Depression Inventory - BDI), respectively, in patients.

Results: Compared to controls, patients showed decreased white matter fibers in the basal ganglia and sensorimotor areas, as well as in the superior temporal regions and the brainstem (Figure1). TWSTRS scores negatively correlated with white matter in the superior parietal lobule, whereas BDI showed positive correlation with associative cerebellar areas, such as the crus 1 (Figure2).
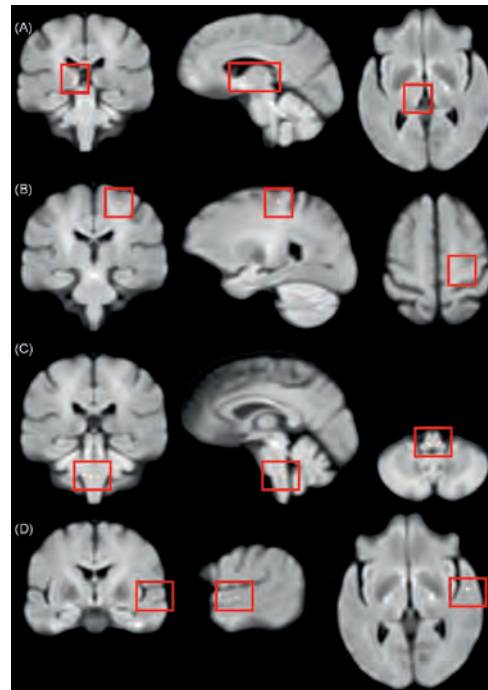
Significant clusters of decreased white matter fibers in CD patients in: (A) the basal ganglia, (B) the sensorimotor regions, (C) the brainstem, and (D) and temporal areas.
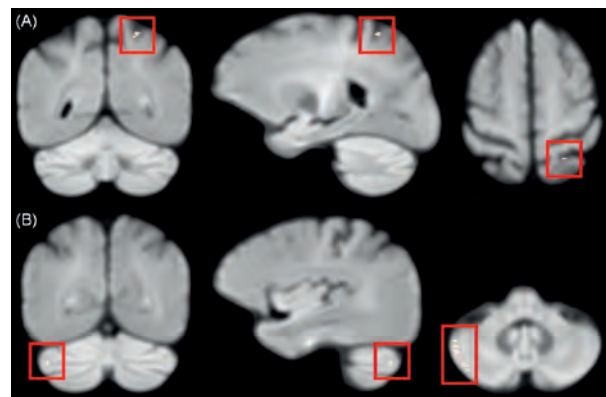
Significant clusters of white matter fibers in CD patients showing: (A) positive correlation with BDI scores, and (B) negative correlation with TWSTRS.

Conclusion: We identified distinct patterns of neural correlates associated with motor and non-motor manifestations of CD. A loss of inhibitory output from the basal ganglia may propagate to several functional networks beyond the motor system. This may result in a progressive maladaptive plasticity, and culminate in overt symptoms of dystonia.

Disclosure: The authors declare no conflict of interest.

OPR-088

Personality and Early Parkinson's disease phenotypes

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Background and aims: Although there is a previous description of a parkinsonian personality characterized as rigid, introverted, and cautious, little is known about personality traits in de novo Parkinson's disease (PD) patients and their relationships with motor and neuropsychiatric symptoms. We intend to investigate these two questions.

Methods: The personality of 193 de novo PD patients was assessed using Cloninger's biosocial model and motor and non-motor symptoms using several clinical scales. We conducted correlations and cluster analysis to investigate the relationship between personality traits, motor, and non-motor symptoms.

Results: PD patients have low novelty seeking, high harm avoidance, and normal reward dependence and persistence scores. Harm avoidance was positively correlated with depression, anxiety, and apathy (rs= [0.435, 0.676], p<0.001) and negatively correlated with quality of life (rs= -0.492, p<0.001). Novelty seeking, reward dependence, and persistence were negatively correlated with apathy (rs= [-0.274, -0.375], p<0.001). Cluster analysis revealed 3 distinct clusters: i) neuropsychiatric phenotype (with high harm avoidance, low novelty seeking, and hypodopaminergic neuropsychiatric symptoms), ii) motor phenotype (with low novelty seeking and higher motor severity), iii) benign phenotype (low harm avoidance and high novelty seeking, reward dependence, and persistence traits clustered with lower symptoms severity and low impulsivity).

Conclusion: Personality in de novo PD seems to play a role in the presence of different clinical phenotypes with harm avoidance and novelty seeking traits having a higher impact on susceptibility to mood disorders. Identification of different PD subgroups may help to investigate if some personality features might influence disease evolution and treatment.

Neuroimaging 2

OPR-089

Longitudinal whole-brain metabolic network changes following acute unilateral vestibulopathy

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Background and aims: Symptoms of acute unilateral vestibulopathy (AUV) partially recover due to adaptive brain plasticity. In this study, we analysed whole-brain metabolic connectivity changes after AUV by longitudinal 18F-FDG-PET imaging.

Methods: 22 patients with AUV underwent resting state 18F-FDG-PET scans in the acute phase (mean: 6d) and after partial behavioural compensation (mean: 6m). PET data were compared to 22 matched controls. Images were flipped reconstructed, registered, filtered, normalized, and segmented (AAL2/3 atlas). Pearson's correlations between all segmented brain regions were performed ($r>0.5/ p<0.001$). Functional metabolic connections between/within hemispheres, and in vestibular/multisensory/motor/cognitive were calculated.

Results: Patients had severe vestibular asymmetry in the acute stage (mean horizontal slow-phase velocity (SPV): 9.9°/sec, subjective visual vertical (SVV): 7.6°), which recovered until 6m after AUV (SPV: 0.7°/sec, SVV: 1.7°). As compared to controls, whole-brain metabolic network analysis indicated a significant drop in the total number of connections, in interhemispheric projections between homotopic regions and especially in vestibular and multisensory cortical networks in the acute stage. In the chronic stage, the asymmetry in interhemispheric connections of homotopic regions persisted. Multisensory network connectivity relatively increased in the ipsilesional hemisphere compared to the early stage. Patients with a persistent caloric vestibular deficit had a higher asymmetry index compared to those with reconstituted peripheral function.

Conclusion: AUV disrupts the symmetry of multisensory metabolic networks between hemispheres persistently and mostly in patients with a chronic peripheral vestibular deficit. These data may be important for the understanding of higher sensory network dysfunction and conversion risk to functional dizziness after AUV.

Disclosure: Nothing to disclose.

OPR-090

A Deep-Learning Approach to Predicting Disease Progression in Multiple Sclerosis Using Magnetic Resonance Imaging

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Background and aims: In this study, we developed an artificial intelligence deep-learning algorithm on a large multicenter cohort of MS patients collected from the Italian Neuroimaging Network Initiative (INNI) to predict disease evolution (based on clinical disability and cognitive impairment) at two-years of follow-up from their baseline MRI features. The performance of the algorithm was then evaluated on an independent test-set and compared to that of two expert physicians.

Methods: For 373 patients, baseline T2-weighted and T1-weighted brain MRI, as well as baseline and two-year clinical and cognitive assessments were collected from the INNI repository. A deep-learning architecture based on convolutional neural networks was implemented (Fig. 1) to predict: (1) clinical worsening (Expanded Disability Status Scale [EDSS]-based model), (2) cognitive deterioration (Symbol Digit Modalities Test [SDMT]-based model), or (3) both (EDSS+SDMT-based model). The method was tested on an independent dataset and compared to the performance of two expert physicians.
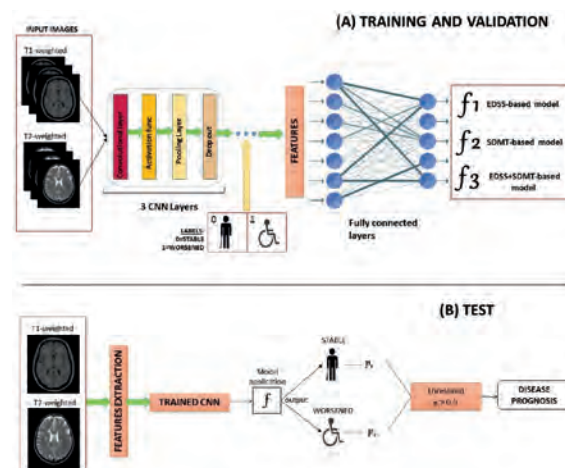
Fig. 1: A schematic overview of the deep-learning network architecture implemented to train and optimize the model (in A), and to finally test it on an independent dataset (in B).

Results: For the independent test-set, the model showed high predictive accuracy for clinical (83.3%) and cognitive (67.7%) worsening, although the highest accuracy was reached when training the algorithm using both EDSS and SDMT information (85.7%). Artificial intelligence classification performance exceeded that of two expert physicians (70% of accuracy for the human raters).

Conclusion: We developed a robust and accurate model for predicting clinical and cognitive worsening of MS patients after two years, based on conventional brain T2-weighted and T1-weighted baseline MRI. This algorithm may be valuable for supporting physicians in their clinical practice for the earlier identification of MS patients at risk of disease worsening.

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OPR-091

Functional brain connectome in ventral and dorsal variants of posterior cortical atrophy

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Background and aims: The study aims at investigating the functional brain connectome architecture in patients with ventral (vPCA) and dorsal (dPCA) variant of posterior cortical atrophy (PCA).

Methods: 36 PCA patients and 69 healthy controls underwent neurologic and cognitive examinations, and a brain MRI. Patients were categorized in vPCA (N=19) and dPCA (N=17) variants based on the symptoms prevalence, and were matched for age, sex, education, MMSE and disease duration. Topological brain network properties and regional functional connectivity (FC) were compared between groups using graph analysis and connectomics.

Results: Relative to controls, only vPCA patients showed global functional network alterations. Lobar network analysis showed common alterations of nodal strength within the occipital area in all PCA patients compared with controls, while vPCA showed additional involvement of temporal, parietal and occipital areas. No differences were observed between PCA variants. At the regional level, compared to controls, each PCA variant showed diffuse FC breakdown. Compared to dPCA, vPCA patients showed further FC breakdown within the occipital and parietal lobe, and between frontal, sensorimotor nodes and basal ganglia.

Conclusion: Our findings suggest the potentially high sensitivity of graph-analysis and connectomic in capturing signs of neurodegeneration in PCA variants. With sociodemographic and clinical features being equal, the vPCA group showed a more severe pattern of FC breakdown. Longitudinal investigations are needed to understand whether patterns associated with each PCA variant are able to predict distinct disease trajectories.

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OPR-092

Association of the Frailty Index with structural brain volumes in The Irish Longitudinal Study on Ageing (TILDA)

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Background and aims: Frailty is a recognised state of vulnerability in older adults. The Frailty Index (FI) measures frailty according to 32 deficits across multiple domains (Table 1) that accumulate with age and could have an impact in brain health. Our aim was to study brain volume signatures of a FI in The Irish Longitudinal Study on Ageing (TILDA).

Methods: We included TILDA wave 3 participants aged 65+ years who took part in a 3T MRI sub-study. Using Freesurfer we measured total cortical grey matter (GM) volume and regional GM volumes according to the Desikan-Killiany atlas. We performed partial correlation analyses with FI and Desikan GM regions volumes adjusted by age, sex and total brain volume; and performed a partial correlation tests to compare total cortical GM volume with each FI item adjusted by age and sex.

Results: In 407 participants, the volumes of regions related with prefrontal cortex and temporal cortex were negatively correlated with the FI and positive correlated with left precuneus (Figure 1). Only FI deficits related with functional impairments, osteoporosis and polypharmacy were associated with total cortex volume (Table 1).

FI item	R	p	FI item	R	p
Difficulty walking 100 m	-0.116	0.020	Cataracts	-0.088	0.079
Poor self rated physical health	-0.098	0.050	Arthritis	-0.014	0.785
Poor self rated vision	-0.110	0.028	Osteoporosis	-0.015	0.764
Poor self rated hearing	-0.107	0.031	Cancer	-0.003	0.946
Daytime sleepiness	-0.068	0.170	Varicose ulcer	-0.007	0.885
Polypharmacy	-0.103	0.038	Difficulty climbing one flight of stairs	-0.029	0.562
Knee pain	-0.114	0.022	Glaucoma/Age related macular degeneration	-0.057	0.256
Urinary incontinence	0.020	0.696	Self rated day-to-day memory	-0.006	0.911
Hypertension	0.008	0.865	Difficulty following a conversation with four people	-0.109	0.028
Angina	0.014	0.775	Difficulty stooping. kneeling or crouching	-0.075	0.131
Heart attack	-	-	Difficulty reaching above shoulder height	-0.088	0.078
Difficulty rising from a chair	-0.022	0.664	Difficulty pushing/pulling large objects	-0.052	0.301
Diabetes	-0.085	0.087	Difficulty lifting/carrying weights >=10lb	-0.042	0.405
High cholesterol	0.032	0.518	Difficulty picking up coin from table	-0.007	0.887
Irregular heart rhythm	0.035	0.479	Feeling lonely	0.026	0.605
Other CVD	-0.043	0.393	Stroke or TIA	-	-

Table 1. Differences in global cortex volume for each item within FI.
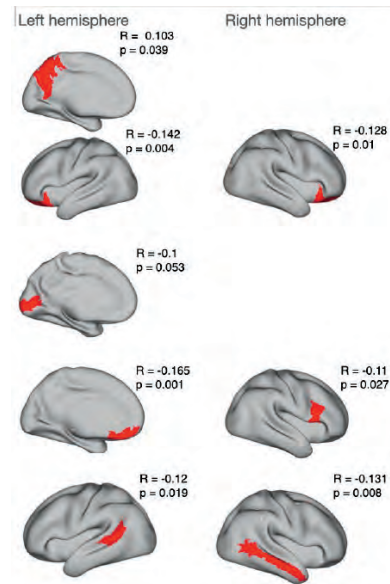
Figure 1. Significant partial correlation coefficient for brain volume by region and FI, adjusted by age, sex and total brain volume.

Conclusion: From a volumetric perspective, results suggest that frailty as captured by a FI may primarily involve the visual-executive-planification coordination systems. Further studies are necessary to replicate this finding with other FIs; compare associations with other frailty measurement tools; complement analyses with connectivity studies. A better understanding of the neuro correlates underlying frailty in older adults is needed for better prevention and treatment of age-related disability.

Disclosure: Nothing to disclose.

OPR-093

White matter microstructural changes in healthy aging: a DTI and NODDI study

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Background and aims: The goal of this study was to assess white matter (WM) integrity changes associated with aging using different diffusion metrics in a cohort of young and older adults.

Methods: 48 young (YC), aged 20–31 years, and 65 old controls (OC), aged 40–85 years, were enrolled and underwent multi-shell diffusion MRI. Fractional anisotropy (FA) and mean diffusivity (MD) maps were computed. Furthermore, Intra-cellular Volume Fraction (ICVF), Orientation Dispersion Index (ODI) and Isotropic Volume Fraction (ISO) maps were estimated using the NODDI model. Tract-Based Spatial Statistic analysis assessed significant metrics variability between the two groups ($p<0.05$, family-wise error corrected, 5,000 permutations).

Results: A widespread age-related reduction of FA was detected in supratentorial regions in OC relative to YC. A focal decrease of ICVF was found in OC relative to YC in the WM frontal fibers, specifically in the anterior sub-regions of corpus callosum, anterior corona radiata, frontal fibers of the superior longitudinal fasciculus, inferior fronto-occipital fasciculus and uncinate fasciculus. A widespread increase of MD and ISO was observed in OC relative to YC replicating the widespread WM alteration pattern obtained by FA results. Furthermore, an increased ODI of the WM fibers in OC relative to YC was identified, involving not only the supratentorial regions but also the cerebellar architecture.

Conclusion: The information provided by multi-shell diffusion MRI acquisition and multi-model reconstruction allowed us to quantify the extent of WM architecture deterioration with aging. Multiple diffusion metrics may lead to a reliable profiling of the healthy brain aging.

Disclosure: Supported by European Research Council (StG-2016_714388_NeuroTRACK).

Neurotraumatology

OPR-094

tDCS in patients with disorders of consciousness: a multicentre randomized double-blind sham-controlled clinical trial

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Background and aims: Left dorsolateral prefrontal cortex (LDLPFC) transcranial direct current stimulation (tDCS) has shown to transiently improve the level of consciousness of severely brain-injured patients with disorders of consciousness (DOC). However, no large-sample multicenter study confirmed its efficacy.
Methods: In this sham-controlled double-blind randomized trial, we investigated whether 4 weeks of tDCS improves consciousness/responsiveness in patients in prolonged DOC during rehabilitation stay. LDLPFC-tDCS was applied for 20 days (five days per week). We used to the Coma Recovery Scale-Revised (CRS-R) weekly and up to 3-months follow-up. We used a mixed general linear model to evaluate behavioral changes (4-week and 3-month) between active and sham groups. Differences between baseline and week-4 and month-3 were analyzed with a Mann-Whitney test.
Results: 62 patients (18 women, 30 MCS, 39 non-TBI, 260 ± 171 days post-injury, 33 active-tDCS) were treated without any serious adverse events. At the group level, no treatment effect was found. Subgroup analyses revealed a significant improvement for the active compared to the sham group for MCS (p=0.015) and TBI (p=0.023). No other comparisons were significant.
Conclusion: Our results suggest that at the group level, tDCS applied during rehabilitation does not significantly enhance patients' signs of consciousness. On the other hand, at 3-month follow-up, the subgroups of MCS and TBI patients demonstrated a better recovery in the treated compared to the sham groups. tDCS should be specifically applied in this subgroups of patients to promote their recovery.
Disclosure: Nothing to disclose.

OPR-095

Early post-traumatic seizures in hospitalized patients with traumatic brain injury

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Background and aims: Early post-traumatic seizures (EPTS) are a well-known complication of traumatic brain injury (TBI). EPTS increase the risk of secondary brain injury and are associated with worse outcomes. Use of seizure prophylaxis medication to prevent EPTS is controversial and not routine in many countries, including Norway. The purpose of this study was to expand the understanding of EPTS by examining incidence and risk factors in hospitalized TBI-patients.
Methods: Adult patients with TBI and neuroradiological evidence of intracranial injury admitted to Oslo University Hospital between 2015 and 2019 were identified from the Oslo TBI Registry – Neurosurgery. Demographic and clinical data including occurrence of seizures were retrieved from the registry. Univariate and multivariable logistic regression analyses were used to investigate risk factors associated with EPTS.
Results: 103 of 1.827 patients (5.6%) had new-onset seizures within the first week after TBI. Alcohol abuse [odds ratio 3.6 (95% confidence interval: 2.3–5.7), p<0.001], moderate and severe brain injury [2.2 (1.3–3.8), p=0.004 and 2.1 (1.2–3.6), p=0.012], brain contusion [1.6 (1.0–2.4), p=0.046] and subdural hematoma [1.6 (1.0–2.6), p=0.052] were associated with EPTS in the multivariable model.
Conclusion: In our material, EPTS occurred in 5.6% of hospital-admitted patients with TBI. Chronic alcohol abuse was the most significant independent risk factor, followed by moderate and severe brain injury. The results contribute to the discussion about preventive treatment of EPTS in certain risk groups.
Disclosure: None of the authors has any conflict of interest to disclose.

OPR-096

Autonomic dysfunction after moderate-severe traumatic brain injury: symptom spectrum and clinical testing outcomes

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Background and aims: Survivors of moderate-severe traumatic brain injury (msTBI) frequently experience troublesome unexplained somatic symptoms. Autonomic dysfunction may contribute to these symptoms. We aimed to provide a clinical description of subjective and objective autonomic dysfunction in msTBI.

Methods: We conducted two cohort studies. Cohort 1 comprises msTBI patients (with a control group) prospectively recruited from a regional referral TBI outpatient clinic, in whom we assessed burden of autonomic symptoms using the Composite Autonomic Symptom Score (COMPASS31) questionnaire. Cohort 2 comprises msTBI patients who had standard clinical autonomic function testing, retrospectively identified from referrals to a national referral autonomics unit.

Results: Cohort 1 comprises 39 msTBI patients (10F:20M, median age 40 years, range 19-76), with median time since injury 19 months (range 6–299), and 44 controls (22F:22M, median age 45, range 25–71). Patients had significantly higher mean scores than controls in the weighted total COMPASS-31 score (p<0.001) (Figure 1), and also gastrointestinal, orthostatic and secretomotor subscores (corrected p<0.05) (Figure 2). Total COMPASS31 score inversely correlated with subjective rating of general health (p<0.001, rs=-0.84). Cohort 2 comprises 18 msTBI patients (7F:11M, median age 44 years, range 21-64), with median time between injury and testing 57.5 months (range 2-416). Clinical autonomic function testing revealed a broad spectrum of autonomic dysfunction in 13/18 patients (Figure 3).
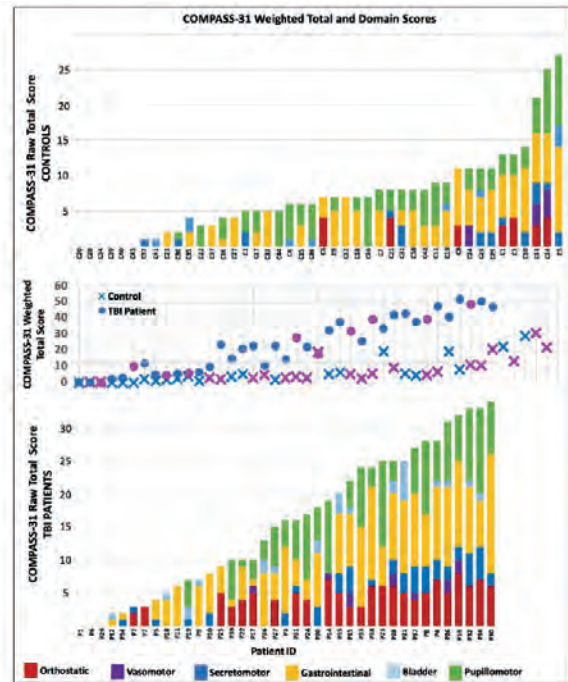
Fig. 1: Symptom burden, with weighted total COMPASS31 score for each patient (middle panel: circles=controls, crosses=TBI & pink=female, blue=male) and corresponding domain subscore distribution (top panel controls, bottom panel TBI).
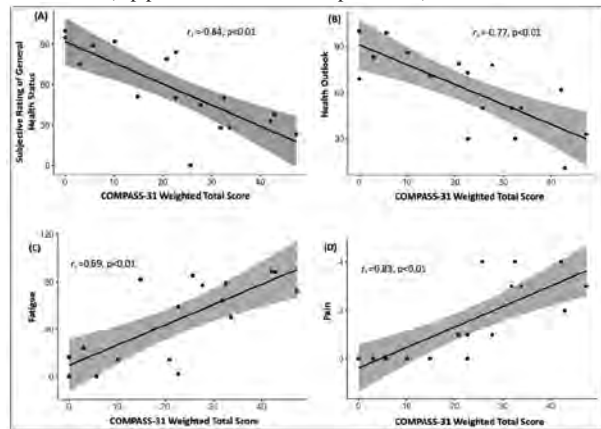
Fig. 2: Relationship between the COMPASS-31 weighted total score and (A) subjective rating of general health status, (B) Health Outlook, (C) Fatigue and (D) Pain.
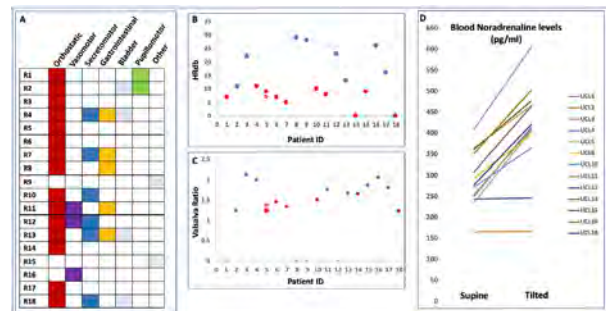
Fig. 3: For each patient (A) reported symptom types, (B) HRDB, measuring respiratory sinus arrhythmia. (C) Valsalva ratio. (D) Supine and tilted blood noradrenaline levels, where available. Red denotes abnormal for age.

Conclusion: Our results provide evidence for clinically relevant autonomic dysfunction after moderate-severe TBI, even at the chronic stage. We advocate for routine enquiry about potential autonomic symptoms, and demonstrate the utility of formal autonomic testing in providing diagnoses.
Disclosure: Nothing to disclose.

OPR-097

CT scans in acute traumatic brain injury: high interrater agreement in the emergency settings and during follow-up

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N. Semenovykh [3], R. Luzin [3], L. Khamidova [2], A. Yakovlev [1],
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Background and aims: Proper evaluation of computer tomography (CT) scans is crucial for prognosis of traumatic brain injury (TBI) outcome and treatment strategy choice; however, in the acute settings it should be done within a limited time period. We evaluated interrater agreement (IRA) of CT findings between interpretation of radiologists in emergency department at time of injury and compared to subsequent readings by radiologists free of time constraints.
Methods: We retrospectively evaluated brain CT scans of 53 patients with acute TBI, performed a non-reference interrater variability test and calculated Cohen's kappa score to compare scan analysis in emergency settings ("A" team) and in the follow up ("R" team).
Results: We found no statistically significant differences in the proportion of positive and negative findings between "A" and "R" team either by type of pathology or its combinations, or by time of day when acute assessment was performed. The highest IRA reaching 100% was observed for depressed skull fracture, epidural hematoma, and intraventricular hemorrhage (Fig. 1). For a linear skull fracture, subdural hematoma, and SAH we also found good IRA: Cohen's Kappa (k) was 0.89, 0.88 and 0.81 respectively. Moderate IRA rate was observed for brain concussions (k=0.58). In most cases, missing findings could be explained by small size and specific location of lesions.
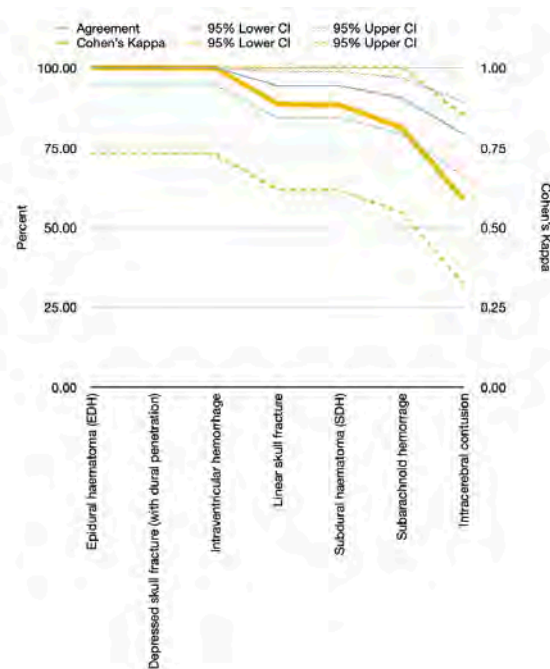
Figure 1. Cohen's Kappa for different type of pathology, analyzed in emergency settings and in the follow-up.
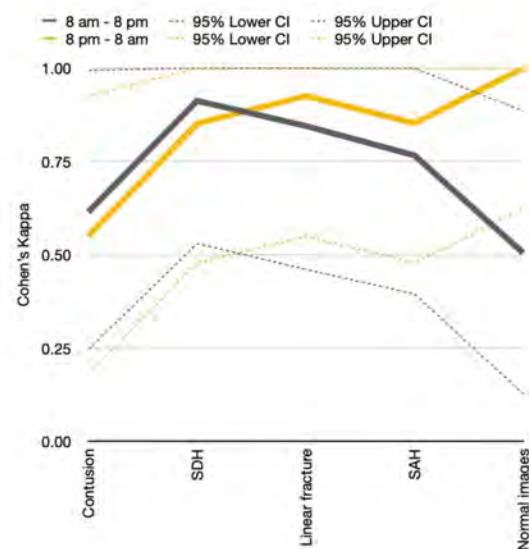
Figure 2. Cohen's Kappa for different type of pathology, analyzed in emergency settings by time of day when acute assessment was performed, and in the follow-up.

Conclusion: The interrater agreement demonstrated that despite time constraints, evaluation of TBI CT scans in emergency settings allows to correctly identify most lesions.
Disclosure: Nothing to disclose.

OPR-098

Risk of traumatic brain haemorrhage in patients on direct oral anticoagulant drugs (DOAC) or vitamin K antagonists (VKA)

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Background and aims: Patients on DOAC or VKA may have an increased risk for Intracranial haemorrhage (ICH) and poor clinical outcomes after mild traumatic brain injury (mTBI). Our aim was to evaluate the risk, incidence and clinical characteristics of ICH in patients who sustained mTBI.

Methods: We collected demographic data and clinical characteristics from the medical records of the 420 consecutive patients and compared them between patients with and without haemorrhage. In the end, we calculated risks and odd-ratio for haemorrhage and DOAC/VKA.

Results: In total, 35 received anticoagulant therapy, and 55 had traumatic haemorrhage (46 had no treatment, 4 VKA, 5 DOAC). Patients with haemorrhages were older (66.1 SD 19.6 vs 56.8 SD 24.5 years), stayed in the hospital longer (12.6 SD 14.7 vs 7.2 SD11.5 days), had higher initial blood sugar (7.7 SD 7.6 vs 6.8 SD 2.3 mmol/L), lower GCS (14.0 SD 2.7 vs 14.7 SD 0.9) and higher mRS at the admission (0.5 SD 1.4 vs 0.2 SD 0.7) and the discharge (1.9 SD 1.9 vs 1.2 SD 1.5). The absolute risk for haemorrhage for DOAC was 9.1%, and for VKA 7.3%, the relative risk was 0.6 and 0.3, and odds-ratio 1.82 (95% CI 0.65 to 5.10) and 2.45 respectively (95% CI 1.08 to 5.53).

Conclusion: The overall risk and incidence for intracranial haemorrhage after mild traumatic brain injury was low. Although the odds ratio for ICH was lower for patients on DOAC than for those on VKA, the difference was insignificant.

Disclosure: Nothing to disclose.

Monday, June 27, 2022
Neurocritical care

OPR-099

Consciousness in Neurocritical Care Cohort Study Using fMRI and EEG (CONNECT-ME): Level of consciousness in ICU

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Background and aims: Functional MRI (fMRI) and EEG in clinically unresponsive patients may reveal signs of covert consciousness. Research in so-called cognitive motor dissociation is primarily based on data from patients with chronic disorders of consciousness (DoC). CONNECT-ME aims to explore and facilitate individualized multimodal assessment for signs of residual consciousness in patients with acute and subacute DoC, using fMRI and EEG in the intensive care unit (ICU).

Methods: We assessed 87 acutely brain-injured adult patients for residual consciousness by clinical evaluation, fMRI (resting-state) and EEG (resting-state and passive stimulations), between 2016–2020. EEG and fMRI data were used as features in a cross-validated machine learning (ML) framework to predict level of consciousness (LoC) during ICU admission. Area under the curve (AUC) of ROC curves was used for comparison of prediction performance.

Results: Of 87 patients (50.0±18 years, 43% women), 51 (59%) were clinically in coma/unresponsive wakefulness (UWS) and 36 (41%) in minimally consciousness state (MCS) or better. During ICU-admission, 31 (36%) patients died, of whom 29 (94%) were in coma/UWS with main cause of death being withdrawal of life-sustaining-therapy due to poor prognosis (n=28). EEG was available for 86 patients, and fMRI for 64 patients. EEG visual, spectral and ML-derived characteristics predicted LoC (coma/UWS vs. ≥MCS) with AUC 0.78±0.06 (p<0.05), while fMRI mean connectivity measures (N=62) predicted LoC with AUC 0.75±0.06 (p<0.01). Combining EEG and fMRI (N=50) resulted in AUC 0.80±0.08; p<0.01.

Conclusion: In patients with acute/subacute DoC, EEG- and fMRI-measures predicted consciousness levels during ICU admission, both alone and in combination.
Disclosure: Nothing to disclose.

OPR-100

The impact of non-convulsive seizures and ictal–interictal continuum on the recovery of patients with a DoC

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Background and aims: Non-convulsive seizures (NCS) represent a confounding clinical factor that may hamper the assessment of consciousness and contribute to the high misdiagnosis rate. Recently, the American Clinical Neurophysiology Society provided definitions for NCS and for an intermediate pattern – the ictal-interictal continuum (IIC) – which cannot be qualified neither as non-convulsive ictal nor as interictal. These patterns with absent or only minimal clinical correlates occur with relative high frequency and are independently associated with a worse outcome in comatose patients. In this study, we investigated the prevalence of NCS/ICC and whether these patterns have a role in recovery of patients with a prolonged disorder of consciousness (DoC).

Methods: We recorded clinical EEG in 137 patients with a prolonged DoC. Patients were diagnosed as unresponsive wakefulness syndrome (UWS) or minimally conscious state (MCS) according to standardized behavioral criteria. The 6-months clinical outcome was dichotomously defined as an improvement in diagnosis (i.e. a MCS who emerged or a UWS who regained at least MCS) versus the absence of improvement. The presence of interictal epileptiform abnormalities or NCS/ICC was evaluated by two blinded board-certified neurophysiologists.

Results: Epileptiform abnormalities were identified in 38% of DoC patients and specifically the NCS/ICC pattern was found in 14.6%. The presence/absence of NCS/ICC was not related to etiology, diagnosis or antiepileptic therapy. Using logistic regression, we found that the presence of NCS/ICC was a significant predictor of lack of clinical improvement (OR 9.95).

Conclusion: The occurrence of NCS/IIC patterns should be carefully investigated to identify treatable causes of unresponsiveness.
Disclosure: This work was supported by ERA PerMed JTC2019 "PerBrain".

OPR-101

Electroencephalography of mechanically ventilated patients at high risk of delirium

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Background and aims: Neurophysiological exploration of ICU delirium is limited. Here, we examined EEG characteristics of medical-surgical critically ill patients with new onset altered consciousness state at high risk for ICU delirium.

Methods: Pre-planned analysis of non-neurological mechanically ventilated medical-surgical ICU subjects, who underwent a prospective multicenter randomized, controlled EEG study (NCT03129438, April 2017– November 2018). EEG characteristics, according to the 2012 ACNS nomenclature, included background activity, rhythmic periodic patterns/epileptic activity, amplitude, frequency, stimulus-induced discharges, triphasic waves, reactivity and NREM sleep. We explored EEG findings in delirious vs. non-delirious patients, specifically focusing on presence of burst-suppression and rhythmic periodic patterns (ictal-interictal continuum), and ictal activity.
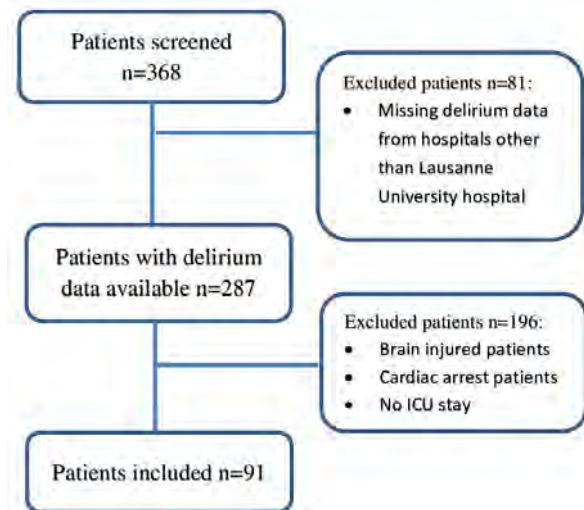
Study flow chart

Results: We analyzed 91 patients (median age, 66 years) who underwent EEG because of new onset altered consciousness state at a median 5 days from admission; 42 patients developed delirium (46%). Burst-suppression (10 vs. 0%, p=0.02), rhythmic/periodic patterns (43% vs. 22%, p=0.03) and epileptiform activity (7 vs. 0%, p=0.05) were more frequent in delirious vs. non-delirious patients. The presence of at least one of these abnormal EEG findings (32/91 patients; 35%) was associated with a significant increase in the likelihood of delirium (42 vs. 15%, p= 0.006). Cumulative dose of sedatives and analgesics, as well as all other EEG characteristics, did not differ significantly between the two groups.
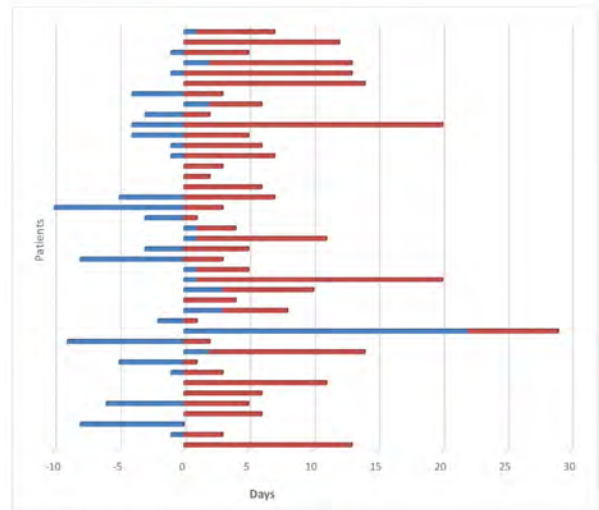
EEG chronologic relationship between delirium duration. In blue: number of days with delirium before EEG; in orange, number of days with delirium after EEG.
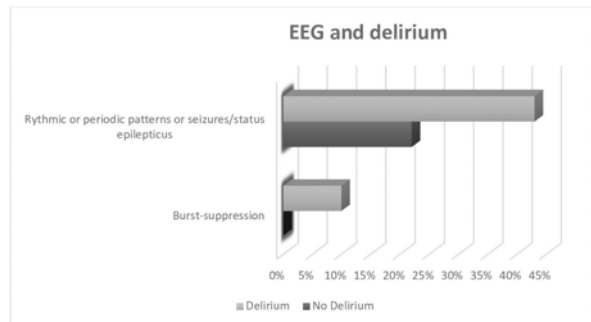
EEG characteristics between two groups

Conclusion: In mechanically ventilated non-neurological critically ill patients with new onset alteration of consciousness, EEG showing burst-suppression, rhythmic or periodic patterns, or seizures/status epilepticus indicate an increased risk of ICU delirium.

Disclosure: Swiss National Science Foundation (SNSF).

OPR-102

Consciousness in Neurocritical Care Cohort Study Using fMRI and EEG (CONNECT-ME): Clinical outcome at 3- and 12-month

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Background and aims: Clinical prognosis in unresponsive patients following brain-injury may be improved with functional MRI (fMRI) and EEG. We investigated prediction of 3- and 12-month outcome in patients with acute/subacute disorders of consciousness (DoC) using fMRI and EEG.

Methods: We assessed 87 acutely brain-injured adult patients in the intensive care unit with clinical and multimodal brain assessment including fMRI (resting state) and EEG (resting state and passive stimulations) between 2016–2020. EEG and fMRI data were used as features in a cross-validated machine-learning framework to predict 3- and 12-month clinical outcome (dichotomized at GOS-E>3). Area under the curve (AUC) of ROC-curves was used for comparison of prediction performance.

Results: Follow-up data was available for 85 patients (97.7%). At 3- and 12-months, 37 (42.5%) and 40 (47.1%) had died, respectively. Prediction performance of 3-month outcome was AUC-ROC: 0.70 ± 0.06 (p=0.07; n=70), 0.57 ± 0.09 (p=0.24; n=62), and 0.65 ± 0.05 (p=0.24; n=50) for EEG, fMRI, and EEG and fMRI combined, respectively. Corresponding prediction performance of 12-month outcome was AUC-ROC: 0.78 ± 0.06 (p<0.01), 0.68 ± 0.05 (p=0.07) and 0.70 ± 0.07 (p<0.05). Unfavorable outcome at 3- and 12-months was significantly associated with age>60 years (OR 3.43, 95% CI 1.0–16.5, p<0.05; OR 8.06 (2.4–38.4), p<0.001), and coma/unresponsive wakefulness at time of EEG/fMRI (OR 3.0 (1.1–8.9), p<0.05; OR 7.38, (2.8–20.8), p<0.001) and at discharge (OR 20.8, (3.9–518), p<0.001; OR 16.1, 95% CI 4.9–77.1, p<0.001), respectively.

Conclusion: We observed evidence that clinical status at 3- and 12-months was predicted by EEG and fMRI, with significantly above chance performance at 12-months. Age and consciousness during admission was also predictive of future clinical outcome.

Disclosure: Nothing to disclose.

OPR-103

Reliable prediction of poor outcome in postanoxic coma using EEG in a four-electrode frontotemporal montage

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Background and aims: EEG background patterns in the first 24h after cardiac arrest (CA) are highly valuable for prognostication in postanoxic coma. However, limited resources in many hospitals hamper widespread implementation of continuous EEG monitoring. In the present study, the reliability of EEG in a four-electrode frontotemporal montage for prediction of poor outcome was investigated.

Methods: Continuous EEG registrations of 154 consecutive cardiac arrest patients were available from a multicenter prospective cohort study. Five-minute EEG epochs at 12 and 24h after CA were reviewed by three blinded experts in both a 9-channel bipolar (standard) montage and a four-channel frontotemporal (FT) montage (T3-Fp1, Fp1-Fp2, Fp2-T4, T3-T4). EEG background patterns were scored according to the American Clinical Neurophysiology Society nomenclature. Poor outcome was defined as a best Cerebral Performance Category score of 3–5 at six months after CA. Interrater agreement was determined using the intraclass correlation coefficient (ICC).

Results: 152 Patients had EEG available at 24h after CA, of which 74 (49%) had poor outcome. Suppression, burst-suppression with identical bursts, or low voltage EEG was present in 25 patients and predicted poor outcome at 24h with 100% specificity (95% CI 95–100%) in both montages. Sensitivity was 34% (95% CI 23–46%) for the standard montage and 31% (95% CI 21–43%) for the FT montage. ICC for scoring EEG background pattern was 0.94 for both montages.

Conclusion: EEG with only four electrodes in a frontotemporal montage seems reliable for prognostication after cardiac arrest. These results suggest the possibility to reduce the number of EEG electrodes without compromising accuracy of prognostication after cardiac arrest.

Disclosure: Nothing to disclose.

OPR-104

Strengths and limits of robotic-guided continuous Transcranial Color Doppler

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Background and aims: Transcranial Color Doppler (TCD) can be used to monitor cerebral blood flow in intensive and operative settings; however, its applicability has been limited because of the need of specialized manpower during the whole examination. We evaluated the strengths and limits of artificial intelligence assisted robotic TCD (AI-TCD) for prolonged monitoring in different clinical settings.

Methods: Instructed sonographers at our two large university centers used AI-TCD (NovaGuide™ Intelligent Ultrasound, NovaSignal Corp, USA) to find the middle cerebral artery flow and automatically track the signal in case of head movements. Patients were investigated in different settings (outpatient clinic, stroke unit, neuro-intensive care unit (ICU), anesthesiology ICU, neuroradiological and cardiological interventional suites and operation theater for carotid endarterectomy). Examinations characteristics including duration, technical aspects and adverse effects were collected.

Results: We performed 47 monitorings on 38 patients (27 in Linz and 11 in Padova). AI-TCD examinations were safe in all patients. Yet, the examination was feasible in 5 of 7 settings. It was not possible during carotid endarterectomy, since the device was interfering with the surgical field, and during endovascular intracranial procedure as the system was not radiotransparent and did not allow radiological intra-procedural control.

Conclusion: AI-TCD allowed excellent and practical continuous data acquisition in most intensive, interventional and acute clinical settings. Further developments are needed to extend the range of settings in which this new technology might be applied.

Disclosure: Nothing to disclose.

Autonomic nervous system diseases

OPR-105

EAN-EFAS Survey on cardiovascular ANS disturbances following a SARS-CoV2 infection or COVID-19 vaccination

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Background and aims: To run a survey among European neurological and interdisciplinary autonomic nervous system (ANS) laboratories on newly-diagnosed or significantly deteriorated cardiovascular ANS disorders following a SARS-CoV2 infection or COVID-19 vaccination.

Methods: We invited 83 laboratories in 22 European countries to answer a web-based survey.

Results: 45 laboratories completed the survey (54%). Postural orthostatic tachycardia syndrome was the most frequently reported newly-diagnosed or deteriorated cardiovascular ANS disorder following a SARS-CoV2 infection or COVID-19 vaccination (Figure 1). 47% of the survey participants reported on persons with orthostatic complaints but negative tilt-table findings after a SARS-CoV2 infection, 16% on patients with new onset of psychogenic pseudosyncope following the infection. Newly-diagnosed ANS disorders were deemed likely associated with the SARS-CoV2 infection or COVID-19 vaccination by 53% and 31% of the responders. Deterioration of previously-diagnosed ANS disorders was deemed likely associated with the infection by 79% of the responders, with the vaccination by 22% thereof. A follow-up was available in 54% of cases. 69% of patients with newly-diagnosed cardiovascular ANS disorders following a SARS-CoV2 infection and 78% of those after a COVID-19 vaccination improved at follow-up. In patients with previously-diagnosed ANS disorders who had worsened after a SARS-CoV2 infection or COVID-19 vaccination, recovery was observed by 50% and 65% of the survey participants.
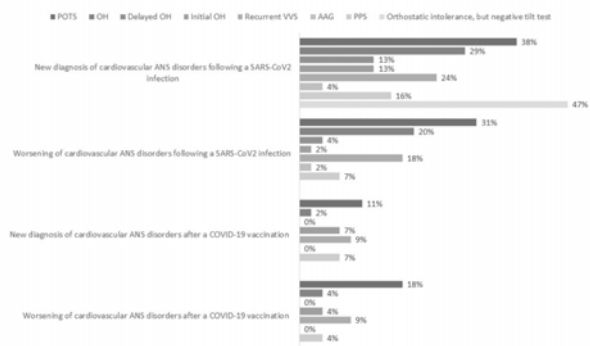
Figure 1: Percentage of European ANS laboratories reporting new diagnosis or significant deterioration of cardiovascular ANS disorders following a SARS-CoV2 infection or COVID-19 vaccination. ANS, autonomic nervous system; POTS, Postural orthostatic tachycardia syndrome.

Conclusion: Cardiovascular ANS disorders may develop or worsen following a SARS-CoV2 infection, while the association with a COVID-19 vaccination remains controversial. A specialized diagnostic work-up helps exclude autonomic disorders in persons with unspecific orthostatic complaints or syncope lookalikes following a SARS-CoV2 infection.

Disclosure: The authors declare no conflicts of interest. This project was approved by the EAN Scientific Committee and by the Board of the European Federation of Autonomic Society. We received administrative support from the EAN Head Office.

OPR-106

Pelvic autonomic dysfunction is common in patients with Pure Autonomic Failure

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Background and aims: Cardiovascular autonomic failure is the hallmark finding in Pure autonomic failure (PAF) however other autonomic functions are likely to be affected. This study aims to characterise genitourinary dysfunction in PAF patients and explore their relationship with cardiovascular autonomic dysfunction.

Methods: In this cross-sectional observational study, PAF patients who underwent cardiovascular autonomic testing completed self-administered questionnaires evaluating urinary and sexual symptoms and a 3-day bladder diary measuring fluid intake and urine output. Demographic, clinical features, disease duration and related medical comorbidities were assessed.

Results: 25 PAF patients (10 males) were included (mean age 71+8 years; disease duration 13+8 years). Lower urinary tract symptoms were reported by 96% (24/25) using the Urinary Symptom Profile and sexual dysfunction was present in 84% using the Arizona Sexual Experience Scale. Overactive bladder symptoms (n=23; 92%; median overactive subscore 8 (IQR 3–11)) were more frequently reported than voiding symptoms (n=19; 76%; median low stream subscore 2 (IQR 1–3)). Four (16%) patients required catheterisation. 22 patients completed a bladder diary and 19 (86%) had nocturnal polyuria (NP), defined as NP index > 0.3 (nocturnal urine volume/24-hour urine volume), mean NP index 0.45 (range, 0.20–0.73). There were no significant correlations between age, disease duration and cardiovascular parameters (orthostatic BP drop, supine hypertension, respiratory sinus arrhythmia, Valsalva ratio) with urogenital parameters including need for catheterisation and degree of NP (p>0.05).

Conclusion: NP and genitourinary symptoms are common in PAF. The pathophysiology of NP in PAF is likely to be multifactorial and may not only be explained by cardiovascular autonomic failure.

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OPR-107

The European Network of Autonomic Nervous System laboratories: an EAN-EFAS survey

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Background and aims: The aim of this EAN-EFAS survey was to identify neurology-driven or interdisciplinary autonomic nervous system (ANS) laboratories in Europe, to describe their personnel, equipment and patient characteristics and to explore differences between European regions.

Methods: We contacted national neurological societies of 51 European countries to identify ANS laboratories in each country. Each identified laboratory, answered a specifically designed survey evaluating personnel, equipment and patient characteristics of the laboratory.

Results: 38 national societies provided information about their country (65%), altogether identifying 83 ANS laboratories in 22 countries, 45 thereof (54%) answered the survey (Figure 1). All laboratories perform cardiovascular and 84% perform sudomotor evaluation. Blood testing for catecholamines and antibodies are performed in 64% and 56%, respectively. 62% of the laboratories perform epidermal nerve fiber density analysis. Each laboratory has a median of 2 consultants (0–10), 1 resident (0–10), 1 technician (0–8), and 1 nurse (0–5). The median number of tilt-up table tests/laboratory/year is 100 (0–4.000). An ANS outpatient clinic is available in 34 (76%) centers with a median of 200 (6–5.544) outpatient visits/year. Inpatient admissions are available in 41 (91%) centers with a median of 20 (0–300) inpatient visits/year. There is a significant difference in available ANS services between different European regions (11/21 countries from south/east/wider Europe vs 11/12 countries from north/west Europe, p=0.021).

Distribution of laboratories for testing of the autonomic nervous system across Europe (Blue indicates county with at least one laboratory, red indicates country with no laboratory, and dark grey indicates country from which no response was obtained).

Conclusion: This survey highlights significant differences in the availability of care for people with ANS disorders, stressing the need to improve access to diagnostic and treatment facilities across Europe.

Disclosure: The authors declare no conflicts of interest. This project was approved by the EAN Scientific Committee and by the Board of the European Federation of Autonomic Society. We received administrative support from the EAN Head Office.

OPR-108

A clinico-genetic study based on the Innsbruck MSA Registry (IMSA-R)

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Background and aims: While genetic factors may contribute to the pathogenesis of Parkinson's disease (PD), multiple system atrophy (MSA) is generally considered a sporadic disease. However, neuropathologically confirmed cases of MSA with positive family history (FH) for MSA and other neurodegenerative disorders have been described. **Methods:** Here we screened the Innsbruck MSA (n=255) and Parkinson Registry (n=368) for patients with MSA or PD providing informative FH for neurodegenerative disorders among 1st to 3rd degree relatives and compared their prevalence with those from published population-based studies. **Results:** Forty percent of MSA and 54% of PD cases (p=0.023) had a positive FH for neurodegenerative disorders, with parkinsonism being most prevalent [18.3% vs. 25.6%; p=0.108]. Familial clustering ($\geq$2 affected relatives) occurred in 9.5% of MSA and 17.3% of PD cases (p=0.065). Median age at onset was comparable between FH-positive MSA and PD cases [55 vs. 56 years; p=0.712], but differed in FH-negative ones [58 vs. 63 years; p=0.036]. Both in PD and in MSA, we observed no differences in the initial clinical presentation between FH-positive and negative cases. The prevalence of first-degree FH for parkinsonism was comparable between the MSA and PD cohort [10.4% (95% CI 6.3–16.6) vs. 17.1% (95% CI 12.6–22.7); p=0.079], whereas both exceeded previously reported prevalence rates in population-based elderly controls [5.6% (95% CI 5.1–6.1); vs. MSA p=0.012; vs. PD p<0.001]. **Conclusion:** The higher prevalence of positive FH for parkinsonism observed in patients with MSA compared to the general population suggests that genetic, yet unidentified, factors may play a role in the pathogenesis of the disease.

OPR-109

Hemodynamic determinants of supine hypertension in neurogenic orthostatic hypotension

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Background and aims: Patients with neurogenic orthostatic hypotension (nOH) often exhibit supine hypertension. The mechanisms underlying supine hypertension are poorly understood.

Methods: We performed a retrospective analysis of continuous blood pressure (BP) patterns in 65 nOH patients who underwent a tilt table test and compared the means of the periods -180 to -20 seconds before, and 170–190 seconds after the head-up tilt. Mean arterial pressure (MAP) and its constituents heart rate (HR), stroke volume (SV) and total peripheral resistance (TPR) were analysed. The measures were compared between two groups, which were split based on the median systolic supine BP.

Results: Patients with nOH and a high supine BP had a higher supine TPR than those with low supine BP. HR and SV in a supine position did not differ between groups. Three minutes after tilt only the MAP differed between the two groups, and HR, SV and TPR did not. Notably, in those with nOH and high supine BP, TPR did not change upon tilting. The differences between the supine values and the values three minutes after tilt indicate a smaller SV fall, smaller TPR increase, and a larger BP decrease in the high supine BP group (Figure 1).
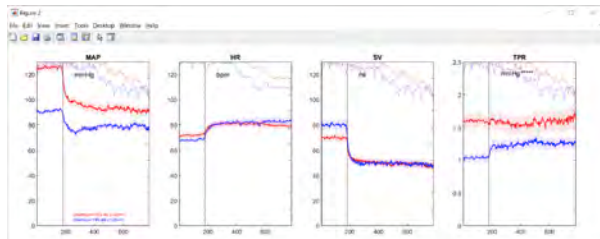
Figure 1

Conclusion: Supine hypertension in nOH is primarily driven by a high TPR in supine position and associated with a larger BP fall upon standing.

Disclosure: The authors declare that there is no competing interest related to this work.

Cerebrovascular diseases: Clinical presentation and cognition

OPR-110

Novel patterns of stroke neural damage link endovascular thrombectomy to the occurrence of spatial delusions

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Background and aims: Behavioural changes are disturbing consequences of stroke, whose occurrence depends on strategic patterns of lesion and disconnection. Spatial delusions are right hemisphere disconnection syndromes characterized by the firm belief of place reduplication, transformation or mislocation. Endovascular thrombectomy may modify the classical anatomical distribution of brain infarcts. We aimed to determine whether endovascular thrombectomy is associated with a higher incidence of spatial delusions and what are the anatomical determinants of this putative association.

Methods: We performed a prospective, cumulative, case-control study, from December/2016 to June/2021. Acute right hemisphere ischemic strokes patients were consecutively included. The main outcome was the occurrence of spatial delusions. Stroke lesions were delimited and structural disconnection maps were inferred based on the tract-wise analysis of 7 Tesla tractographies.

Results: In a sample composed by 78 cases and 212 stroke controls, endovascular thrombectomy was significantly associated with the occurrence of spatial delusions (multivariate linear regression model including age, clinical severity, vascular territory, inter-hospital transfer and endovenous thrombolysis: OR 2.46, 95% CI 1.18 to 5.16, p=0.017). The structural disruption proportion and the beta coefficient maps associated with endovascular thrombectomy had a significantly higher spatial correlation with the structural disruption maps of cases than controls (p<0.001;Fig.1).

Endovascular thrombectomy was found to share with spatial delusions significant clusters of lesion and structural disconnection (p<0.05) overlapping thalamo-orbitofrontal fibers and anterior temporal regions (Fig.2).
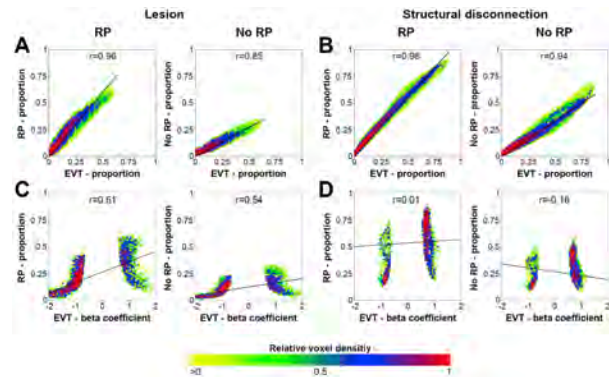
Figure 1:. Spatial correlations between: proportion map of endovascular thrombectomy (EVT) and voxel lesion/disconnection (A/B); beta coefficient map of endovascular thrombectomy and voxel lesion/disconnection (C/D). RP, reduplicative paramnesia.
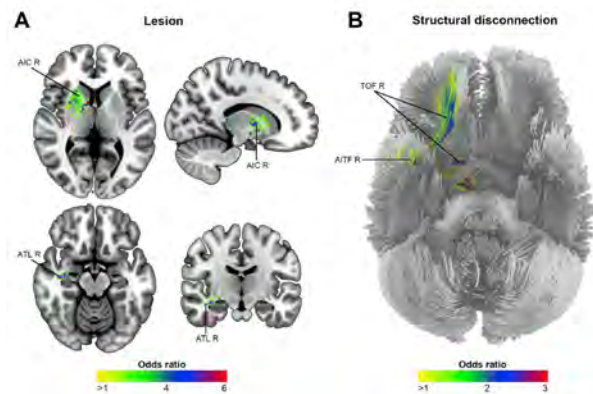
Figure 2:. Statistically significant clusters of the conjunction analysis between the structural disconnectome map of reduplicative paramnesia and the endovascular thrombectomy associated lesion/disconnection maps (A/B;), regressing for confounders.

Conclusion: This study suggests that endovascular thrombectomy is an independent predictor of the occurrence of spatial delusions after right hemisphere stroke, by novel patterns of lesion and structural disconnection.

Disclosure: Nothing to disclose.

OPR-111

Remember that? Previous stroke as independent recurrence risk factor for global transient amnesia

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Background and aims: Transient global amnesia (TGA) is generally described as a sole and benign event. Recurrence varies between 2,9–26,3% and risk factors (RF) are poorly defined. Our aim was to describe a population of patients diagnosed with TGA in the emergency department (ED) and evaluate possible RF for recurrence and development of dementia.

Methods: Retrospective study of data from patients discharged from the ED with the diagnosis of TGA between 2010–2020 with descriptive and comparative analysis for identification of recurrence RF.

Results: 124 patients were included, 84 were female(68%) and mean age was 63 years (SD±8). Most episodes lasted between 3 and 6 hours(23%). One possible trigger was identified in 49 patients(41%). 12 patients had, at least, another episode(10%), most of which occurred after 1 year. Gender, age, episode duration, reported trigger, headache, vascular RF, blood glucose, hemoglobin A1C, MRI and EEG alterations weren't associated with recurrence. Previous stroke history was associated with a new episode [OR: 9, (CI 95% 1.2–77.5), p=0,036]. In the follow-up, 22 patients had an alternative diagnosis (13%). The most frequent were functional disorder (n=6) and epileptic transient amnesia (n=8). In our population, only 1 patient had a diagnosis of dementia within 5 years follow-up.

Conclusion: We present a relatively large population with long follow-up and TGA diagnosis. Recurrence was similar to those reported in the literature and the episode's intrinsic characteristics did not predict recurrence. Notably, the presence of a previous stroke was associated significantly with new episodes, which, to our knowledge, is not described in the existing literature.

Disclosure: Nothing to disclose.

OPR-112

Masseter area is associated with cognitive and motor performance but not with white matter hyperintensity volume

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Background and aims: Masseter sarcopenia is an indicator of physical frailty, which in turn is associated with vascular aging. Vascular aging is associated with cognitive impairment and functional decline. However, documentation on the relation between masseter sarcopenia and cognitive impairment, and the relation to cerebral small vessel disease findings in brain imaging is lacking. We aimed to identify potential correlation between masseter area, cognitive and motor performance, and white matter hyperintensities (WMH).

Methods: The Helsinki Small Vessel Disease study comprised 152 patients (age 65–75 years) who underwent brain magnetic resonance imaging (MRI) and comprehensive neuropsychological and clinical evaluation. WMH volume was obtained with automated segmentation. Masseter muscle area was evaluated visually according to previously set standards.

Results: Analysed with linear regression models adjusted for age, sex, and education, masseter area was significantly associated with global cognition (stand.β 0.28, p=0.001), processing speed (β 0.28, p=0.001), and executive functioning (β 0.21, p=0.013) but not with memory (β 0.16, p=0.055). Masseter area was also associated with Timed Up and Go test (β -0.26, p=0.004) and walking speed (β 0.27, p=0.003), but not with grip strength (β 0.12, p=0.057) after adjustments. No association was found between masseter area and WMH volume (β 0.03, p=0.771). Additional controlling for missing teeth had no effect on the results.

Conclusion: We found that masseter area is associated with both cognitive and motor performance. However, WMH volume did not correlate with masseter area, so according to our study WMH volume does not seem to be the link between sarcopenia and cognitive impairment.

Disclosure: JK and JL are shareholders at Combinostics Oy. JL has received lecture fees from Merck and Sanofi (paid to the employer). The other authors report no competing of interests.

OPR-113

The effect of neurosychological findings of stroke on the risk of recurrent stroke

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Background and aims: In patients characterized by executive dysfunction, vascular depression has been clinically termed as "depression-executive dysfunction syndrome". Despite enthusiasm for this approach, few studies have examined the predictive utility of cognitive functions in understanding the course and outcome of post-stroke depression (PSD).

Methods: The current study involved the patients with ischemic stroke who were admitted during the time period from April 2017 to December 2018. Data were obtained from the evaluations performed by the research staff involved in the clinical research study. All participants were provided a large battery of neuropsychological tests that covered cognitive domains relevant to the understanding of depression. To determine which factors were independently associated with stroke recurrence and cardiovascular event, a multiple logistic regression method was performed using variables found to be significant (p<0.05) in the univariate analyses.

Results: The study included 440 patients who had depression. After 52 weeks of follow-up, 371 patients (84%) completed the study. Among vascular risk factors age, hypertension, large-artery disease and atrial fibrillation were significantly higher in patients with stroke recurrence. In addition, executive function disorder (p=0.001), reduced processing speed (p=0.01), episodic memory disorder (p=0.005) and language processing disorder (p=0.001) were significantly associated with stroke recurrence.

Conclusion: The current study supports the importance of executive dysfunctions in predicting recurrent strokes. This result warrants further studies to demonstrate the effects of depression treatment on stroke recurrence.

Disclosure: Nothing to disclose.

OPR-114

EEG for post-stroke delirium monitoring

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Background and aims: Establishing the diagnosis of post-stroke delirium (PSD) remains challenging, especially in patients with dysphasia. The EEG parameter relative delta power (RDP) has been associated with the presence of postoperative delirium; however, it remains unclear whether these results can be extrapolated to patients with PSD. The aim of this study was to explore whether RDP may differentiate between patients with and without delirium after left middle cerebral artery (MCA) infarction.

Methods: In a dataset of 514 patients with acute ischemic stroke (AIS), we used a retrospective chart review based on DSM-5 criteria to diagnose PSD within the first week after stroke onset. A subset of 20 patients was randomly selected, all with left MCA infarction: 10 with and 10 without PSD. For each patient, the first 8 artifact-free epochs of 8 seconds were selected and RDP (0.5–4Hz) was computed using a fast Fourier transformation and averaged over all channels and epochs. Fp1 and Fp2 were excluded. RDP was compared using a Mann-Whitney-U-test.

Results: Median RDP among all channels and epochs, was significant higher in patients with PSD (0.587; IQR 0.241) compared to patients without PSD (0.408; IQR 0.183) (p-value=0.043). When studying difference in RDP between patients with and without PSD among all derivations (channel against average reference), RDP in P3 was associated with the lowest p-value (0.009).

Conclusion: Preliminary results suggest that RDP differs between patients with and without PSD after left MCA infarction, implicating a potential role of this EEG parameter for objective PSD monitoring.

Disclosure: Nothing to disclose.

OPR-115

Crossed cerebellar diaschisis worsens the clinical presentation in large vessel occlusion acute ischemic stroke

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Background and aims: The cerebellum modulates both motor function and higher cortical processes through cortico-cerebellar loops. Crossed cerebellar diaschisis (CCD) refers to the association between a local supratentorial brain lesion and a decrease of contralateral cerebellar blood flow and metabolic activity. The aim of this study is to determine the prevalence of CCD by whole brain perfusion CT (PCT) realized in acute ischemic stroke due to anterior circulation large vessel occlusion (LVO) and the clinical and radiologic factors that affect the occurrence of crossed cerebellar diaschisis.

Methods: Patients with anterior LVO who benefited from both PCT and mechanical thrombectomy were retrospectively identified from our stroke alert registry (January 2017 to July 2021). CCD was defined as lower blood volume and flow in the cerebellum contralateral to stroke on PCT. Clinical and radiological factors were compared between patient with and without CCD.

Results: Out of the 296 thrombectomy considered, 131 patients met inclusion criteria. CCD was present in 89 patients (68%). NIHSS at admission was significantly higher when CCD was present (11.5 ± 8.3 vs 18.0 ± 6.1, p<0.001). CCD was also associated with higher volume of ischemic core ($13.5ml\pm26.1$ vs $32ml\pm35.8$, p=0.001) and hypoperfusion ($68.9ml\pm50.9$ vs $119ml\pm60.2$, p<0.001).

Conclusion: CCD occurs in 68% of patients with anterior LVO and is associated with higher NIHSS on admission and with higher ischemic penumbra and core volumes. These results suggest that part of the LVO initial clinical deficit may be related to superimposed cerebellar dysfunction.

Disclosure: Nothing to disclose.

Neurogenetics 1

OPR-116

Characterisation of the St. Gallen von Hippel-Lindau disease-Cohort: confirmatory and surprising results

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Background and aims: The von Hippel-Lindau (VHL) disease is a rare autosomal dominant tumour predisposition syndrome. Penetrance is greater than 90% by the age of 65 years. VHL disease is caused by genetic aberration of the short arm of chromosome 3 (3p25-p26), 50% of germline mutations arise spontaneously (non-familial). Retinal capillary hemangioblastoma, cystadenoma of the epididymis or the broad ligament and endolymphatic sac tumours were the earliest tumours that developed. CNS and/or spinal hemangioblastomas, phaeochromocytomas and pancreatic cysts appeared somewhat later. Clear cell renal cell carcinomas and pancreatic neuroendocrine tumours were the last to be diagnosed.

Methods: To evaluate the genotype and phenotype of the St. Gallen VHL cohort and to disclose novel tumour manifestations and comorbidities.

Results: The cohort comprised 31 patients from 16 different families. The age of all patients ranged from 24 to 73 years. The median age is 43 years. Three of the 31 patients had already died. The most common organ lesions were renal cysts (87%), pancreatic cysts (87%), spinal hemangioblastomas (74%), infratentorial hemangioblastomas (71%) and retinal angiomas (61%). Rare tumours were hemangioblastomas of peripheral nerves (13%), cystadenoma of the epididymis (13%), supratentorial hemangioblastomas (10%) and pancreatic neuroendocrine tumours (7%).

Conclusion: We here provide a comprehensive genotype/phenotype characterisation of a large cohort of the von-Hippel Lindau disease in Switzerland. Formally unknown comorbidities, unusual manifestation sites of supratentorial hemangioblastomas, trigeminal neuralgia, hemangioblastomas of the peripheral nerves among other findings will be reported. Intra-familiar heterogeneity is obvious, but may be related to pre-symptomatic testing in familiar cases

Disclosure: Nothing to disclose.

OPR-117

Clinico-genetic spectrum of limb-girdle muscular weakness in Austria: a multi-centre cohort study

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Background and aims: Molecular diagnosis of hereditary myopathies with limb-girdle muscular weakness (LGW), a genetically heterogeneous group of diseases, remains challenging to this date. In our study, we aimed to present clinical data of a large cohort of patients, unravelling the genetic nature of LGW.

Methods: Patients with LGW and a suspected association with hereditary myopathies were included in this nationwide cohort study. Demographic and clinical parameters associated with genetic aetiologies were evaluated. Furthermore, we assessed the predictive value of these parameters for the identification of causative variants in genetic analyses.

Results: Molecular diagnoses were identified in 62% (75/121) of the study cohort. Next-generation sequencing (NGS) identified a higher proportion of solved cases than single gene testing (77.3% vs. 22.3%). The median time from symptom onset to genetic diagnosis was 8.9 years (IQR 3.7–19.9) for single gene testing and 17.8 years (IQR 7.9–27.8) for NGS. Variants in the genes for CAPN3 (n=9), FKRP (n=9), ANO5 (n=8), DYSF (n=8) and SGCA (n=5) were the five most common molecular diagnoses, together accounting for 32.2%. Causative variants were significantly associated with a younger age at symptom onset (p=0.043), elevated CK activity levels (p=0.024) and myopathic changes on electromyography (p=0.007), but inversely associated with isolated upper limb weakness at onset.
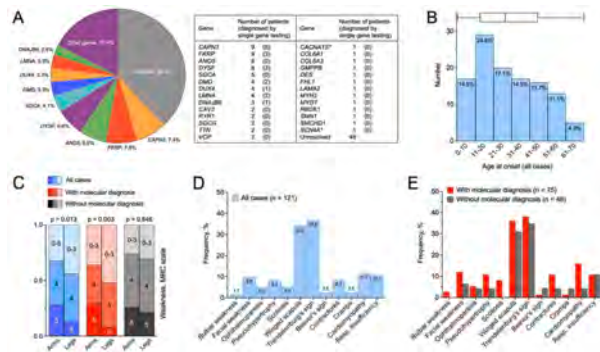
Fig. 1 Genetic spectrum and clinical characteristics of patients with LGW. (A) Causative variants. (B) Age at onset. (C) Affected muscle groups. Frequency of clinical symptoms in total cohort (D) and in patients with or without molecular diagnosis.
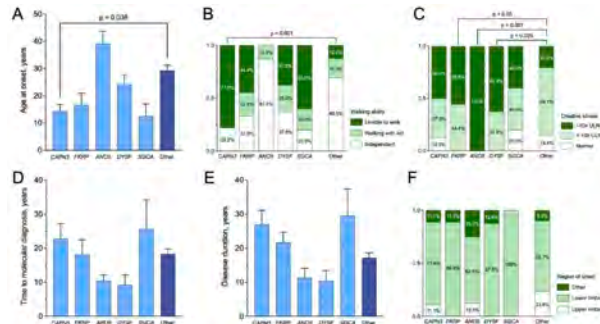
Fig. 2 Demographic and clinical characterisation of common genetic aetiologies in patients with LGW. (A) Disease onset. (B) Waling ability. (C) Creatine kinase levels. (D) Time to molecular diagnosis. (E) disease duration. (F) region of onset.

Conclusion: We suggest early application of NGS in patients with LGW to avoid diagnostic delays. In addition, clinical factors predictive of specific molecular diagnosis may help in the selection of patients for genetic analyses, especially in centres with limited access to sequencing.

Disclosure: The study was financially supported by Sanofi Genzyme.

OPR-118

MAPT p.R406W carriers present with a nonconforming clinical phenotype

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Background and aims: MAPT p.R406W is an autosomal dominantly inherited missense mutation associated with FTLD with an amnestic, AD-like phenotype. Our group first described a carrier pedigree (labeled ADG) in 2003, with 47 relatives. We aim to delineate phenotypic and genetic characteristics of MAPT p.R406W carriers through 19-year follow-up, and to provide first data on mutation frequency in FTD and AD.

Methods: We extended the ADG pedigree, obtained data over 19 years on symptoms, biomarkers and neuropathology. Furthermore, we screened FTD (n=647) and AD (n=1100) patient cohorts for new carriers.

Full ADG pedigree. A pattern of autosomal dominant inheritance may be discerned.

Results: The ADG family now counts 38 mutation carriers. 7 unrelated carriers were identified in AD and FTD cohorts. Inclusion of additional relatives procured 56 mutation carriers (39 affected). p.R406W mutation frequencies were 0.62% (FTD) and 0.27% (AD). All probands shared genetic kinship, suggesting a common ancestor. Average onset age and disease duration were 60.9 and 12.4 years (ranges 54–69, 5–25). Remarkably, two distinct phenotypes (clinical AD(n=10) or bvFTD(n=9)) emerged. bvFTD patients had significantly worse prognosis. Disinhibition/aggression were highly common (100% of bvFTD, 40% of AD patients). CSF amyloid-β1-42 was decreased in all 5 patients with CSF data, 2/5 with concomitant tau elevation. Neuropathology was FTLD-tau, notably showing only 3R-tau-isoforms.
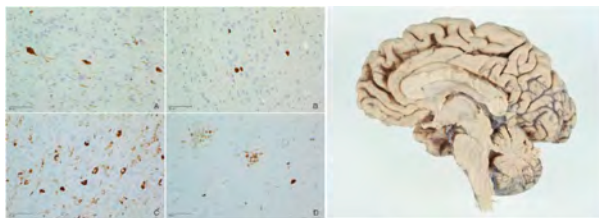
Neuropathologic findings in patient with p.R406W-associated bvFTD.
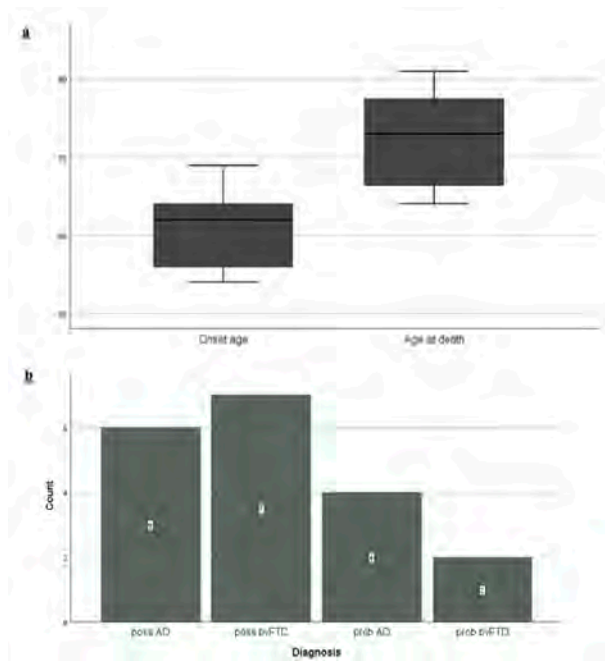
Clinical profile of p.R406W mutation carriers. A wide spread in onset age and age at death can be seen, as well as variable clinical diagnoses. This figure illustrates the tremendous heterogeneity of the clinical phenotype.

Conclusion: We are first to report MAPT p.R406W mutation frequencies, unexpectedly high in FTD ànd AD. Contrary to previous reports, we observed a unique phenotypic shift in Belgian p.R406W carriers, with prominent behavioral symptoms, 47.4% with bvFTD. Surprisingly, CSF biomarkers showed decreased amyloid-β1-42, and neuropathology was FTLD-tau with isolated 3R-tau, highly unusual findings for this tauopathy.
Disclosure: Nothing to disclose.

OPR-119

Potential radiological biomarkers for the m.3243A>G-related MELAS syndrome

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Background and aims: The m.3243A>G variant is the most common cause of adult mitochondrial disease and has heterogeneous clinical manifestations, including mitochondrial encephalomyopathy, lactic acidosis and stroke-like episodes (MELAS) syndrome. Around 20% of patients with the m.3243A>G variant develop MELAS syndrome, and several clinical predictors including heteroplasmy, have been identified. This study sought to identify potential radiological biomarkers of MELAS syndrome.

Methods: 17 patients with the m.3243A>G variants were recruited; seven had MELAS syndrome, and 10 were without the syndrome. All patients were scanned on a Siemens 3T scanner using a 3D T1w anatomical protocol. 24 age- and gender-matched controls were included (Philips scanner).

Results: The mean (SD) age of patients were 40.3 years (12.6), and the mean age-corrected blood heteroplasmy was similar between the MELAS and non-MELAS groups (69% vs 68%, $p > 0.05$). Patients with MELAS syndrome had a significantly smaller mean total intracranial volume (TICV) ($p < 0.001$) (Figure 1), widespread cerebral and cerebellar volume loss ($p < 0.001$) than non-MELAS and control groups. The cognition score of the Newcastle Mitochondrial Disease Rating Scale was strongly correlated with TICV ($r = -0.804$, $p < 0.001$). Significant regional reductions in cortical thicknesses were observed in parts of the temporal lobe in MELAS and non-MELAS groups than in the control group ($p < 0.05$).

Conclusion: TICV is emerging as a promising radiological biomarker that can predict individuals with the m.3243A>G variant at risk of developing MELAS syndrome. The clinical significance and underlying mechanisms of temporal lobe atrophy in non-MELAS patients warrant further investigation.

Disclosure: Nothing to disclose.
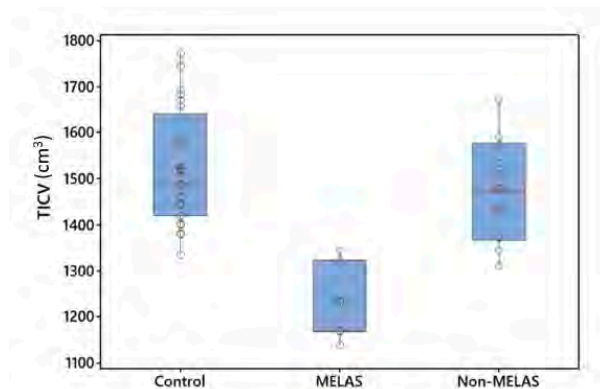
Figure 1. Boxplots of total intracranial volume. The circle with cross symbol denotes the mean value. MELAS= mitochondrial encephalomyopathy, lactic acidosis and stroke-like episodes.

MS and related disorders: Predictors for MS outcome

OPR-120

Does Cognitive Impairment Predict Physical Disability Progression? Evidence from EXPAND, a Phase 3 Long-Term SPMS Study

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Background and aims: Assess the predictive value of cognitive processing speed (CPS), using the Symbol Digit Modalities Test (SDMT) score, on the time-to-wheelchair (T2W) disability progression milestone in secondary progressive multiple sclerosis (SPMS) patients from the Phase 3 EXPAND study.

Methods: Patients from the core and core+extension parts (core+EP) of EXPAND were categorized into quartiles by baseline SDMT score and on-study (Month 0–24) SDMT change (worst-WQ [Q1], intermediate [Q2–Q3], best-BQ [Q4]). The predictive value of these baseline and on-study change categories for time-to-wheelchair (T2W: Expanded Disability Status Scale [EDSS] score ≥ 7) after up to 5-years of the core+EP was assessed for the total study population. The predictive value of on-study change was also assessed separately in the siponimod-group (patients received consistent treatment during the core and the subsequent EP).

Results: Risk of T2W was significantly higher in the WQ vs BQ by baseline SDMT (HRWQ/BQ=1.81, p=0.007). On-study SDMT change was predictive of subsequent T2W in both the total study population (HRWQ/BQ=1.73, p=0.046) and in the siponimod arm (HRWQ/BQ=1.93, p=0.047).

Table:	$HR_{WQ/BQ}$ (95% CI) for T2W (sustained till end of follow-up)
Baseline SDMT as a predictor of disability progression	
Total study population (n=1,628)	1.81 (1.17;2.78), p=0.007
On-study SDMT change (M0–24) as a predictor of subsequent progression	
Total study population (n=1,119)	1.73 (1.01, 2.96), p=0.046
Siponimod group (n=761)	1.93 (1.01, 3.70), p=0.047

Model for baseline: Cox regression, adjusted for treatment, age, gender, baseline EDSS, baseline SDMT quartile, and treatment-by-baseline SDMT quartile interaction

Model for on-study: Cox regression, adjusted for treatment, age, gender, baseline EDSS, baseline SDMT, on-study change in SDMT quartile

Abbreviations: BQ, best quartile; EDSS, expanded disability status scale score =7; EP, extension part; SDMT, symbol digit modalities test; WQ, worst quartile

Conclusion: In line with previous smaller studies, these findings from the EXPAND study confirm that CPS, considered an indirect measure of thalamic network efficiency and functional brain reserve, may have predictive value for long-term physical disability progression. Monitoring CPS in daily practice might therefore help identify patients at increased risk of progressing.

Disclosure: This study was funded by Novartis Pharma AG, Basel, Switzerland. The detailed author disclosures will be presented in the subsequent presentation.

OPR-121

Confirmed disability improvement and sustainability in secondary progressive multiple sclerosis placebo-arm patients

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Background and aims: This study evaluates secondary progressive multiple sclerosis (SPMS) patients with a confirmed disability improvement (CDI) and its sustainability through 24 months in the Multiple Sclerosis Outcome Assessments Consortium (MSOAC) Placebo Database.

Methods: SPMS patients aged from 18 to 61 years with baseline Expanded Disability Status Scale (EDSS) scores between 3 and 6.5 in the MSOAC Placebo Database were identified. CDI was defined as ≥1.0-point decrease from EDSS baseline score ≤5.0 or ≥0.5-point decrease from EDSS baseline score ≥5.5 at 9-months confirmed at 12-months (cohort I) and at 12-months confirmed at 15-months (cohort II). Endpoints included mean duration of CDI (calculated from confirmation) and percentage of patients maintaining CDI status through 24 months.

Results: 553 SPMS patients were identified; 6.3% (28/444) and 7.0% (30/430) of eligible patients had CDI in cohorts I and II respectively. The majority were females; baseline EDSS scores were ≥5.5 for 75.0% of cohort I and 83.3% of cohort II (Table 1). Mean duration of CDI was 7.2 months in cohort I and 5.7 months in cohort II. Of the SPMS patients, 3.2% (cohort I) and 3.7% (cohort II) maintained CDI through 24 months (Table 2).

Table 1. Baseline characteristics of SPMS* improvers

Demographics	Cohort I 9 months confirmed at 12 months (n=28)	Cohort II 12 months confirmed at 15 months (n=30)
Age, years		
Mean (SD)	50 (6.1)	49.4 (6.7)
Median (min, max)	51 (36, 60)	51 (36, 60)
Sex, n (%)		
Female	20 (71.4)	22 (73.3)
Male	8 (28.6)	8 (26.7)
Baseline EDSS score, n (%)		
≤5	7 (25.0)	5 (16.7)
≥5.5	21 (75.0)	25 (83.3)

*SPMS includes both active and nonactive patients.

EDSS, Expanded Disability Status Scale; SD, standard deviation; SPMS, secondary progressive multiple sclerosis.

Table 1: Baseline characteristics of SPMS* improvers

Parameter	Overall[a]			Recently diagnosed[b]		
	Ofatumumab	Teriflunomide	p-value	Ofatumumab	Teriflunomide	p-value
Change in SDMT score from baseline to Month 24, mean (SE)	n=492 3.50 (0.358)	n=468 2.39 (0.365)	0.030	n=245 4.29 (0.489)	n=238 2.56 (0.492)	0.012
Percentage of patients with >=4-point sustained improvement on SDMT, % (n/N)[c]	25.0 (233/946)	19.6 (180/936)	0.005	26.9 (118/443)	20.2 (91/454)	0.018

[a]Mean age (SD): 38.2 (9.1) years.
[b]Mean age (SD): 35.9 (9.2) years.
[c]Cognitive status during the study was classified as improved, if 6mCCI was sustained until end of study (regardless whether 6mCCD status was met at an earlier visit-window). 6mCCD is defined as a decrease from baseline in SDMT score by >=4-point sustained for >=6 months. 6mCCI is defined as an increase from baseline in SDMT by >=4 points sustained for >=6 months.
6mCCD, 6-month confirmed cognitive decline; 6mCCI, 6-month confirmed cognitive improvement; SDMT, Symbol Digit Modalities Test; SD, standard deviation; SE, standard error.

Table 2: Sustained improvement in patients with SPMS*

Conclusion: CDI was observed in ~6–7% of SPMS patients evaluated in clinical trial placebo arms, with ~3–4% maintaining CDI through 24 months. More transformational treatments are needed to improve disability in SPMS.

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OPR-122

Emergency medical care for multiple sclerosis: A five-year population study in the Campania Region (South Italy)

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Background and aims: Emergency hospital admissions are common in multiple sclerosis (MS), and can highlight unmet medical needs. We aim to evaluate burden, predictors and outcomes of MS emergency admissions.

Methods: This is a population-based study, conducted in the Campania Region (South Italy) from 2015 to 2019, using hospital discharge records, drug prescriptions, and outpatients. The risk of emergency hospital admissions and the likelihood of worse outcomes were evaluated using Cox-regression and multinomial logistic regression models, respectively, in relation to age, sex, disease modifying treatments (DMTs), comorbidities and adherence.

Results: We recorded 1.225 emergency admissions for 1.001 patients (out of 5765 prevalent MS patients), overall costing 4.143,764.67 EUR. The risk of emergency admissions increased with age (HR=1.02; 95%CI=1.01,1.03; p<0.01), and comorbidities (HR=1.62; p<0.01), and decreased in patients using DMTs (interferon beta/peg-interferon beta/glatiramer acetate HR=0.19; p<0.01; teriflunomide/dimethyl-fumarate/fingolimod HR=0.18; p<0.01; and alemtuzumab/cladribine/natalizumab/ocrelizumab HR=0.21; p<0.01), and with higher adherence (HR=0.18; 0.26; p<0.01). Following emergency admission, older age was associated with probability of death (n=63) (OR=1.06; p<0.01), and discharge to long-term facility (n=65) (OR=1.03; p=0.01).

Conclusion: With 17% people with MS requiring emergency medical care over 5 years, improved management of DMTs and comorbidities could potentially reduce their medical, social and financial burden.

Disclosure: Nothing to disclose.

OPR-123

Brain Age in Multiple Sclerosis: A comparison of traditional machine learning and deep learning methods

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Background and aims: Brain age is a numerical predicted measure of biological age attained by combining magnetic resonance imaging (MRI) brain scans and artificial intelligence methods. Our main objective was to compare a deep learning (DL) simple fully convoluted neural network (SFCN) model with an established feature-based machine learning (ML) model for brain age estimation in a large longitudinal cohort of people with multiple sclerosis (PwMS).

Methods: PwMS with eligible MRI data were retrospectively analyzed (n=1.515). Clinical and demographic data are summarized in Table 1 and Figure 1. 3D T1-weighted MRIs from eight scanners were processed using in-house ML and DL models. Pearson´s correlation and linear mixed effect (LME) models were used for associations between brain age, age and clinical variables.
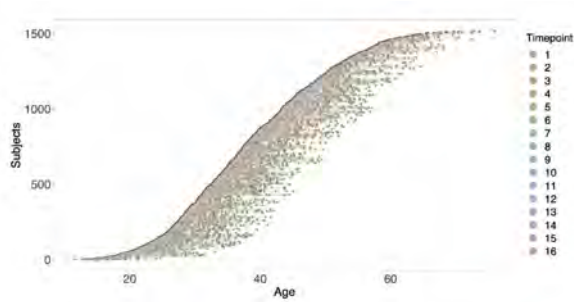
Figure 1 An overview of the multiple sclerosis cohort. We depicted every multiple sclerosis subject in ascending order based on age at the first scan, with chronological age on the x-axis, and the follow-up period as an individual horizontal line. The colour of the circles indicates the number of total MRI scans included for that specific subject

Table 1. Baseline Group Characteristics

Clinical Values	MS (n = 1515)	EDSS ≤3.5 (n = 1064)	EDSS 4.0 - 6.0 (n = 110)	EDSS >6.0 (n = 35)
Sex, No.(%) females	1098 (72.5)	774 (72.7)	77 (70.0)	24 (68.6)
Age, mean (SD, range)	38.9 (11.6, 64.2)	37.5 (11.1, 64.2)	44.5 (11.8, 50.4)	46.1 (11.8, 45.5)
Disease Duration, mean (SD, range)	5.6 (7.2, 53.5)	5.0 (6.7, 51.2)	8.8 (7.8, 38.0)	13.9 (11.0, 41.4)
EDSS, median (IQR)	2.0 (2.0)	1.5 (1.0)	4.5 (1.5)	6.5 (0.5)
Age at diagnosis, mean (SD)	36.5 (11.0)	35.3 (10.6)	39.8 (11.3)	37.3 (12.7)
Year of MS, median	2010	2010	2004	2000
DMTs, No.(%)				
None	59.9	575 (54.0)	59 (53.6)	17 (48.6)
Effective	31.3	377 (35.4)	38 (34.5)	13 (37.1)
Highly effective	8.4	106 (10.0)	12 (10.9)	5 (14.3)
Other	7 (0.5)	6 (0.6)	1 (0.9)	N/A

MS: multiple sclerosis; EDSS: extended disability status scale; DMTs: disease-modifying therapies

Results: Correlations between the estimated brain age and chronological age were stronger for DL estimations (CI=0.89-0.90, r=0.90) than for ML estimations (CI=0.74-0.76, r=0.75), Figure 2. Using LME models, we observed increasing brain age to be significantly associated with higher Expanded Disability Status Scale (EDSS) for both the DL estimates (t=5.3, CI=0.17-0.37) and the ML estimates (t=3.7, CI=0.16-0.51) and longer disease duration (t=5.8, CI=0.08-0.15, and t=6.5, CI=0.15-0.28, respectively).
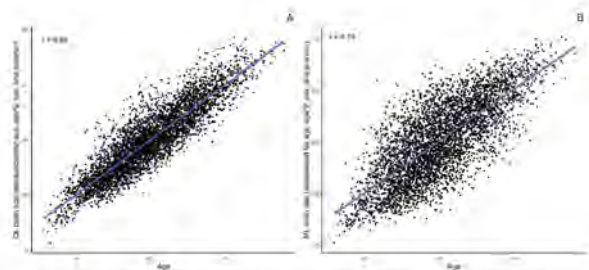
Figure 2. A visualisation of the correlation between age and brain age estimates. Both DL (A) and ML (B) estimates were evaluated [...]

Conclusion: Both brain age models revealed significant associations with EDSS and disease duration. The DL model may be of higher clinical value due to a stronger association to EDSS than ML. However, further research is needed.

Disclosure: EAH, SB, PBH, MKB, PS, AM, TO, EGC, JH, HFH, FP and TG received honoraria from different pharmaceutical companies and grants. All other authors report no relevant disclosures.

Ageing and dementia 2

OPR-124

Visuospatial Navigation Strategies in Typical and Atypical Aging

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Background and aims: Spatial navigation and visuospatial function impairment are typical for early Alzheimer´s disease (AD). We used a realistic-looking virtual environment to analyse different aspects of visuospatial processing and spatial navigation performance in typical and atypical aging.

Methods: 219 participants: amnestic mild cognitive impairment (aMCI, n=75), mild AD dementia (n=66) and cognitively normal older adults (CN, n=78) underwent cognitive evaluation, MRI brain scan, biomarker assessment and spatial navigation testing in a virtual realistic-looking "Intersections" test. Test consisted of three tasks: i) egocentric "route repetition", where participants repeated the route through a virtual city, ii) allocentric "route retracing", where participants indicated their way back, and iii) allocentric "different approach direction" where participants indicated their positions from different perspectives at each intersection with two same and two unique houses. Participants were asked to report used navigation strategy (sequence-of-directions, stimulus-response, using specific or non-specific landmarks).

Results: aMCI and mild AD dementia groups performed worse compared to CN in all tasks (p<0.05). The most commonly used navigation strategy in both, route repetition and route retracing tasks, was Sequence-of-directions (≥68.6%) and looking at the specific landmarks in the different approach direction tasks (≥52.9%) in aMCI and CN groups. Non-specific strategies were most common in dementia group (p<0.05). Using non-specific strategies across all groups was associated with worse performance (p<0.05).

Conclusion: More effective visuospatial strategies were associated with better navigation performance. The results demonstrate that a realistic and ecologically valid spatial navigation test can differentiate between typical and atypical aging.

Disclosure: ENOCH no. CZ.02.1.01/0.0/0.0/16_019/0000 868; the Ministry of Health, University Hospital Motol, Prague grant no. 00064203; Institutional Support of Excellence 2. LF UK grant no. 6990332; Grant Agency of Charles University grant no. 327821

OPR-125

Abstract withdrawn

OPR-126

Dementia and antipsychotics are associated with significantly higher mortality in patients with COVID-19

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Background and aims: Dementia and cognitive decline are discussed as risk factors for severe/lethal outcome of the coronavirus disease 2019 (COVID-19). We aimed to determine whether the presence of dementia is associated with higher in-hospital mortality in patients with COVID-19.

Methods: We conducted an open-cohort observational study based on electronic patient records from seven geriatric care clinics in Stockholm, Sweden between March 1st, 2020 and January 8th, 2021. In total, we identified 4,680 patients, out of which 480 (10.3%) patients had diagnosis of both COVID-19 and dementia, 2,361 (50.4%) had COVID-19 and were dementia-free and 1,839 (39.3%) had dementia without COVID-19. Patients' age, sex, oxygen saturation, comorbidities, and medication prescription (cardiovascular and psychotropic medication) were registered at admission. The first and second wave of the COVID-19 pandemic were divided by the date August 31st, 2020. The hazard ratios (HRs) with 95% confidence intervals (CIs) of in-hospital mortality associated with dementia were obtained using proportional hazards regression with time since entry as time scale.

Results: Dementia was independently associated with 59% higher in-hospital mortality among COVID-19 patients compared to dementia-free patients at admission [HR 1.59 (1.26–2.01)]. In addition, the prescription of antipsychotic medication was associated with substantially higher mortality among patients without dementia [2.79 (2.05–3.80); vs dementia 1.32 (0.84–2.09)].
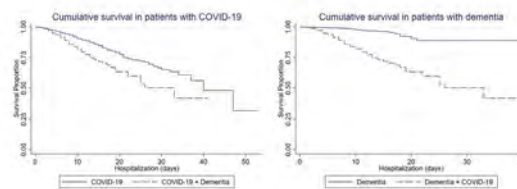
Figure 1. Kaplan-Meier cumulative survival curve during hospitalization by dementia and COVID-19 status.

Conclusion: Dementia is a risk factor for short-term mortality in geriatric patients hospitalized due to COVID-19. Antipsychotic medication seems to be a further risk factor among patients without dementia. Our results may help identify high-risk patients in need of more specialized care when infected with COVID-19.

Disclosure: Authors declare no conflict of interest.

OPR-127

Sleep disorders and incident dementia: a nationwide observational cohort study

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Background and aims: Several studies have examined the role of sleep disturbances as a risk factor for dementia, however most of these studies involve smaller cohorts, short time intervals, and often rely on retrospective surveys and self-reported exposure data. Our aim was to examine the association between sleep disorders and late-onset dementia in an entire population.

Methods: In a nationwide cohort with 40-year follow-up we assessed associations between sleep disorder diagnoses and late-onset dementia using Danish register data. Incidence rate ratios (IRR) were calculated using Poisson regression.

Results: The cohort consisted of 1,491,276 people. Those with any sleep disorder had a 17% higher risk of dementia (IRR 1.17, 95% CI 1.11–1.24) compared to people with no sleep disorder after adjusting for age, sex, calendar year, education, and somatic and psychiatric comorbidities. IRR was significantly increased only for dementia within 5 years of sleep disorder diagnosis.

Conclusion: Our findings show a greater short-term risk of dementia following a sleep disorder diagnosis, while we found weaker evidence of a long-term risk. This could potentially point towards sleep disorders as an early symptom of dementia. Further research is needed to distinguish sleep disorders as an early symptom of dementia, a risk factor, or both.

Disclosure: Prof. Waldemar served as a consultant or speaker for Roche, Biogen, and Novo Nordisk (honorarium to department and without honorarium). Dr. Spira received honoraria for serving as a consultant to Merck and from Springer Nature Switzerland AG for guest editing special issues of Current Sleep Medicine Reports.

OPR-128

Life' Simple 7 and rate of cognitive decline in preclinical dementia: a population-based study

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Background and aims: We investigated whether vascular risk factors (VRFs) are associated with rate of cognitive decline in the preclinical dementia phase.

Methods: The population-based study included 1,449 participants aged ≥ 60 years (M = 69.99, SD=9.25) from the Swedish National Study on Aging and Care-Kungsholmen, who underwent repeated neuropsychological testing (episodic memory, semantic memory, verbal fluency, and perceptual speed) across 12 years. VRFs were assessed with the Life's Simple 7 (LS7) score at baseline and included smoking, diet, physical activity, body mass index, plasma glucose, total serum cholesterol, and blood pressure. Participants were categorised as having poor or intermediate/optimal cardiovascular health. Level and change in cognitive performance as a function of LS7 categories and future dementia status (DSM-IV criteria) were estimated using linear mixed-effects models.

Results: Participants in a preclinical dementia phase were more likely to have a poorer LS7 score initially compared to those who remained dementia-free. For young-old individuals (<72 years), poor diet was associated with an accelerated perceptual speed decline (β=-0.05, 95% CI -0.08 to -0.02) and a poor plasma glucose score was associated with faster rates of verbal fluency (β=-0.019, -0.09 to -0.01) and global cognitive (β=-0.028, -0.06 to 0.00) decline in the preclinical dementia group.

Conclusion: The association between VRFs and cognitive decline was most pronounced in young-old individuals in a preclinical phase of dementia and driven mostly by diet and glucose.

Disclosure: All authors have no conflict of interest to declare.

OPR-129

Sensitivity to early amyloid increases with higher education in individuals with subjective cognitive decline

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Background and aims: Evidence suggests that higher educated patients with mild cognitive impairment (MCI) can tolerate more neuropathology than lower educated patients with similar clinical impairment. It is not known whether this observation also accounts for individuals with subjective cognitive decline plus (SCD+).

Methods: Data of 197 SCD+ individuals, 227 MCI and 157 AD patients were included, which were collected as part of the AMYPAD-DPMS cohort. First, median education in years was computed across the AD-spectrum groups for each of the 8 European sites. Next, using a median split, the AD-spectrum cohorts were separately categorized into a higher and lower educated group, excluding subjects with median education. Afterwards, the higher and lower educated AD-spectrum groups were matched for age, sex and cognitive function (MMSE) using propensity score matching in R, leading to the following sample (low/high education): 54/54 SCD+, 70/81 MCI and 56/65 AD patients. Global amyloid load was compared between education groups using Centiloid (CL) information derived from Flutemetamol and Flourbetaben PET scans. Significance level was set to $p < 0.05$.

Results: Higher educated SCD+ subjects presented significantly ($p < 0.001$) lower CL values (M(CL)=16.48) than lower educated SCD+ subjects (M(CL)=32.17), whereas the opposite effect ($p < 0.046$) was observed in the MCI cohort and no difference was found in the AD group.
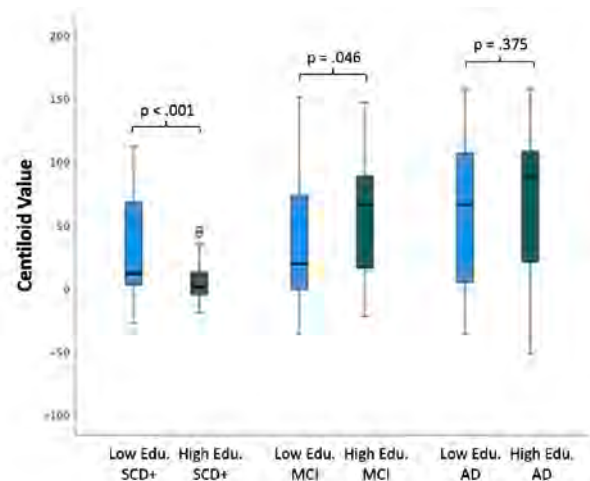
Group comparisons between the low and high educated SCD+, MCI and AD groups, respectively.

Conclusion: These results indicate that sensitivity to early amyloid accumulation may increase with higher education in stages of SCD, whereas higher education appears to support compensation to amyloid burden in early clinical stages of the disease.

Disclosure: Nothing to disclose.

MS and related disorders: Treatments and multiple sclerosis

OPR-130

Improvement in Cognitive Processing Speed with Ofatumumab in Patients with Relapsing Multiple Sclerosis

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Background and aims: In the Phase 3 ASCLEPIOS I/II trials, ofatumumab significantly reduced inflammatory disease activity and relapses, and delayed disability worsening in patients with relapsing multiple sclerosis (RMS). Here, we report the effect of ofatumumab on cognitive processing speed (CPS).

Methods: We analysed the change in Symbol Digit Modalities Test (SDMT) score (baseline to Month 24; derived from a mixed model for repeated measures), proportion of patients with ≥4-point sustained improvement on SDMT (by categorical analysis), and time-to-first 6-month confirmed cognitive improvement (6mCCI; ≥4-point improvement on SDMT) in the overall population and in a subgroup of patients recently diagnosed (RD; within the last 3 years). Time-to-first 6mCCI was also analysed in a subgroup of patients with/without (SDMT score ≤/>43) baseline cognitive impairment.

Results: Ofatumumab significantly improved SDMT scores from baseline to Month 24 in both the overall and RD populations; improvement was more pronounced in the RD subgroup (Table 1). More patients on ofatumumab had ≥4-point sustained improvement on SDMT versus teriflunomide in both the overall and RD populations (Table 1). Ofatumumab numerically increased the probability of time-to-first 6mCCI (hazard ratio [95% confidence intervals]) in the overall population (1.14 [0.96, 1.36]), RD subgroup (1.19 [0.93, 1.52]) and patients without baseline cognitive impairment (1.23 [0.98, 1.56]).

Parameter	Overall[a]			Recently diagnosed[b]		
	Ofatumumab	Teriflunomide	p-value	Ofatumumab	Teriflunomide	p-value
Change in SDMT score from baseline to Month 24, mean (SE)	n=492 3.50 (0.358)	n=468 2.39 (0.365)	0.030	n=245 4.29 (0.489)	n=238 2.56 (0.492)	0.012
Percentage of patients with >=4-point sustained improvement on SDMT, % (n/N)[c]	25.0 (233/946)	19.6 (180/936)	0.005	26.9 (118/443)	20.2 (91/454)	0.018

[a]Mean age (SD): 38.2 (9.1) years.
[b]Mean age (SD): 35.9 (9.2) years.
[c]Cognitive status during the study was classified as improved, if 6mCCI was sustained until end of study (regardless whether 6mCCD status was met at an earlier visit-window). 6mCCD is defined as a decrease from baseline in SDMT score by >=4-point sustained for >=6 months. 6mCCI is defined as an increase from baseline in SDMT by >=4 points sustained for >=6 months.
6mCCD, 6-month confirmed cognitive decline; 6mCCI, 6-month confirmed cognitive improvement; SDMT, Symbol Digit Modalities Test; SD, standard deviation; SE, standard error.

Table 1: Effect of ofatumumab versus teriflunomide on cognitive processing speed

Conclusion: Ofatumumab was associated with more clinically meaningful improvements in CPS versus teriflunomide when measured by change in SDMT in both the overall and RD populations. Early treatment initiation with ofatumumab may enhance CPS improvement in patients with RMS by efficiently suppressing inflammation.
Disclosure: The study was supported by Novartis Pharma AG, Switzerland. The detailed author disclosures will be presented in the subsequent presentation.

OPR-131

Effects of evobrutinib, a Bruton's tyrosine kinase inhibitor, on slowly expanding lesions: a marker of tissue loss in MS

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Background and aims: Slowly expanding lesions (SELs) are chronically active, demyelinated multiple sclerosis (MS) lesions, likely driven by sustained microglia/macrophage activity, resulting in irreversible neural tissue damage and axonal loss. Objective: evaluate the effect of evobrutinib, a Bruton's tyrosine kinase inhibitor (BTKi), vs comparator on SEL volume from baseline to Week (W)48 in a Phase II trial (NCT02975349) in relapsing MS.

Methods: SELs were identified, via magnetic resonance imaging, as radially expanding areas of pre-existing T2 lesions ($\geq$10 contiguous voxels; ~30mm^3). SEL volume analysis, stratified by baseline T2 lesion volume tertiles, was based on W48/end-of-treatment values (completers and discontinuers); treatment effect was analysed via stratified Hodges–Lehman estimate of distribution shift and stratified Wilcoxon rank-sum test. Evobrutinib dose groups (25mg once-daily [QD], n=50; 75mg QD, n=51; 75mg twice-daily [BID], n=53) were compared with placebo/evobrutinib 25mg QD (n=53; Table).

Results: Relative to comparator, SEL volume decreased with increasing evobrutinib dose (25mg QD, -136.5mm^3 [95% CI: -618.0;309.0], p=0.505; 75mg QD, -246.0mm^3 [-712.0;97.0], p=0.192; 75mg BID, -474.5mm^3 [-1,098.0;-3.0], p=0.047). SEL volume was significantly reduced for evobrutinib high-dose (75mg QD + BID) vs low-dose (placebo + evobrutinib 25mg QD) within these subgroups: baseline EDSS $\geq$3.5 (-652.0mm^3 [95% CI: -1,507.0;-100.0], p=0.020); relapsing-remitting MS (-317.0mm^3 [-731.5;-29.0], p=0.025); longer disease duration (>=8.5 years; -729.3mm^3 [-1,706.5;-20.0], p=0.040).

Conclusion: Evobrutinib reduces SEL volume in a dose-dependent manner in relapsing MS. The reduction is especially apparent in patients with more advanced disease. This is the first evidence that a BTKi impacts brain lesions associated with chronic inflammation and tissue loss, potentially via microglia.

Disclosure: Study was sponsored by Merck Healthcare KGaA (CrossRef Funder ID: 10.13039/100009945), detailed author disclosures will be included in the presentation.

	Placebo/Evobrutinib 25 mg QD (n=53)	Evobrutinib 25 mg QD (n=50)	Evobrutinib 75 mg QD (n=51)	Evobrutinib 75 mg BID (n=53)
Sex, n (%)				
Male	14 (26.4)	18 (36.0)	16 (31.4)	17 (32.1)
Female	39 (73.6)	32 (64.0)	35 (68.6)	36 (67.9)
Age, years (mean ±SD)	41.6 ±10.8	42.4 ±9.4	42.9 ±10.1	42.2 ±11.5
Time since MS onset, years, n (%)				
<8.5 years	32 (60.4)	26 (52.0)	20 (39.2)	23 (43.4)
>=8.5 years	21 (39.6)	23 (46.0)	31 (60.8)	30 (56.6)
Type of MS				
RRMS	47 (88.7)	42 (84.0)	43 (84.3)	47 (88.7)
SPMS	6 (11.3)	8 (16.0)	8 (15.7)	6 (11.3)
Number of relapses in 2 years pre-randomisation, n (%)				
<=1 relapse (non-HDA)	26 (49.1)	27 (54.0)	18 (35.3)	25 (47.2)
>=2 relapses (HDA)	27 (50.9)	23 (46.0)	33 (64.7)	28 (52.8)
EDSS score, n (%)				
<=3	27 (50.9)	28 (56.0)	22 (43.1)	28 (52.8)
>=3.5	26 (49.1)	22 (44.0)	29 (56.9)	25 (47.2)
T2 lesion volume, cc (mean ±SD)	15.9 ±12.6	13.8 ±11.7	14.0 ±12.2	19.0 ±13.5

mITT analysis set.
BID, twice daily; EDSS, Expanded Disability Status Scale; HDA, high disease activity; mITT, modified intention-to-treat; MS, multiple sclerosis; QD, once daily; RRMS, relapsing-remitting MS; SD, standard deviation; SPMS, secondary-progressive MS.

Table: Baseline characteristics

OPR-132

Tracking the immune response to SARS-CoV-2 mRNA vaccines in ofatumumab treated RMS patients in a multicenter study

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Background and aims: Initial and booster vaccination with the newly developed SARS-CoV-2 mRNA vaccines efficiently protect healthy individuals against COVID-19. As only limited data is available for Multiple Sclerosis (MS) patients with immunosuppressive treatment, this study aims to comprehend the impact of ofatumumab treatment on mounting cellular and humoral immune responses to SARS-CoV-2 mRNA vaccines.

Methods: KYRIOS is an open-label, two-cohort study including 40 MS patients at 8 sites in Germany. Patients receive initial or booster SARS-CoV-2 mRNA vaccination either before (cohort 1) or at least 4 weeks after starting ofatumumab treatment (cohort 2). The impact of ofatumumab treatment on development of SARS-CoV-2 reactive T-cells (primary endpoint) and neutralizing antibodies (secondary endpoint) will be evaluated. Furthermore, immune responses will be monitored and phenotypically described for up to 18 months.

Results: Results of an interim analysis show that SARS-CoV-2 mRNA vaccines can induce cellular and humoral immune responses in ofatumumab-treated patients. Immune responses could be detected as soon as 1 week after the initial vaccination cycle for all patients receiving their initial SARS-CoV-2 vaccines during stable ofatumumab treatment (n=4) or before ofatumumab initiation (n=5). The interim analysis further shows the effect of ofatumumab treatment on development of immune responses after booster vaccines (n=23).

Conclusion: The KYRIOS study demonstrates for the first time that ofatumumab treated patients can mount specific immune responses towards SARS-CoV-2 mRNA vaccines. The results further suggest that both, humoral and cellular immune response, need to be considered for interpretation of vaccine efficacy and are in line with other recently published studies.

Disclosure: This study is sponsored by Novartis Pharma Vertriebs GmbH.

OPR-133

Assessing the immune response to SARS-CoV-2 mRNA vaccines in SPMS patients treated with siponimod (clinical trial)

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Background and aims: SARS-CoV-2 mRNA vaccines are a key factor for fighting the COVID-19 pandemic across the globe. However, data are lacking on the efficacy of these vaccines to induce cellular and humoral immune responses in patients with secondary progressive multiple sclerosis (SPMS) on disease-modifying therapies (DMTs) both over time and after a booster vaccination.

Methods: AMA-VACC is prospective, open-label, three-cohort study including 41 multiple sclerosis patients at ten sites in Germany. Cohort 1 receives SARS-CoV-2 mRNA vaccination during continuous siponimod treatment, cohort 2 interrupts siponimod treatment for the purpose of a full vaccination cycle and cohort 3 is vaccinated during continuous treatment with first-line DMTs (dimethylfumarate, glatirameracetate, interferons, teriflunomide) or no current treatment in clinical routine. Development of neutralizing antibodies (primary endpoint) as well as detection of SARS-CoV-2 specific T-cells (secondary endpoint) are assessed after initial and booster vaccination and monitored for up to 6 months.

Results: Results of previous interim analysis showed that the majority of patients treated with siponimod can mount an immune response after SARS-CoV-2 mRNA vaccination. Here, longitudinal data will be presented describing for the first time the level of cellular and humoral immune response for up to 6 months after vaccination and the effect of booster vaccines in siponimod treated patients.

Conclusion: This analysis will provide data on the maintenance of humoral and cellular immune response after SARS-CoV-2 vaccination in siponimod treated patients and enable physicians and patients to make an informed decision on the coordination of SARS-CoV-2 mRNA (booster) vaccination and SPMS treatment.

Disclosure: This study is sponsored by Novartis Pharma GmbH.

OPR-134

Longer-term Safety of Ofatumumab in Patients With Relapsing Multiple Sclerosis

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Background and aims: In the Phase 3 ASCLEPIOS I/II trials, ofatumumab treatment up to 30 months had favourable safety profile and was generally well-tolerated in relapsing multiple sclerosis (RMS) patients. Here, we aim to assess the longer-term safety and tolerability of ofatumumab treatment for up to 4 years.

Methods: Patients completing the core ASCLEPIOS I/II, APOLITOS and APLIOS trials could enter ALITHIOS, an ongoing, open-label extension study. We analysed the cumulative safety data for up to 4 years with ofatumumab (cut-off: 25-Sep-2021) in the overall (n=1,969), continuous (ofatumumab in core+extension; n=1,292) and newly-switched (teriflunomide core and ofatumumab extension; n=677) groups. The proportion of patients with treatment-emergent adverse events (TEAEs), serious AEs (SAEs), serious infections including opportunistic infections, and malignancies will be assessed. Laboratory parameters including neutrophils, lymphocytes, and serum immunoglobulin (Ig)G and IgM levels and association with serious infections will be analysed.

Results: Baseline demographics and disease characteristics are presented in Table1. In the previously reported data (cut-off: 29-Jan-2021; treatment for ~3.5 years), 83.8% of patients had ≥1 AEs (exposure-adjusted incidence rate/100 patient-years [EAIR], 148.7) and 9.7% had ≥1 SAEs (EAIR, 4.8) with a low incidence of serious infections (2.9%; EAIR, 1.4) and malignancies (0.6%; EAIR, 0.3). Updated cumulative clinical safety data with ofatumumab for up to 4 years will be presented at the congress.

	Ofatumumab Continuous (N=1292)	Ofatumumab Newly Switched (N=677)		Ofatumumab Overall (N=1969)
		Baseline of Core Study (N=677)	Baseline of Extension Study (N=677)	
Age, years (mean±SD)	38.0±9.06	38.2±9.22	40.1±9.21	38.7±9.16
Age group - n (%)				
18 to 30 years	312 (24.1)	156 (23.0)	116 (17.1)	428 (21.7)
31 to 40 years	438 (33.9)	244 (36.0)	239 (35.3)	677 (34.4)
41 to 55 years	539 (41.7)	277 (40.9)	288 (42.5)	827 (42.0)
> 55 years	3 (0.2)	0	34 (5.0)	37 (1.9)
BMI (kg/m²)	25.61±6.16	25.69±5.83	25.61±5.85	25.61±6.05
Female, n (%)	889 (68.8)	456 (67.4)	456 (67.4)	1345 (68.3)
Time since diagnosis, years (mean±SD)	5.87±6.31	5.45±6.00	7.33±6.01	6.37±6.25
EDSS score at baseline, (mean±SD)	2.90±1.33	2.77±1.32	2.81±1.46	2.87±1.38
IgG levels at baseline (mean±SD); g/L	10.31± 2.24	10.35±2.09	10.23±2.14	10.28±2.21
IgM levels at baseline (mean±SD); g/L	1.34± 0.65	1.36±0.74	1.14±0.67	1.27±0.66

EDSS, Expanded Disability Status Scale; Gd+ Gadolinium-enhancing, Nfl, neurofilament light chain; OMB, ofatumumab; SD, standard deviation

For OMB newly-switched patients, their baseline values from extension study contribute to the overall summary.

Baseline Demographics and Disease Characteristics

Conclusion: Safety findings for upto 3.5 years showed ofatumumab treatment to be well-tolerated with no new safety risks identified. This additional safety data up to 4 years will inform physicians on the longer-term safety profile of ofatumumab in RMS patients.

Disclosure: The study was supported by Novartis Pharma AG, Switzerland. The detailed author disclosures will be presented in the subsequent presentation.

OPR-135

Efficacy and safety of ocrelizumab in a treatment-naive, early RMS population: 7-year data from the OPERA OLE trials

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Background and aims: The benefits and risks of highly effective therapy as a first-line treatment early in relapsing multiple sclerosis (RMS) should inform evidence-based therapeutic decisions; this subgroup analysis examined disease activity and progression in a treatment-naive, early (diagnosis ≤2 years) RMS subpopulation treated with ocrelizumab (OCR) over >7 years (n=756), from the Phase III OPERA trials (NCT01247324/NCT01412333).

Methods: Participants were randomised to OCR or interferon (IFN)-beta 1a during the 96-week double-blind period (DBP). During open-label extension (OLE), participants continued OCR (OCR-OCR) or switched to OCR (IFN-OCR). Efficacy endpoints included no evidence of disease activity (NEDA) with MRI rebaselining at Week (W)24 (absence of: Protocol-defined relapses [PDR], 24W-confirmed disability progression [24W-CDP], contrast-enhancing T1-weighted and new/enlarging T2-weighted lesions). Safety measures included incidence/nature of adverse events (AEs).

Results: Of n=756 (OCR 375; IFN 381) analysed participants, 70% remained on treatment for ≥7.4 years (OCR 73%; IFN 67%). Versus IFN, higher proportions of OCR-treated participants at W96 had NEDA (72% vs 44%; p<0.001); no 24W-CDP (92% vs 88%; p=0.086); no evidence of MRI activity (95% vs 62%; p<0.001); no PDR (83% vs 73%; p=0.0015). OCR-OCR participants maintained benefits through OLE W286 vs IFN-OCR: NEDA (51% vs 28%; p<0.001); no 24W-CDP (81% vs 76%; p=0.14); no evidence of MRI activity (90% vs 56%; p<0.001); no PDR (76% vs 66%; p=0.0032 [Table 1]). AE, serious AE and serious infection rates over 7 years remained similar to the DBP (Table 2).

Table 1. Proportion of participants with NEDA and its components at Week 96 and OLE Week 286

Proportion of participants (%)	DBP (Week 96)			DBP+OLE (Week 286)[a]		
	IFN	OCR	P-value	IFN-OCR	OCR-OCR	P-value
With NEDA	43.93	72.46	<0.001	28.00	50.97	<0.001
With no 24W-CDP	88.45	92.27	0.086	76.38	80.80	0.1403
With no PDR	72.70	82.67	0.0015	66.14	76.27	0.0032
With no evidence of MRI activity	62.20	94.93	<0.001	56.17	89.60	<0.001

[a]Clinical cut-off date: 27 November 2020.

24W-CDP, 24-week confirmed disability progression; DBP, double-blind period; IFN, interferon; NEDA, no evidence of disease activity; OCR, ocrelizumab; OLE, open-label extension; PDR, protocol-defined relapse.

AE Rate per 100 PY (95% CI)	OPERA			OCR all-exposure clinical trials[a]
	DBP (Week 96)		DBP+OLE (Week 286)[a]	
	IFN (n=381; 659.7 PY)	OCR (n=374, 663.7 PY)	OCR (n=668; 4,178.7 PY)	(n=5,688; 21,675 PY)
Any AEs	298 (285–311)	289 (277–303)	201 (197–205)	238 (236–240)
AEs leading to discontinuation	4.4 (2.9–6.3)	1.8 (0.9–3.2)	1.2 (0.9–1.6)	1.0 (0.8–1.1)
SAEs	4.7 (3.2–6.7)	4.2 (2.8–6.1)	6.0 (5.3–6.8)	7.3 (7.0–7.7)
Fatal outcomes	0.15 (0.00–0.84)	0.00 (0.00–0.56)	0.10 (0.03–0.25)	0.21 (0.15–0.28)
Malignancies	0.15 (0.00–0.84)	0.30 (0.04–1.09)	0.50 (0.31–0.77)	0.48 (0.39–0.58)
Infections and infestations	66.85 (60.75–73.40)	84.10 (77.25–91.35)	69.76 (67.25–72.34)	72.68 (71.55–73.83)
Serious Infections	1.97 (1.05–3.37)	0.30 (0.04–1.09)	1.38 (1.03–1.77)	2.25 (2.06–2.46)

[a]Clinical cut-off date: 27 November 2020.

AE, adverse event; CI, confidence interval; DBP, double-blind period; IFN, interferon; OCR, ocrelizumab; OLE, open-label extension; SAE, serious adverse event; PY, patient years.

Table 2: Rates of AEs per 100 patient years (PY) in the DBP, DBP+OLE and the OCR all-exposure population (subsets of the safety population, n=755)

Conclusion: In this treatment-naive, early RMS population, long-term safety and efficacy data support the use of ocrelizumab as first-line therapy.

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MS and related disorders: Biomarkers and MRI in neuroinflammatory diseases

OPR-136

Serum Glial Fibrillary Acidic Protein: A Biomarker of Disease Progression in Multiple Sclerosis

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Background and aims: Neurodegeneration and astrocytic activation are pathological hallmarks of progressive multiple sclerosis (MS) and can be quantified by serum neurofilament light chain (sNfL) and glial fibrillary acidic protein (sGFAP). We investigated sNfL and sGFAP as tools for stratifying progressive MS patients based on progression and disease activity status.

Methods: sNfL and sGFAP were analyzed in 259 progressive MS patients within 6-months from first confirmed EDSS≥3 corresponding with our "baseline". Progressive patients were classified as "active/non-active" based on new brain/spinal cord lesions or relapses in the two years prior to baseline or during follow-up. Statistical analysis on log-transformed sGFAP/sNfL assessed the baseline association with demographic, clinical, MRI features as well as associations with future disability and cognition.

Results: Baseline sNfL was higher in progressive patients with disease activity during the first two years of follow-up (β=1.17, p=0.042) and during the entire follow-up available (β=1.2, p=0.013). Neither sNfL nor sGFAP discriminated between active status prior to baseline. Baseline sGFAP levels were positively associated with higher risk of 6-months confirmed disease progression (6mCDP,adjusted-HR:1.71). The association was stronger in patients with low sNfL (adjusted-HR:2.44). The change, but not the absolute value of sNfL, was prognostic for 6mCDP (adjusted-HR:1.46, p:0.003). Elevated sNfL levels were associated with future cognitive decline (β= -0.79, p=0.028).

Table. Association between baseline levels of biomarkers and 6-month confirmed progression on the EDSS

Group	Predictor	Association with confirmed progression	Adjusted association with confirmed progression
All	sNfL (continuous)	1.04 (0.79, 1.39); p=0.782	1.11 (0.83, 1.49); p=0.488
	sNfL		
	Quintile 1	Reference	Reference
	Quintile 2	1.75 (1.07, 2.87); p=0.027	1.72 (1.04, 2.84); p=0.035
	Quintile 3	1.18 (0.69, 2.04); p=0.544	1.16 (0.66, 2.05); p=0.601
	Quintile 4	1.04 (0.60, 1.78); p=0.900	1.08 (0.61, 1.89); p=0.799
	Quintile 5	1.11 (0.66, 1.88); p=0.696	1.14 (0.67, 1.95); p=0.627
Low sGFAP	sNfL (continuous)	1.10 (0.74, 1.64); p=0.643	1.20 (0.76, 1.89); p=0.437
	sNfL		
	Quintile 1	Reference	Reference
	Quintile 2	2.41 (1.24, 4.69); p=0.009	2.09 (1.04, 4.21); p=0.040
	Quintile 3	1.27 (0.60, 2.69); p=0.537	1.12 (0.50, 2.52); p=0.782
	Quintile 4	1.29 (0.55, 3.04); p=0.556	1.32 (0.52, 3.33); p=0.556
	Quintile 5	1.67 (0.68, 4.12); p=0.261	1.65 (0.65, 4.21); p=0.294
All	sGFAP (continuous)	1.47 (1.05, 2.05); p=0.028	1.71 (1.19, 2.45); p=0.004
	sGFAP		
	Quintile 1	Reference	Reference
	Quintile 2	1.27 (0.74, 2.18); p=0.390	1.33 (0.77, 2.29); p=0.311
	Quintile 3	1.17 (0.69, 1.99); p=0.568	1.34 (0.77, 2.32); p=0.305
	Quintile 4	1.48 (0.89, 2.48); p=0.134	1.61 (0.94, 2.75); p=0.084
	Quintile 5	1.67 (1.00, 2.81); p=0.052	1.24 (1.26, 3.98); p=0.006
Low sNfL	sGFAP (continuous)	2.21 (1.27, 3.84); p=0.005	2.44 (1.32, 4.52); p=0.005
	sGFAP		
	Quintile 1	Reference	Reference
	Quintile 2	2.01 (1.04, 3.88); p=0.037	2.10 (1.07, 4.14); p=0.032
	Quintile 3	1.59 (0.82, 3.09); p=0.173	2.35 (1.13, 5.00); p=0.026
	Quintile 4	2.02 (1.06, 3.84); p=0.033	2.01 (1.02, 3.98); p=0.044
	Quintile 5	2.90 (1.32, 6.40); p=0.008	3.86 (1.60, 9.31); p=0.003

Legend: Estimates are presented as hazard ratio and 95% confidence interval from Cox regression model. Adjusted analyses included the measure of interest and age, sex, EDSS, relapse and treatment. Low sGFAP: only patients with sGFAP levels below the median; Low sNfL: only patients with sNfL levels below the median; sGFAP: serum glial fibrillary acidic protein; sNfL: serum neurofilament light chain.

Conclusion: Higher levels of sGFAP were an indicator of progression, whereas sNfL reflected acute disease activity in our progressive MS cohort. Thus, sGFAP and sNfL levels may be used to stratify progressive MS patients at enrollment in clinical research studies and clinical trials.

OPR-137

A Highly Sensitive Proteomic Immunoassay to Identify Novel Serum Biomarkers for Multiple Sclerosis Disease Progression

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Background and aims: Progression independent of relapse activity (PIRA) is common in relapsing remitting multiple sclerosis (RRMS), even under high-efficacious disease modifying treatment such as natalizumab, yet specific blood biomarkers are currently lacking. Our objective was to identify novel biomarkers associated with PIRA using a proteomics approach.

Methods: In this longitudinal cohort study of 84 natalizumab-treated RRMS patients, 1,472 proteins were assessed using the Olink Explore panel (Proximity Extension Assay) at baseline (prior to natalizumab initiation) and after 3 months and 24 months of natalizumab treatment. Annual clinical and radiological data on disease activity and progression were collected for a median of 5.2 years, including relapses, Expanded Disability Status Scale (EDSS), 9-hole peg test, timed 25-foot walk test and lesion, whole brain, ventricle and thalamus volume by Freesurfer's Sequence Adaptive Multimodal SEGmentation (SAMSEG) tool. EDSS plus status (progressor or non-progressor) was determined between year 1 and last follow-up, correcting for relapse associated worsening. Relevant proteins were selected based on statistically significant effects on EDSS-plus status and brain atrophy measures.

Results: EDSS plus progressors (n=40) and non-progressors (n=44) showed comparable low rates of clinical and radiological disease activity at baseline and follow-up. Up to 3 serum proteins were found to be significantly up- or downregulated in progressors compared to non-progressors at the 3 and 24 month timepoint, including some involved in the complement pathway and myelination. Additional proteins were significantly associated to and predictive of brain atrophy.

Conclusion: We identified several potential serum biomarkers associated with PIRA and brain atrophy in natalizumab-treated RRMS.

Disclosure: Nothing to disclose.

OPR-138

Monoaminergic network abnormalities: a fingerprint for multiple sclerosis-related fatigue and depression

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Background and aims: Fatigue and depression are extremely frequent in MS; however, their pathophysiological correlates are not completely unveiled. We explored monoaminergic network functional abnormalities in MS patients and their correlation with fatigue and depression by applying PET-constrained independent component analysis (ICA) to resting state (RS) functional MRI (fMRI) data.

Methods: We enrolled 213 MS patients and 62 healthy controls (HC), who underwent neurological, fatigue, depression and RS fMRI assessment. We excluded patients with cognitive impairment assessed through the symbol digit modality test and patients with depression or fatigue due to disease-modifying treatments. Patterns of dopamine, noradrenaline- and serotonin-dependent RS functional connectivity (FC) were derived by ICA, constrained to PET atlases for dopamine, noradrenaline and serotonin transporters, previously obtained in HC's brain.

Results: Compared to HC, MS patients showed abnormalities in all three explored monoaminergic networks, mostly with decreased monoamine-dependent RS FC in frontal regions and subcortical areas including the cerebellum and thalamus, and increased RS FC in temporo-parieto-occipital cortical areas, including bilateral precunei. MS-related fatigue was associated with decreased dopamine-dependent RS FC in the left thalamus and left cerebellum, and increased serotonin-dependent RS FC in the left middle occipital gyrus. MS-related depression was associated with more distributed abnormalities involving the three explored monoaminergic networks, resulting in overall reduced monoamine-dependent RS fMRI FC in the frontal lobe, limbic areas and precuneus.

Conclusion: MS patients presented diffuse monoaminergic network functional dysregulation. Specific alterations in these networks were associated with fatigue and depression, providing a pathological fingerprint for these bothersome symptoms and putative targets for their treatment.

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OPR-139

MAGNON – Contribution of Lublin Criteria and quantitative MRI-Analysis for daily clinical routine of MS Patients

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Background and aims: Revised Lublin criteria provide a definition of remitting and progressing Multiple Sclerosis to classify disease activity of patients with Secondary Progressive Multiple Sclerosis (SPMS). However, Lublin criteria are only rarely used in clinical practice, like quantitative and standardized MRI analyses, which are often not part of standard routine care in patient management. MAGNON aims to evaluate if standardized quantification of MRI data and assessment of MS patients based on the Lublin criteria could help to classify disease activity.

Methods: 1,000 MRI scans of patients with SPMS or suspected SPMS will be provided by 50 centers in Germany between 2020–2022. The analysis of standardized MRI data will comprise a volumetric quantification of brain and thalamic volumes as well as T2-lesion-volume and number using a centralised automatic processing pipeline (Biometrica MS®, jung diagnostics GmbH). Percentage brain volume change is computed when follow-up scans are available. The value of standardized MRI analysis and the impact on patient assessment, including potential changes in Lublin classification, is evaluated.

Results: Latest interim analysis data (n=650) show that already one stand-alone standardized MRI scan can provide insights on disease activity and progression. Moreover, physicians stated that already one stand-alone MRI suggested a change in MS treatment for about 40% of their patients with suspected SPMS.

Conclusion: MAGNON interim results indicate that quantification of lesion volume as well as brain and thalamic atrophy on routine MRI may facilitate the individual assessment of disease activity and progression according to the Lublin criteria and thus enhance individualized patient care.

Disclosure: This data collection is funded by Novartis Pharma GmbH, Germany.

OPR-140

Exploring in vivo multiple sclerosis brain microstructural damage through T1w/T2w-ratio: a multicenter study

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Background and aims: The T1-weighted (w)/T2w-ratio may be clinically feasible to investigate microstructural damage in multiple sclerosis (MS). The aims of this study were to evaluate white matter (WM) and gray matter (GM) T1w/T2w-ratio in healthy controls (HC) and MS patients, and its association with clinical disability.

Methods: In this cross-sectional study, 270 HC and 434 MS patients were retrospectively selected from seven European sites. T1w/T2w-ratio was obtained from brain T2w and T1w scans after intensity calibration using eyes and temporal muscle.

Results: In HC, T1w/T2w-ratio increased until 50-60 years in WM and GM. Compared to HC, T1w/T2w-ratio was significantly lower in lesions of all phenotypes, and in normal-appearing (NA) WM and cortex of relapsing-remitting (RR) and secondary progressive (SP) MS (p≤0.026), but it was significantly higher in the striatum and pallidum of RR, SP and primary progressive (PP) MS (p≤0.04). In relapse-onset MS, T1w/T2w-ratio was significantly lower in lesions and NAWM already at Expanded Disability Status Scale [EDSS]<3.0 and in the cortex only for EDSS≥3.0 (p≤0.02). Conversely, T1w/T2w-ratio was significantly higher in the striatum and pallidum for EDSS≥4.0 (p≤0.005). In PPMS, striatum and pallidum showed significantly higher T1w/T2w-ratio beyond EDSS=6.0 (p≤0.001). In MS, longer disease duration, higher EDSS, higher brain lesional volume, and lower normalized brain volume were associated with lower

lesional and cortical T1w/T2w-ratio and a higher T1w/T2w-ratio in the striatum and pallidum (β from -1.17 to 0.29, p≤0.04).

Conclusion: T1w/T2w-ratio is a clinically relevant marker sensitive to demyelination, neurodegeneration, and iron accumulation occurring in the different MS phases.

Disclosure: MM is supported by a MAGNIMS/ECTRIMS research fellowship. FB is supported by the NIHR biomedical research centre at UCLH. This work is partially supported by the Ministry of Education and Science, Republic of Serbia (project 175031).

OPR-141

CYBA genotypes may influence disease severity and recovery in patients with Guillain Barré syndrome

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Background and aims: The NOX2 enzyme expressed by myeloid cells, including inflammatory M1 macrophages, generates potentially neurotoxic reactive oxygen species (ROS). Single nucleotide polymorphisms (SNP) within the gene encoding the functional NOX2 subunit CYBA impact on the magnitude of NOX2-derived ROS formation from myeloid cells. We have recently reported that genetic variation at CYBA influences disease severity and time to progression among patients with multiple sclerosis (Törnell et al., Eur J Neurol, in press 2022). In this retrospective study, we determined the potential impact of variants of CYBA SNPs (rs1049254 and rs4673) for severity and recovery time among patients with Guillain-Barré syndrome (GBS).

Methods: 100 patients with GBS were followed for median 15 (range 0.5–86) months with clinical parameters sequentially recorded. 31% of the patients were female, and the median age at diagnosis was 52 years (range 17–85). DNA was isolated from serum samples for genotyping at rs1049254 and rs4673 using the TaqMan SNP genotyping kit.

Results: CYBA alleles linked to reduced NOX2-derived ROS formation, i.e. rs1049254/G and rs4673/A, were associated with reduced likelihood of requirement of assisted ventilation (p=0.01, Fisher's exact test, Figure 1A). Additionally, a higher frequency of low-ROS alleles was associated with shorter time to independent walking (p<0.001, log-rank test, Figure 1B).
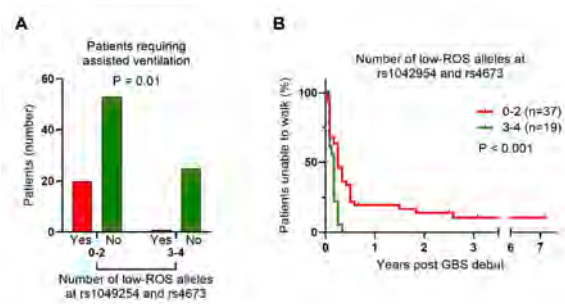
Figure 1: Patients Patients with Guillain Barré syndrome carrying 3-4 low-ROS alleles rs1049254/G and rs4673/A experienced reduced likelihood of requirement of assisted ventilation (A) and a shorter time to independent walking (B).

Conclusion: These results implicate NOX2-derived ROS in GBS pathophysiology and suggest that patients carrying low-ROS CYBA alleles show favorable outcomes in terms of disease severity and in the phase of recovery.

Disclosure: None of the authors report conflicting interests. The study was supported by Swedish State via the ALF agreement (grant no. ALFGBG-724881) and the Sahlgrenska Academy at University of Gothenburg.

Cerebrovascular diseases: Basic and translational stroke research

OPR-142

IPSC-derived mural cells to model the effects of hyperglicemia on the neurovascular unit

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Background and aims: The neurovascular unit (NVU) is a functional domain that constitutes the blood-brain barrier and contributes to a variety of trophic and signaling functions. Recent studies have highlighted a potential role of non-neuronal NVU constituents, such as mural cells, in the development of cognitive impairment. Moreover, a link between vascular risk factors for cognitive impairment, namely type 2 diabetes, and neurovascular dysfunction has been established. The aims of this project are to establish an in vitro model of mural cells (pericytes and vascular smooth muscle cells (VSMCs)) derived from induced pluripotent stem cells (iPSCs) and to assess the effects of changes in glucose homeostasis on mural cells' functionality.

Methods: We used a two-step protocol to differentiate neural crest cells and then mural cells from iPSCs. We also assessed cell contractility in response to endothelin-1, a potent vasoconstrictor, under basal conditions and following hyperglycaemic (25 mM), normoglycaemic (5.5 mM) and hypoglycaemic (0 mM) conditioning for 24 hours.

Results: We managed to obtain a mixed population of mural cells, although it was not possible to differentiate two distinct populations of pericytes and VSMCs. The cells were indeed able to contract in reaction to an endothelial vasoconstrictor stimulus. Contractile response seemed to be better after normoglycaemic conditioning compared to hypo- and hyperglycaemic one.

Conclusion: Further studies are needed in order to better characterize differences between pericytes and VSMCs that could be translated in more efficient differentiation protocols. Nevertheless, our preliminary results seem to confirm a potential relationship between impairment in glucose homeostasis and mural cells dysfunction.

Disclosure: The authors have nothing to disclose.

OPR-143

The Renin-Angiotensin-Aldosterone-System modulates astrocytes and their crosstalk with microglia and neurons

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Background and aims: Astrocytes are the most abundant central nervous system (CNS) cell type and are fundamentally involved in homeostasis, neuroprotection, and synaptic plasticity. The renin-angiotensin-aldosterone system regulates arterial blood pressure through endothelial cells and perivascular musculature. Moreover, astrocytes express angiotensin II type 1 and 2 receptors. However, their role in astrocytic function has not yet been elucidated. We hypothesized that the angiotensin II receptors impact astrocyte function as revealed in an in vitro system mimicking cerebral ischemia.

Methods: Astrocytes were exposed to telmisartan or PD123319 (angiotensin II type 1 and 2 receptor-blockers) under normal conditions (control) or deprivation from oxygen and glucose (OGD). Conditioned medium (CM) of astrocytes was harvested to elucidate astrocyte-mediated indirect effects on microglia and cortical neurons.

Results: Telmisartan increased the survival of astrocytes during acute and prolonged ischemic conditions in vitro without affecting their proliferation rate or disturbing their expression of S100A10, a marker of activation. PD123319 resulted in both increased expression of S100A10 and proliferation rate. The CM of telmisartan-stimulated astrocytes reduced the expression of pro-inflammatory mediators in microglia, while PD123319-stimulated astrocytes increased the expression of pro-inflammatory markers in microglia with simultaneous reduction of anti-inflammatory markers. Increased neuronal activity was observed after treatment of neurons with CM of telmisartan- as well as PD123319-stimulated astrocytes.

Conclusion: Data show that angiotensin II receptors have functional relevance for astrocytes and modulate both astrocytes' phenotype and functionality. The effects of modulation of angiotensin II receptors on astrocytes might potentially serve as a therapeutic target in human stroke.

Disclosure: The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

OPR-144

Electrocorticographic band changes during infarct progression and spreading depolarizations in gyrencephalic brain

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Background and aims: Characterization of temporal and anatomical electrocorticographic changes occurring after a Middle Cerebral Artery occlusion (MCAo), including those caused by Spreading Depolarizations (SDs) as outcome biomarkers.

Methods: The left medial cerebral arteries were clipped in six Landrace swine. Five electrodes were placed bilaterally over the parietal and frontal cortex corresponding to the irrigation territory of the MCA and the Anterior Cerebral Artery (ACA). Five-minute ECoG signal segments were obtained before, 0, 4, 8, and 12 hours after the artery occlusion, and before, during, and after the negative DC shift of SDs. The power spectrum of signals was decomposed into the delta, theta, alpha, beta, and gamma bands.
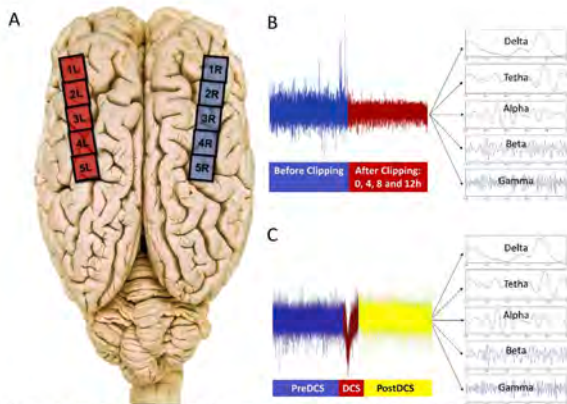
Figure 1. Placement of the electrodes and signal gathering

Results: After the artery clipping, channels located near to the MCAo (nMCAo) registered permanent power drop in all the frequencies. Channels far from the MCAo (fMCAo), coinciding with the penumbra, exhibited constant shrinkage of fast waves mainly alpha, and progressive decline in delta and theta. After 8 hours, the ACA channel recorded power decay in all the frequencies except gamma. During the DC shift, all brain oscillations were abated at MCA and ACA channels. Delta, theta, and alpha remained collapsed in the fMCAo channels, whereas no power reductions were observed in the ACA channel after the DC shift.
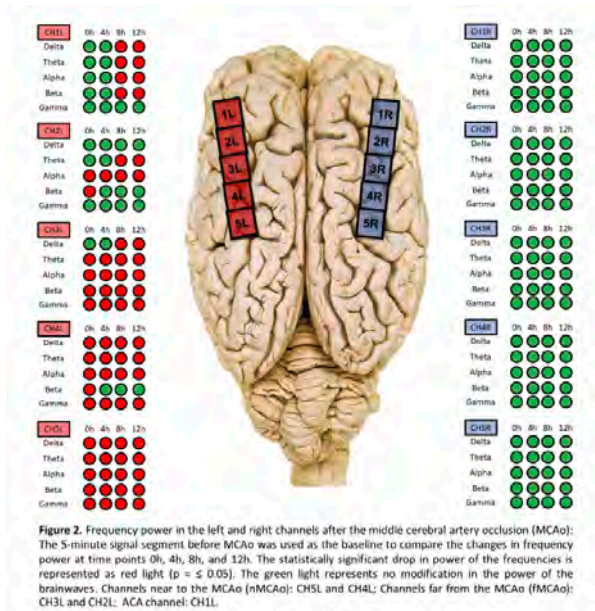
Figure 2. Frequency power in the left and right channels after the middle cerebral artery occlusion (MCAo)
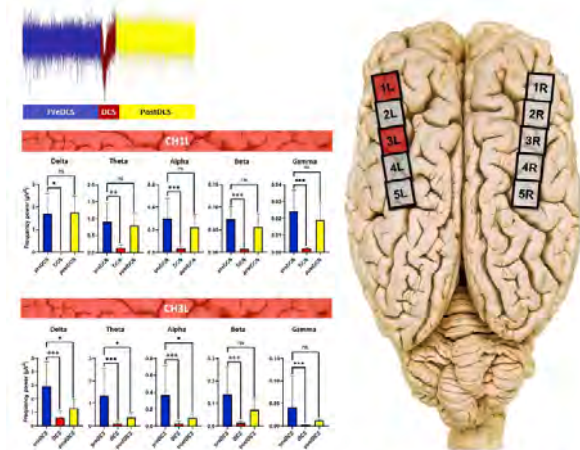
Figure 3. Frequency power in the left channels during and after the DC shift of the SDs

Conclusion: ECoG can identify the penumbra zone and monitor infarct progression. Secondary brain injury was observed in the irrigation territory of ACA after 8 hours of blood constraints at MCA. SDs generate drastic frequency disturbances regardless of the cortical location, causing sequelae at the presumable salvable brain tissue.

Disclosure: Nothing to disclose.

OPR-145

Thrombo-CARE - histological and immunohistochemical analysis of clots to differentiate stroke etiology

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Background and aims: Despite extensive diagnostic efforts, etiology of stroke remains unclear in about 20% of patients. The establishment of mechanical thrombectomy offers the possibility to enhance etiological determination by histological and immunohistochemical analysis of retrieved thrombotic material.

Methods: Clots from 200 consecutive patients undergoing mechanical thrombectomy in a neurovascular center were investigated by Hematoxylin and Eosin, CD3 and CD45 staining. Semiquantitative and computer-based automatic image analysis defined histological composition and relative fractions of immune stained areas. Results were initially correlated with strokes of known etiology. Subsequently, thrombi of unknown source were characterized with regard to their (immuno-)histological profile attempting etiological classification.

Results: 198 samples were accessible for analysis. Mixed histology appeared in 123 (62%), thrombocyte/fibrin-rich in 45 (23%) and erythrocyte-rich histology in 18 (9%) patients. Etiology was classified as cardio-embolic in 87 (44%), arterio-embolic in 37 (19%) and undetermined in 26 (13%) patients. 20 patients with cardio-embolic stroke had thrombocyte/fibrin-rich clots, five patients with arterio-embolic stroke. eight patients with arterio-embolic stroke had erythrocyte-rich clots, one patient with cardio-embolic stroke. Associations between histology and etiological groups were significant (p=0.0061). Associations between immune staining and all etiological groups were not significant. Clots from embolic strokes of undetermined source (ESUS) presented similar histological features as cardio-embolic ones.

Conclusion: Erythrocyte-rich thrombi were significantly associated with arterio-embolic stroke, thrombocyte/fibrin-rich thrombi with cardio-embolic stroke. Many patients with ESUS shared similar histological clot features as cardio-embolic strokes. Patients with ESUS and thrombocyte/fibrin-rich clots especially require long-term cardiac rhythm monitoring and may benefit from oral anticoagulation.

Disclosure: Nothing to disclose.

OPR-146

Distribution of five clinically important neuroglial proteins in the human brain

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Background and aims: Glial fibrillary acidic protein (GFAP), myelin basic protein (MBP), neurofilament light chain (NFL), Tau and ubiquitin carboxy-terminal hydrolase L1 (UCHL1) are five neuroglial proteins that are used as biomarkers of tissue damage in the nervous system. There is incomplete knowledge of their quantitative distribution in the CNS, limiting the interpretability of circulating levels of these proteins. The aim with this study was to quantitate the concentration of GFAP, MBP, NFL, Tau and UCHL1 in different anatomical regions in the CNS, thereby creating a map of how these proteins are distributed in the in the human brain and spinal cord.

Methods: Tissue homogenates from 17 selected anatomical regions in the CNS, from ten deceased donors were analysed with ELISA for each protein of interest. When appropriate, the protein concentrations were adjusted for post-mortem interval.

Results: The concentration of GFAP, MBP, NFL, Tau and UCHL1 varied substantially between different CNS regions. The concentration of MBP were tenfold higher in white matter compared with cerebral cortex, whereas Tau showed an inverse pattern. GFAP, NFL and Tau displayed an anteroposterior gradient in cerebral white matter. The cerebellum had relatively low concentrations of all the investigated proteins.
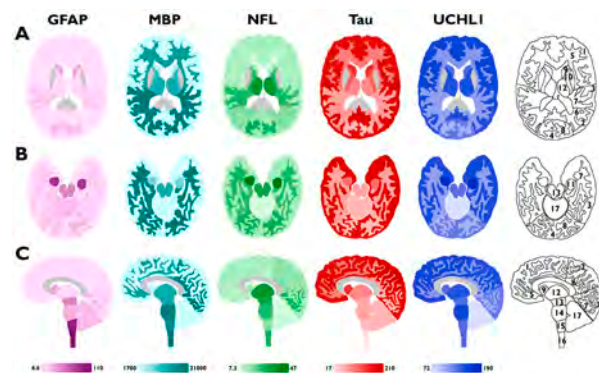
Figure 1 A-C. (A) axial cranial, (B) axial caudal, and (C) sagittal sections of the CNS. The bar below every section shows the colour gradient used between the minimum and maximum value for each neuroglial protein. Darker colour represents higher values.

Conclusion: This study investigated the tissue content of GFAP, MBP, NFL, Tau and UCHL1 in different anatomical CNS regions, and the results show a substantial variation between CNS regions and investigated proteins. This information can be used as a reference when interpreting circulating levels of these proteins in relation to localisation and extent of a CNS damaging disease.

Disclosure: The authours reports no competing interests.

OPR-147

Circulating endothelial progenitor cells (cEPC) as a putative predictive cellular biomarker in Moyamoya arteriopathy

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Background and aims: Moyamoya arteriopathy (MA) is a rare cerebrovascular disorder characterized by ischemic/hemorrhagic strokes. The pathophysiology is unknown. Circulating endothelial progenitor cells (cEPC) have been hypothesized to contribute to vascular remodeling of MA. Our aim is to evaluate if % cEPC could be used as a cellular prognostic or predictive biomarker in MA patients.

Methods: 75 MA patients of GEN-O-MA project, 34 healthy donors (HD) and 20 subjects with unrelated diseases (ACVD) were recruited. Clinical data and peripheral blood samples were collected. Percentage of cEPC ((cEPC/(µl))/(WBC/(µl)) x 100), defined as CD45dimCD133+CD34+, was measured by FACS.

Results: Our previous comparison did not show significative differences of % cEPC in peripheral blood of MA, HD and ACVD. Nevertheless, the selection of a patient subgroup (Caucasian, adults, with a pre-surgical sampling) resulted in a substantial decrease of % cEPC in MA as compared to HD. Here, such an evidence became more significant as far as the size of MA subgroup raised. Pediatric patients instead exhibited an increase in % cEPC as compared to age/sex matched HD. Moreover, an analysis was performed to correlate % cEPC value to clinical features, prognosis and disease severity within the MA group.

Conclusion: Our findings suggest that % cEPC value could be a promising "circulating cellular biomarker" for a better patient stratification in MA. The validation of these results on a larger population could provide a new reliable biological marker in support to neuroimaging data, to date the only available prognostic tool for MA patient management.

Disclosure: Nothing to disclose.

Neurogenetics 2

OPR-148

Repeat expansion size predicts age of onset in RFC1 CANVAS and disease spectrum

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Background and aims: Biallelic repeat expansions in RFC1 have been identified as the cause of cerebellar ataxia, neuropathy, vestibular areflexia syndrome (CANVAS). Based on the first descriptions, RFC1 disease has variable phenotype, onset and progression, however the factors underlying this heterogeneity are still largely unknown.

Methods: We investigated the effect of the repeat expansion size on age at onset, clinical phenotype and disease course in a multicenter cohort of 316 patients with biallelic AAGGG RFC1 repeat expansions confirmed by Southern Blotting. Furthermore, we assessed the stability of the repeat during intergenerational transmission in 19 families.

Results: Median age at onset of imbalance was 55 years and median disease duration at last follow-up was 10 years. At last examination, 45% of patients showed a full-blown CANVAS, 16% isolated sensory neuropathy and 39% neuropathy with cerebellar or vestibular involvement. RFC1 expansion ranged from 249 to 3,885 repeats. An inverse correlation, which was stronger for the smaller allele, was observed between the repeat size and age at neurological onset. A larger expansion was also predictive of a more complex phenotype and a faster progression to disabling manifestations. RFC1 expansion appeared stable during parental transmission, with no or minimal variation in most cases.
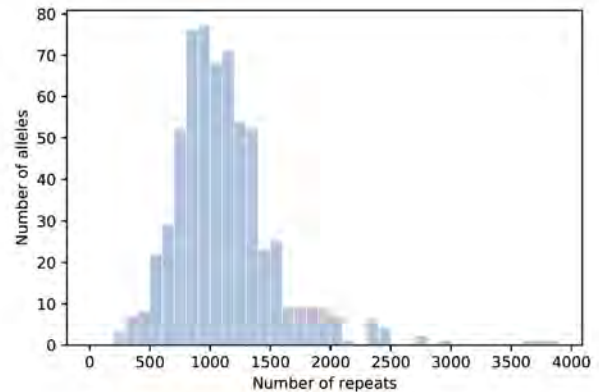
Distribution of the size of the AAGGG repeat expansions in our cohort.
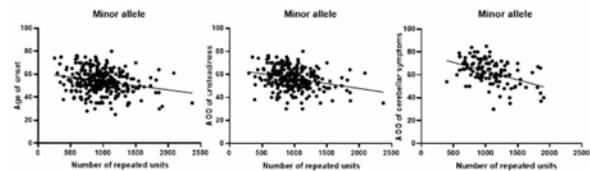
Correlation between the size of the minor RFC1 allele and age of onset, age at onset of unsteadiness and age at onset of cerebellar symptoms.
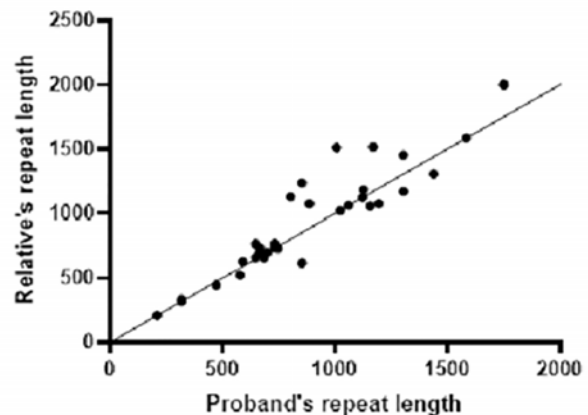
Relationship between the repeat length in probands and first-degree relatives.

Conclusion: RFC1 disorder shows heterogenous clinical presentation and disease course. A smaller expansion has a favorable prognostic role and is associated with later disease onset, later appearance of cerebellar symptoms and delayed need for walking aids. Southern blotting is recommended after PCR screening in all RFC1 positive cases to better inform patients on their prognosis.

Disclosure: EAN Research Fellowship 2021.

OPR-149

Brain metabolic profile and longitudinal changes in the presymptomatic phase of GRN-associated frontotemporal dementia

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Background and aims: Progranulin gene (GRN) mutations are among the main genetic causes of frontotemporal dementia (FTD). Previous biomarker-based studies shed light on pathophysiological changes occurring during the presymptomatic phase. FDG-PET may be useful to capture early signs of brain dysfunction, before structural changes; however, there is a lack of longitudinal investigations assessing brain metabolic changes in GRN-associated FTD. This study aimed at characterizing the dynamic profile of brain hypometabolism in presymptomatic GRN carriers and its position in preclinical pathochronology.

Methods: This prospective study analysed 27 preysmptomatic GRN carriers and 31 demographically comparable non-carriers issued from the Predict-PGRN study (NCT04014673). Participants were evaluated over 5 years with cognitive/behavioral assessments, plasma neurofilament measurements, brain MRI and FDG-PET imaging. PET data were analysed with voxel-wise comparisons, metabolic percent annual changes maps (PET-PAC) and region of interest-based approach.

Results: The median age at inclusion was 42 years, ≥15 years before expected disease onset. Since their inclusion, carriers displayed significant hypometabolism involving superior and middle temporal gyri, in absence of cortical atrophy or any cognitive changes. During follow-up accelerated metabolic decline (up to 20%/year) occurred in the lateral temporal region, as well as in temporal pole and superior occipital gyrus. Metabolic changes in temporal cortex were associated with increase in neurofilaments.

Figure 1: Cross-sectional voxel-wise analysis of brain glucose metabolism in presymptomatic GRN carriers compared to controls at baseline, showing a cluster of hypometabolism in the left middle temporal gyrus (p<0.001, uncorrected).
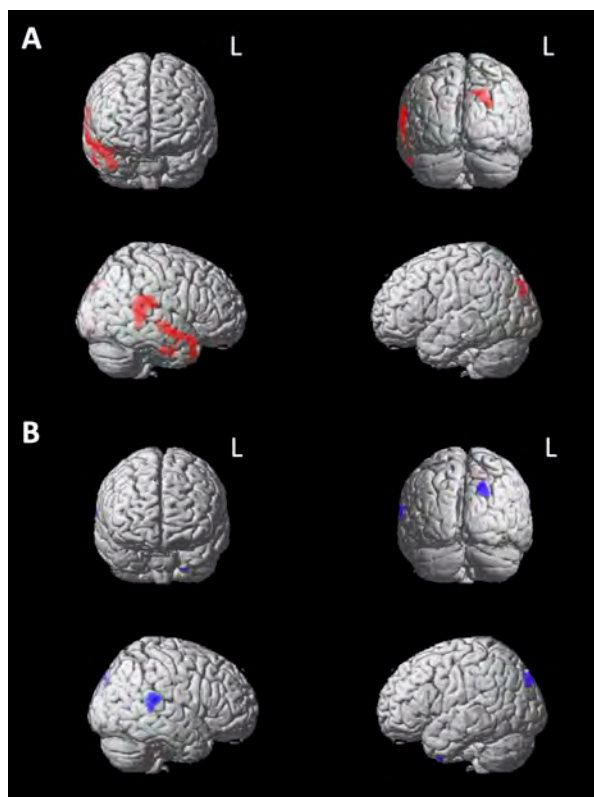
Figure 2: Longitudinal decrease of glucose metabolism in carriers during the 5-year follow-up, peaking in right superior/middle temporal lobe, from pairwise voxel-based t-tests (A) and PET-PAC maps (B) (p<0.001, FDR cluster-level corrected).

Conclusion: Brain metabolic changes are present since the earliest phases of GRN disease. They highlight the lateral temporal lobe as hub of lesional accumulation, heralding subsequent spreading and neurodegeneration. Their annualised change rates may serve as valuable biomarkers to assess the efficacy of therapeutic trials in presymptomatic carriers.

OPR-150

Whole exome sequencing in 444 families with rare paediatric neurological disorders in Central Asia and Transcaucasia

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Background and aims: Little is known about the genetics of rare paediatric neurological disorders (RPND) in Central Asia and Transcaucasia (CAT). Additionally, ethnic groups from CAT are largely underrepresented in reference population genetic databases. Here, we report the results of proband and trio research whole-exome sequencing (WES) in 444 families with RPND from five CAT countries.

Methods: In 2018 the "University College London (UCL)-Central Asia-Transcaucasia disease diversity project" was initiated, and hitherto, ~2,000 families with RPND from CAT have been recruited. To date, proband or trio research WES data is available from 444 families. WES, variant filtering, dynamic re-analysis of WES data, and variant confirmation/segregation analysis by Sanger sequencing were performed at UCL as previously described (PMID: 29343805).

Results: Almost half of the cohort (47%) were probands from consanguineous unions mostly originating from Azerbaijan and Tajikistan (Figure 1). Families with multiple affected members made of 14% of the cohort. A mean age of the probands at the time of recruitment was 8.7±7.5 years. Clinical phenotypes were classified into 5 diagnostic categories (Table 1). Trio WES was performed on 36% of families while proband WES was done in 64%. Overall 179 families (40%) received a molecular diagnosis with causative variants identified in known disease-associated genes (Figure 1, Table 1). Firm novel genes were found in 2% and putative candidate genes were identified in 8% of the families (Table 2). Several actionable genes improved clinical management.

Figure 1 The results of research WES in 444 families with rare paediatric neurological disorders in CAT
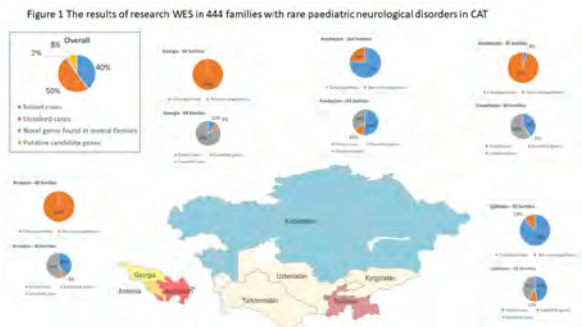
Table 1 Diagnostic categories and known disease genes found in the CAT cohort

Table 2 Novel candidate genes identified in this study

Conclusion: This is the first large-scale research WES study in RPND in CAT. The study showed a good diagnostic rate.

Disclosure: Authors have no disclosures.

OPR-151

Long-term clinical benefit of idebenone in LHON: Results from the prospective, natural history-controlled LEROS study

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Background and aims: Idebenone is approved in Europe for treating Leber's hereditary optic neuropathy (LHON) – a rare mitochondrial disorder resulting in vision loss. Controlled data detailing long-term treatment is sparse.

Methods: Patients with LHON onset ≤5 years prior were enrolled and stratified by time since onset: subacute/dynamic (≤1 year) and chronic (>1 year). The primary outcome measure was clinically relevant benefit (CRB=clinically relevant recovery and/or stabilisation of visual acuity [VA]) from baseline after 12 months of treatment. Data from 181 patients treated up to 24 months were compared to an external natural history (NH) cohort (372 patients), matched by time since disease onset.

Results: The primary endpoint was met (42.3% CRB in treated subacute/dynamic eyes at 12 months [60/142] vs 20.7% [40/193] in matched NH cohort eyes [p=0.0020]); this difference was maintained after 24 months (52.9% [64/121] vs 36.0% [27/75] [p=0.0297]). A similar result was observed in chronic patients at 12 months (50.3% [72/143] vs 38.6% [59/153] [p=0.0087]). In subacute/dynamic eyes, CRB was largely driven by stabilisation of VA at 12 months (64.5% [20/31] vs 22.5% [9/40] [p=0.0005]), while in chronic eyes by recovery of VA (32.9% [47/143] vs 19.6% [30/153] [p=0.0034]).

Conclusion: In LEROS, long-term treatment with idebenone resulted in prolonged clinical benefit in patients with LHON. This benefit was largely driven by preventing significant VA loss in the subacute/dynamic phase, and by VA recovery in the chronic phase.

Disclosure: TK has received research support and personal fees from Santhera Pharmaceuticals and Chiesi GmbH. LT and XL are employees of Chiesi Farmaceutici S.p.A.LEROS was funded by Santhera Pharmaceuticals. TK, VC, PYWM: Research support and/or compensation from Santhera Pharmaceuticals, Chiesi GmbH and GenSight Biologics. LT, XL: Employees of Chiesi Farmaceutici S.p.A.

Neuro-oncology 2

OPR-152

CAR T-cell therapy in BOlogNa - NEUrotoxicity TReatment and Assessment in Lymphoma: the CARBON-NEUTRAL study

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Background and aims: To investigate clinical, laboratory and instrumental characteristics of chimeric antigen receptor (CAR) T-cells therapy-related neurotoxicity.

Methods: In this prospective, monocentric study, consecutive patients affected by refractory B-cell non-Hodgkin lymphoma were included. Patients were comprehensively screened (neurological examination, EEG, brain MRI, nerve conduction study, neuropsychological evaluation) before infusion. From the day of CAR T-cells infusion, patients underwent serial examinations to monitor development of neurotoxicity (Figure 1).
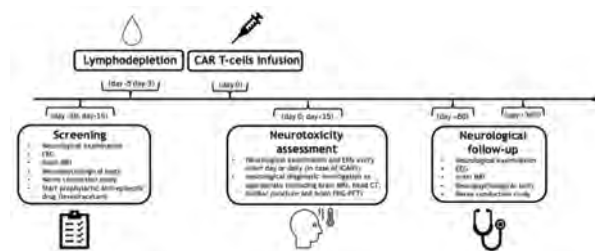
Figure 1: Neurological assessment protocol comprehensive of screening, toxicity monitoring and follow-up.

Results: Of 103 consecutive patients candidate to receive anti-CD19 CAR T-cells infusion, 45% (n=46) were treated and included in the study (Figure 2). Median age at infusion was 56.5 years and 13 patients (28%) were females. Seventeen patients (37%) developed neurotoxicity characterized by encephalopathy frequently associated with language disturbances (65%) and frontal lobe dysfunction (65%). A predominant frontal lobe involvement was also supported by ancillary tests (EEG, neuropsychological evaluation and brain FGD-PET). Median time at onset and duration were five and eight days, respectively. EEG abnormalities at baseline represented a negative prognostic factor (OR=10.027; CI=1.509-66.628; p=0.017). Notably, CRS was invariably present prior to or concomitant with neurotoxicity, and all patients who exhibited severe CRS developed neurotoxicity. A strong correlation between CRS and neurotoxicity was observed in all clinical and laboratory explored parameters (Figure 3). Fourteen patients had complete neurological resolution, whereas three patients died secondary to systemic complications, of whom only one with neurotoxicity (fulminant cerebral oedema).
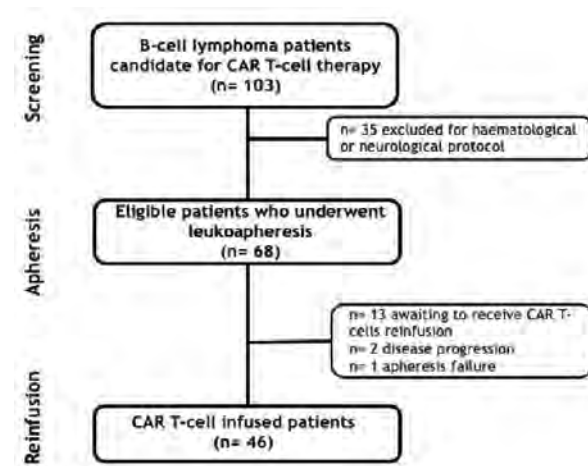
Figure 2: Eligibility flow chart of patients with B-cell lymphoma who received CAR T-cell therapy.
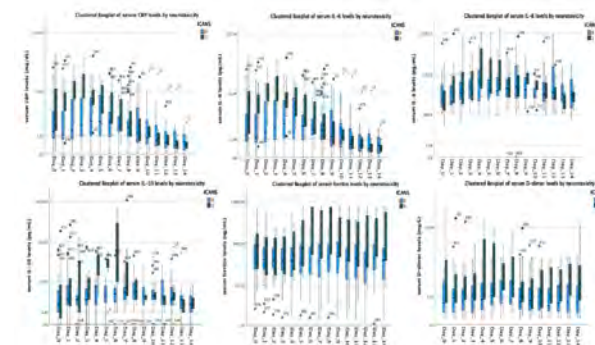
Figure 3: Serum level of CRP, IL-6, IL-8, IL-10, ferritin and D-dimer during the first two-weeks from CAR T-cells infusion in ICANS patients (blue boxes) and patient who did not develop neurotoxicity (green boxes).

Conclusion: Neurotoxicity related to CAR T-cell therapy exhibits a distinctive clinical and investigative signature, namely frontal predominant encephalopathy, and is strictly related to CRS, arguably involving cytokine-mediated neuroinflammatory mechanisms.

Disclosure: Nothing to disclose.

OPR-153

Neratinib for treatment of leptomeningeal metastases from HER2-positive breast cancer in extended access program

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Background and aims: The aim of the study was to evaluate the activity of neratinib in leptomeningeal metastases (LM) from HER2-positive breast cancer (BC) after the failure of multiple treatments.

Methods: Adult patients with a newly diagnosed LM (LANO criteria) from HER2-positive BC with KPS ≥60 were included. Coexistence of BM that have or not received radiotherapy and previous antineoplastic drugs for systemic disease were allowed, with the exclusion of lapatinib. Primary endpoint was the overall survival (OS). Secondary endpoints were progression-free survival (PFS), neurological benefit, radiological response, and tolerability.

Results: Nine patients have been enrolled with a median age of 44 years, and a median KPS of 80. Median time since LM onset from the diagnosis of primary BC was 42 months, after a median number of adjuvant treatments before LM of 3. Three patients developed LM alone, and other 6 had LM associated with BM. Six-months and 1-year OS were 66.7% and 22.3%, respectively, with a median OS of 8 months (95%CI 3-13*). Median PFS was 3.5 months (95%CI 2-6) after the start of treatment. A neurological improvement was reported in 2/9 patients (22.2%), while in other 4/9 patients (44.5%) was achieved a neurological stabilization lasting for a median time of 5 months (95%CI 2-19). The best radiological response was a stable disease in 5/9 patients (55.6%). A CSF clearance was observed in 1 patient (11.1%). Two patients (22.2%) had mild diarrhea correlated with neratinib.

Conclusion: Neratinib might be a safe and effective treatment in LM from heavily pretreated HER2-positive BC

Disclosure: The Authors declare that have no conflict of interest.

OPR-154

Long term neurological safety in B-cell lymphoma patients treated with CAR T-cell therapy: a prospective cohort study

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Background and aims: Anti-CD19 CAR T-cell therapy has transformed the standart of care for patients with relapsed and refractory hematologic malignancies, but is frequently associated with acute neurotoxicity. Yet, long-term neurological safety is still unknown.

Methods: We here report a long-term, prospective, follow-up study of an adult patient population with aggressive B-cell lymphoma, treated with CAR – T cell therapy in our center between October 2018 and August 2019 All patients underwent neurological examination, neuropsychological assessment, cerebral MRI and completed self-administrated questionnaires, both at baseline and two-years after CAR T-cells infusions.

Results: 52 patients were included, 33 had tumour progression or died, leaving 19 disease-free patients for long-term evaluation (at 2 years). None of these patients developed new neurological deficits or MRI changes when compared to baseline. Cognitive performances showed no difference before and two years later after for all evaluated patients, including in patients who had developed acute neurotoxicity after CAR T-cells. In self-questionnaire assessments, anxiety and depression complaints significantly (?) improved at two years when compared to baseline.
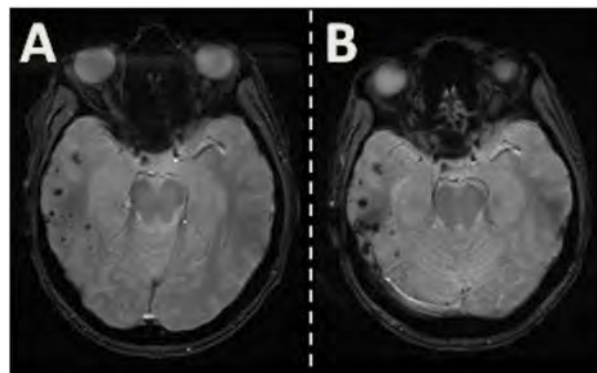
Brain MRI: T2* weighted images of patient with multiple micro bleeds at baseline (A) and at two years (B) after CAR T-cell treatment.

Conclusion: This study suggests a long-term neurological safety for CAR-T cell therapy as neither neurocognitive disorders, nor neurologic impairments, nor modifications of cerebral imaging were observed two years after CAR T-cell infusions.

Disclosure: Nothing to disclose.

OPR-155

Risk factors for temozolomide-induced myelotoxicity and effect of dose adjustments on prognosis of glioblastoma patients

N. Grun [1], J. Osinga [1], A. Van der Vegt [1], F. Van den Elzen [1], C. Den Otter [1], T. Postma [1], M. Schuur [1], P. De Witt Hamer [2], A. Bruynzeel [3], F. Lagerwaard [3], M. Van Linde [4], I. Bartelink [5], B. Lissenberg-Witte [6], M. Kouwenhoven [1]

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Background and aims: Temozolomide (TMZ) is generally well-tolerated in patients treated for glioblastoma; a malignant primary brain tumor with poor prognosis. Still, 16% of the patients develop severe myelotoxicity during standard first line treatment. In this study, we evaluate risk factors for severe myelotoxicity and prognosis of toxicity-dictated treatment adjustments.

Methods: Retrospective cohort study of patients treated with standard treatment between 2000–2021; 359 patients with glioblastoma were included. We identified risk factors for myelotoxicity by logistic regression, determined decrease in thrombocytes to identify patients at risk for severe thrombocytopenia during chemoradiation with ROC analysis and used Kaplan- Meier analysis for survival analyses.

Results: Females (OR 12,807; [95% CI: 5,488–29,884]) and patients >50 years (OR 3,473 [1,373–8,785]) were at risk for severe myelotoxicity. Females were more at risk for severe thrombocytopenia (OR 9,667 [4,164–22,442]) compared to men. A decrease in thrombocyte counts of ≥31.22% identified patients who developed severe thrombocytopenia with a sensitivity of 100% and specificity of 80.5% (AUC 0.952 [0.910–0.994]). The median survival of patients discontinuing adjuvant treatment was reduced compared to patients who received 6 courses TMZ with or without dose reduction (14 vs 21 months; p=0.004).

Conclusion: Females and patients >50 years were at risk for myelotoxicity. Patients with a decrease in thrombocytes of ≥31.22% during chemoradiation were at risk for severe thrombocytopenia. Discontinuation of adjuvant TMZ treatment negatively impacted prognosis, dose reductions during the adjuvant phase did not affect survival in patients with glioblastoma.

Disclosure: Nothing to disclose.

ePresentations

Saturday, June 25, 2022
COVID-19 & Infectious diseases 1

EPR-001

Sleep quality of myasthenia gravis patients during the coronavirus disease-19 pandemic

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Background and aims: The coronavirus disease 2019 (COVID-19) is the largest pandemic of our times. Sleep disturbances are underestimated symptoms in myasthenia gravis (MG) patients because the main focus is on other neurological complaints. The aim was to assess the self-perceived quality of sleep (QoS) in patients with MG, during the coronavirus disease-2019 outbreak.
Methods: The study included 57 patients with MG and 68 healthy control (HC) subjects. We collected socio-demographic and clinical data, and also used the following questionnaires: Pittsburgh sleep quality index (PSQI), a revised 15-item Myasthenia Gravis Quality of Life Questionnaire (MGQOL15r), Hamilton scales for the assessment of anxiety (HAM-A) and depression (HAMD). The actual severity of the clinical manifestation was estimated using MG activities of daily life (MGADL). We assessed patients in April 2020 and April and May 2021, using the same questionnaires.
Results: Patients with MG had higher scores on PSQI than HC on booth time points (p<0.01). Patients with higher scores on MGQOL15r, HAM-A, and HAM-D scales had higher scores on PSQI (p<0.01). Patients with higher scores on MGADL (p<0.01), females, and unemployed patients had higher scores on PSQI (p<0.05). We noticed a statistically significant difference between the results at these two-time points in PSQI scores (p<0.05), which was better one year later. Higher scores on MGADL were an independent predictor of the worse PSQI scores.
Conclusion: Lower levels of QoS correlate with worse life quality, some clinical and socio-demographic variables in MG patients, especially with higher disease severity.
Disclosure: Tha authors have nothing to disclose.

EPR-002

Neurological complications of COVID-19 in hospitalized patients: a comparison between the first and successive waves

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Background and aims: Although previous studies have already described the neurological complications of SARS-CoV-2 infection and its prognostic relevance, uncertainty remains among epidemiological differences through different waves of the pandemic. We aim to describe the spectrum of neurological manifestations in hospitalized patients with SARS-CoV-2 infection in our hospital, and to assess for potential differences between the first (from March to August, 2020) and successive waves of the pandemic.
Methods: Retrospective, single-centre cohort study including all patients hospitalized due to SARS-CoV-2 infection who required assessment by a neurologist for the presence of new-onset neurological symptoms during the first year of the pandemic (March 2020 to March 2021). We analysed for epidemiological, clinical, paraclinical, treatment and outcome differences between the first and successive waves.
Results: Of 5525 patients hospitalized with SARS-CoV-2 infection, 128 (2.3%) met the inclusion criteria (60.2% men, mean age 68.5±13.3 years-old). The most common diagnosis was ischemic stroke (29.7%), followed by COVID-19-related encephalopathy (14%) and polyneuropathy (8.5%), being other diagnosis less frequent. COVID-19-related encephalopathy, polyneuropathy, mononeuropathy and myopathy were more frequent in patients hospitalized in the ICU (p<0.02). Overall mortality rate was 21.9%, being stroke the only diagnosis associated with higher mortality (p<0.02). We found no statistical differences between the first and successive waves.
Conclusion: During the pandemic, prevalence of neurological symptoms of new onset was low. The most common diagnosis was ischemic stroke, which was associated with a higher mortality rate. Although this study did not find differences in neurological complications between the several waves, further studies are needed.
Disclosure: Nothing to disclose.

EPR-003

Abstract withdrawn.

EPR-004

Impact of the COVID-19 epidemic on medication of patients with Multiple Sclerosis in Bologna (Northern Italy)

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Background and aims: Multiple Sclerosis (MS), a chronic inflammatory disease of the central nervous system, requires complex diagnostic and therapeutic management. Adherence to Disease Modifying Drugs (DMDs) is associated with reduced relapse rates and disease progression. Lockdown measures during COVID-19 epidemic may have impacted the consistency of treatment with DMDs among people with MS. We aimed to investigate if the COVID-19 epidemic was associated with variations in the adherence to DMD treatment in people with MS (PwMS) in the Local Health Trust of Bologna (LHTB), Italy.

Methods: Population-based cohort study. PwMS were identified through administrative databases using a validated algorithm. Univariate and multivariate logistic regression with cluster-robust standard errors were performed to assess the association between adherence to DMDs (defined as proportion of days covered $\geq 80\%$) and a reference period: COVID-19 (March 1st, 2020 – February 28th, 2021) vs pre-COVID-19 (March 1st, 2019 – February 29th, 2020) years. Sensitivity analyses were carried out to support the main results.

Results: The COVID-19 and the pre-COVID-19 MS cohorts treated with DMDs included 578 and 653 patients, respectively. Adherence to DMDs therapies declined from 68.2% (pre-COVID-19 year) to 63.4% (COVID-19 year). People in the COVID-19 cohort were 19% less likely to be adherent than people cared for during the same period in the pre-COVID-19 year (adjusted OR: 0.81 (95% CI: 0.67-0.97)).

Conclusion: The COVID-19 epidemic and the associated restrictive public health measures may have had a causal role in the observed significant reduction in the adherence to pharmacological therapies with DMDs of PwMS assisted by the LHTB.

Disclosure: Nothing to disclose.

EPR-005

Serum CGRPalpha and beta levels are increased in COVID-19 inpatients

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Background and aims: Calcitonin gene-related peptide (CGRP) is the key molecule in migraine pain. Interestingly, CGRP infusion in volunteers induces headache (theoretically via CGRPalpha) and diarrhea (through CGRPbeta), two common symptoms in COVID-19 patients, which has raised the hypothesis that excess in CGRP release might contribute to COVID-19 pathophysiology. We aimed to analyze CGRPalpha and beta in COVID-19 patients.

Methods: CGRPalpha (Abbexa, UK) and CGRPbeta (CUSABIO, China) levels were assessed by ELISA from morning blood samples in 51 (mean age=59.5, range= 27–91; 56.8% females) COVID-19 inpatients and 61 healthy controls (mean age=54.2, range=28–91; 68.8% females) with no headache history.

Results: CGRPalpha levels were significantly increased in COVID-19 inpatients (57.3+/-34.1 pg/mL) vs healthy controls (44.5+/-26.5 pg/mL) (+22.4%; p<0.01) (Figure 1). CGRPalpha levels were significantly raised (p<0.05) in COVID-19 inpatients experiencing headache (55.2+/-34.4 pg/mL; n=25) or diarrhea (63.7+/-38.3 pg/mL; n=26) vs controls (Figure 2). CGRPbeta levels were also significantly elevated in COVID-19 inpatients (6,3+/-2.6 pg/mL) vs controls (4.95+/-4.42 pg/mL) (+26.2%; p<0.0008) (Figure 1), though this increase was numerically clear (6,3+/-2.4; +26,2%) and stadistical significant (p=0.0035) for COVID-19 patients with diarrhea but not for those experiencing headache (5.1+/-2.2; +3%) (Figure 2).
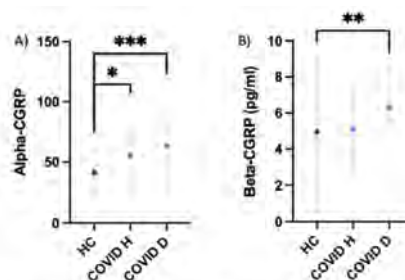
Figure 2.- Comparison of A) CGRPα and B) CGRPβ levels in pg/mL between Covid-19 inpatients classified whether they experienced headache (COVID H) and diarrhea (COVID D) and healthy controls (HC). Data is shown as mean ± standard deviation *p<0.05; **p>0.01; ***p>0.0001.
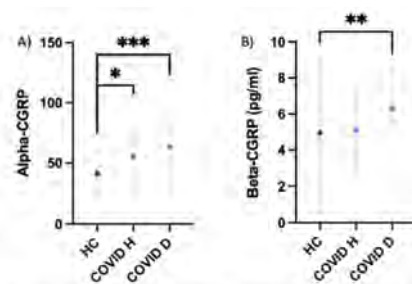
Figure 2.- Comparison of A) CGRPα and B) CGRPβ levels in pg/mL between Covid-19 inpatients classified whether they experienced headache (COVID H) and diarrhea (COVID D) and healthy controls (HC). Data is shown as mean ± standard deviation *p<0.05; **p>0.01; ***p>0.0001.

Conclusion: We show for the first time an increase in both plasma CGRPalpha and beta levels in COVID-19 inpatients, which suggest a role for this ubiquitous neuropeptide in the clinical manifestations of this disease. While both subtypes seemed to be released in patients with headache, an increase in CGRPbeta was seen predominantly in patients with diarrhea.

Disclosure: Supported by grants from ISCIII (PI20/01358) and IDIVAL (INNVAL 20/25).

EPR-006

Autonomic dysfunction in non-critically-ill COVID-19 patients: an observational, cross-sectional, study.

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Background and aims: Evidence are emerging about a neurological involvement of Sars-Cov-2. Autonomic disfunction in patients recovering from acute Coronavirus Infectious Disease-19 (COVID-19) has been recently described, while for the acute phase of the disease clear evidence is lacking. The aim of the study was to assess the prevalence of orthostatic hypotension (OH) and of self-reported dysautonomic symptoms in a cohort of non-critically-ill COVID-19 patients.

Methods: In this observational, cross-sectional study, we compared 38 non-critically-ill patients with COVID-19 (COVID+ group) to 38 healthy volunteers (COVID– group), enrolled between May 1st, 2021 to December 20th, 2021. The autonomic assessment was performed through a self-reported questionnaire, the composite autonomic symptom score 31 (COMPASS31), and a lying-to-standing orthostatic stress test. For the univariate analysis we adopted the Wilcoxon-signed rank test and the Fisher' exact test, respectively for numerical and categorical variables. The significant results were then adjusted for concomitant pharmacological treatments assumed by study participants through a multivariable ordinal logistic regression or a logistic regression, as appropriate.

Results: The prevalence of OH ion and the total scores of COMPASS31 were significantly higher in the COVID+ group than controls. In the univariate analysis, significant differences between groups emerged in the secretomotor, orthostatic intolerance and gastrointestinal COMPASS31 domains. All these results maintained the statistical significance after the adjustment for the aforementioned variables, except for the differences in the gastrointestinal domain of COMPASS31.

Table 1. Results of COMPASS31 and lying-to-standing orthostatic stress test univariate analysis. Categorical variables are expressed as number (n) and percentage (%), while numerical variables as median and interquartile range (IQR1 – IQR3). For categorical variables, we adopted the Fisher's exact test. Numerical variables were analyzed by means of Wilcoxon signed-rank test. Significance was set at p<0.05. We can see highlighted the results that reached a statistical significance. Abbreviations: COVID, coronavirus nfectious disease.

	COVID+ (n=38)	COVID– (n=38)	Wilcoxon signed-rank test		Fisher's exact test
			Z-test	P	P
COMPASS-31					
Total score	10 (4 - 25)	3 (2 - 8)	154.500	0.002	
Domain 1 (orthostatic intolerance)	0 (0 - 12)	0 (0 - 0)	25.000	0.014	
Domain 2 (vasomotor)	0 (0 - 0)	0 (0 - 0)	6.000	0.083	
Domain 3 (secretomotor)	0 (0 - 6)	0 (0 - 0)	7.500	<0.001	
Domain 4 (gastrointestinal)	4 (1 - 6)	2 (0 - 4)	166.000	0.041	
Domain 5 (bladder)	0 (0 - 1)	0 (0 - 0)	43.000	0.550	
Domain 6 (pupillomotor)	0 (0 - 1)	1 (0 - 1)	217.500	0.285	
Pathologic score (>17)	14 (36.8%)	5 (13.2%)			0.032
Orthostatic hypotension test					
Supine position					
Diastolic pressure (mmHg)	71 (65 - 78)	75 (66 - 80)	375.500	0.717	
Systolic pressure (mmHg)	131 (111 - 140)	126 (118 - 140)	335.000	0.803	
Heart rate (bpm)	74 (66 - 80)	68 (62 - 75)	208.500	0.050	
Orthostatic position					
Diastolic pressure (mmHg)	67 (61 - 75)	75 (70 - 84)	506.000	0.020	
Systolic pressure (mmHg)	118 (107 - 129)	125 (119 - 144)	525.000	0.025	
Heart rate (bpm)	77 (72 - 81)	68 (65 - 75)	104.500	<0.001	
Δ Diastolic pressure (mmHg)	2 (-3 - 10)	-1 (-8 - 2)	199.000	0.013	
Δ Systolic pressure (mmHg)	7 (-1 - 21)	0 (-5 - 5)	120.000	0.002	
Δ Heart rate (bpm)	3 (-3 - 10)	-1 (-4 - 5)	260.500	0.110	
Orthostatic Hypotension	17 (44.7%)	2 (5.3%)			<0.001
Systolic Orthostatic Hypotension	10 (26.3%)	0 (0%)			0.001
Diastolic Orthostatic Hypotension	10 (26.3%)	2 (5.3%)			0.025

Table 2. A table depicting the results of the multivariate comparisons between COVID+ and COVID– group, after the adjustment for concomitant drugs assumed by the study participants. Abbreviations: CI, confidence interval.

	Effect variable	Adjusted value (95%CI)	p
Orthostatic Hypotension test			
Orthostatic Hypotension	Odds ratio	16.00 (3.22 - 79.48)	p=0.001
Diastolic pressure (mmHg)	Beta	-6.66 (-11.98 - -1.33)	p=0.015
Systolic pressure (mmHg)	Beta	-7.52 (-14,62 - -0.420)	p=0.038
COMPASS31			
Total score	Beta	7.86 (2.60 - 13.12)	p=0.004
Domain 1 (orthostatic intolerance)	Beta	4.42 (0.85 - 8.00)	p=0.016
Domain 3 (secretomotor)	Beta	2.32 (1.03 - 3.61)	p=0.001
Domain 4 (gastrointestinal)	Beta	1.34 (-0.07 - 2.74)	p=0.061
Pathologic score (>17)	Odds ratio	3.60 (1.10 - 11.85)	p=0.035

Conclusion: Our results suggest that an autonomic dysfunction could be an early manifestation of COVID-19, even in the contest of not-critical forms of the infection.
Disclosure: The authors declare no finactial desclosures.

EPR-007
Abstract withdrawn

EPR-008

Identification of new pneumococcal virulence genes in a larval zebrafish meningitis model

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Background and aims: A previous whole genome sequencing (WGS) study of Streptococcus pneumoniae strains cultured from pneumococcal meningitis patients identified several genes associated with disease severity. We now validated the role of these genes in a larval zebrafish pneumococcal meningitis model.
Methods: Pneumococcal genes with the strongest association with disease severity were evaluated (P-value< 1.0x10–3). We created pneumococcal knock-out strains in the S. pneumonia D39 strain using homologous recombination. Zebrafish larvae were injected with wild-type or mutant pneumococci in the hindbrain ventricle at 2 days post fertilization. For survival experiments, mortality was scored for 60 zebrafish/group until 72 hours post injection (hpi). The competitive index was measured by co-injection of fluorescent wild-type and mutant strains. At 24 hpi, 30 zebrafish/group were homogenized and plated on agar plates. The next day, colony-forming units were counted and the mutant/wild-type ratio was determined.
Results: In the WGS study 36 pneumococcal genes were associated with mortality or unfavorable outcome of pneumococcal meningitis. To date, knockout mutant strains were constructed for 14 of 36 genes (Figure 1). In zebrafish survival experiments, infection with 4 of 14 mutants resulted in higher zebrafish survival compared to infection with the wild type strain (Figure 2). In competitive index experiments, 2 of 4 mutants showed a decreased fitness compared to the wild type strain (Figure 3).

Table 1

Gene code	Gene name	Associated with mortality or unfavorable outcome	P-value	Knockout made
SPV_1180	SPV_1180	Unfavorable outcome	3,69E-05	Yes
SPV_0701	SPV_0701	Mortality	4,07E-05	No
SPV_1018	zmpA	Unfavorable outcome	4,41E-05	Yes
SPV_0047	SPV_0047	Mortality	4,44E-05	No
SPV_0986	SPV_0986	Mortality	4,44E-05	No
SPV_1743	SPV_1743	Mortality	5,44E-05	No
SPV_0600	divIB	Unfavorable outcome	5,98E-05	No
SPV_0761	SPV_0761	Unfavorable outcome	6,69E-05	No
SPV_1250	nadE	Unfavorable outcome	6,75E-05	No
SPV_2129/SPV_2132	intergenic	Unfavorable outcome	9,77E-05	Yes
SPV_1373	SPV_1373	Unfavorable outcome	1,31E-04	Yes
SPV_1060	lepA	Unfavorable outcome	1,34E-04	Yes
SPV_0897	mesH	Unfavorable outcome	1,39E-04	Yes
SPV_2143	intergenic	Unfavorable outcome	1,44E-04	No
SPV_0883	intergenic	Unfavorable outcome	1,44E-04	Yes
SPV_0238	leuS	Unfavorable outcome	1,54E-04	No
SPV_2327	SPV_2327	Unfavorable outcome	1,54E-04	No
SPV_0115	HlyD	Mortality	1,55E-04	Yes
SPV_0652	livJ	Unfavorable outcome	1,65E-04	Yes
SPV_0239	ydaF_1	Unfavorable outcome	1,82E-04	Yes
SPV_1393	SPV_1393	Unfavorable outcome	1,85E-04	Yes
SPV_1344	SPV_1344	Unfavorable outcome	1,95E-04	No
SPV_2022	clpC_2	Unfavorable outcome	1,96E-04	Yes
SPV_0492	SPV_0492	Unfavorable outcome	2,25E-04	Yes
SPV2268/SPV_1013	intergenic	Mortality	2,27E-04	No
SPV_1664	treP	Unfavorable outcome	2,30E-04	Yes
SPV_0063	strH	Unfavorable outcome	2,38E-04	No
SPV_1062	recN	Unfavorable outcome	2,50E-04	No
SPV_1044	lacR	Unfavorable outcome	2,54E-04	No
SPV_0918/SPV_2288	intergenic	Mortality	2,56E-04	No
SPV_2143	intergenic	Mortality	3,02E-04	No
SPV_0507	SPV_0507	Mortality	3,41E-04	No
SPV_2022	clpC_2	Mortality	4,90E-04	No
SPV_0615	glnH3	Mortality	8,07E-04	No
SPV_0242	SPV_0242	Mortality	8,33E-04	No
SPV_0454	hsdM	Mortality	9,52E-04	No

Pneumococcal genes associated with patient outcome in pneumococcal meninningitis.

Figure 2: survival curves of zebrafish larvae infected with pneumococcal knock-out mutants (blue) or wild-type pneumococcus (yellow). Significance is calculated with the logrank test.
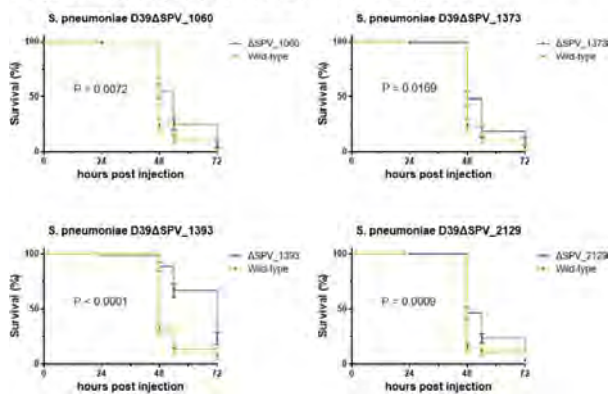
Survival curves of zebrafish larvae after hindbrain injection with wild type or mutant pneumococcal strains

Figure 3: Competitive index of the mutant compared to the wild-type pneumococcus. Zebrafish are represented by individual points, median and interquartile range is showed in red. Significance is calculated with the one-sample Wilcoxon test.
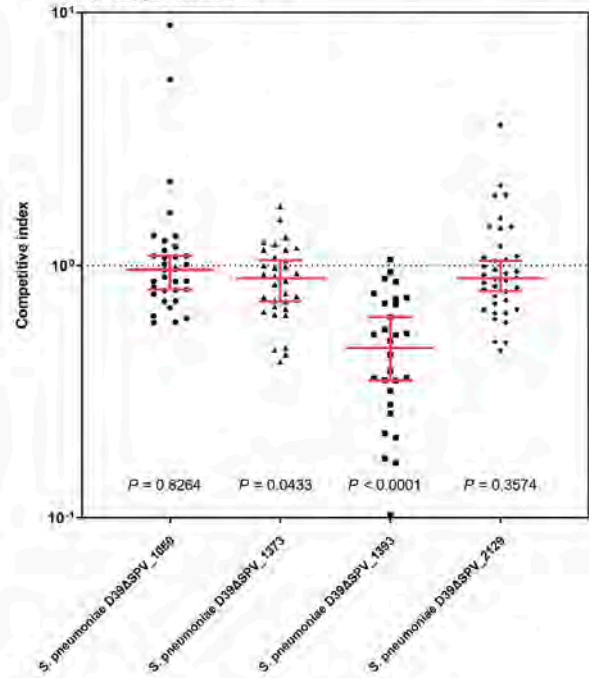
Competitive index of the mutant compared to the wild type pneumococcal strain.

Conclusion: By combining WGS of clinical pneumococcal isolates with a larval zebrafish meningitis model we identified four pneumococcal genes (SPV_1060, SPV_1373, SPV_1393 and SPV_2129) as putative virulence genes associated with disease severity in pneumococcal meningitis.

Disclosure: We have no competing interest to disclose.

EPR-009

Delirium in COVID-19 patients with ARDS: comparison with other etiologies

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Background and aims: A variety of neurological complications are associated with COVID-19, including delirium following intensive care unit (ICU) stay. However, it is still unclear if brain dysfunction is higher in patients with acute respiratory distress syndrome (ARDS)-related COVID-19 compared to other etiologies.

Methods: We conducted a retrospective cohort study at our hospital. We identified 381 ARDS patients admitted between December 2017 and June 2021; after exclusions for lack of consent, 311 were kept in the final analysis (253 with COVID-19 and 58 with other causes). Delirium could be assessed in 231 survivors using a confusion assessment method-ICU scale. We adjusted estimations for potential confounders.

Results: Patients with COVID-19 were more prone to develop delirium than controls (69.1% vs 60.5%): However, patients with COVID-19 had higher body mass index and SAPSII, longer mechanical ventilation and higher sedation doses (propofol, dexmedetomidine). When correcting for these factor COVID-19 patients did not have a higher risk of delirium (adjusted odds ratio (OR) (95% CI): 0.59 (0.25–1.43), p=0,274). Similarly, COVID-19 related ARDS had no impact on all-causes mortality at 30 days (adjusted OR (95% CI): 0.75 (0.30–1.85), p=0.529) and 6 months (adjusted OR (95% CI): 0.58 (0.28–1.2), p=0.145). Neurological complications affecting the central nervous system (adjusted OR (95%): 1.52 (0.32–7.32), p=0.604) and the peripheral nervous system (adjusted OR: 2.73 (0.90–8.32), p=0,070)) were not higher in the COVID-19 group.

Conclusion: In this cohort, patients with ARDS related to COVID-19 did not present higher rate of delirium, neurological complications or mortality than ARDS from other etiologies.

Disclosure: Authors report no disclosures.

Movement disorders 1

EPR-010

Predictors of Motor Symptom Response with Levodopa-Carbidopa Intestinal Gel in Advanced PD: COSMOS Post Hoc Analysis

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Background and aims: Levodopa-carbidopa intestinal gel (LCIG), delivered continuously into the small intestine, improves symptoms in patients with advanced Parkinson's Disease (APD). This post-hoc analysis aimed to identify predictors of optimal motor response with LCIG in APD patients.

Methods: Data were collected retrospectively and cross-sectionally from patients with APD (≥12 months LCIG; COSMOS study [NCT03362879]). Three post hoc multiple linear regression analyses were conducted with several independent variables (Table). Dependent variables included difference in dyskinesia duration (ΔDyskinesia, Analysis 1), difference in 'off' period (ΔOff, Analysis 2), and difference in number of motor symptoms (ΔMotor, Analysis 3).

Results: Analyses included 409 patients with APD; significant associations reported below (Table). Dyskinesia was negatively associated with baseline dyskinesia duration and time from PD diagnosis to motor fluctuation onset (P<0.0001, t=?14.3; P=0.0178, t=?2.4) and positively associated with time from PD diagnosis to LCIG initiation (P=0.0108, t=2.6). ?Off was negatively associated with baseline 'off' period and time from PD diagnosis to motor fluctuation onset (P<0.0001, t=-16.5; P=0.0246, t=-2.3) and positively associated with time from PD diagnosis to LCIG initiation (P=0.0001, t=3.8). Motor was positively associated with age at patient visit (P=0.0002, t=3.8) and negatively associated with baseline number of motor symptoms (P<0.0001, t=-9.7).

Analysis: (dependent variable)[a]	Significant Independent Variable	Estimate ± SE	t for H0: Parameter= Theta0 (95% CI)	P value
Analysis 1: Difference in dyskinesia duration (hours) (number of observations used =267)[b]	Dyskinesia duration (before LCIG initiation) (hours)	−0.8 ± 0.1	−14.3 (−0.9− −0.7)	<0.0001
	Time from PD diagnosis to motor fluctuation onset (years)[c]	−0.1 ± 0.1	−2.4 (−0.3−0.0)	0.0178
	Total LEDD without rescue medication with LCIG (at LCIG initiation) (mg)[d]	0.0 ± 0.0	−2.3 (0.0−0.0)	0.0224
	Time from PD diagnosis to LCIG initiation (years)[e]	0.1 ± 0.0	2.6 (0.0−0.2)	0.0108
Analysis 2: Difference in 'off' period (hours) (number of observations used =275)[b]	'Off' state time (before LCIG initiation) (hours)	−0.9 ± 0.1	−16.5 (−1.0− −0.8)	<0.0001
	Time from PD diagnosis to motor fluctuation onset (years)[f]	−0.2 ± 0.1	−2.3 (−0.3−0.0)	0.0246
	Time from PD diagnosis to LCIG initiation (years)[g]	0.2 ± 0.0	3.8 (0.1−0.3)	0.0001
Analysis 3: Difference in number of motor symptoms (number of observations used =409)	Age at patient visit (years)	0.1 ± 0.0	3.8 (0.0−0.1)	0.0002
	Number of motor symptoms (before LCIG initiation)	−0.6 ± 0.1	−9.7 (−0.7− −0.5)	<0.0001

CI, confidence interval; LEDD, levodopa equivalent daily doses; LCIG, levodopa carbidopa intestinal gel; PD, Parkinson's Disease. [a] All analyses included the following independent variables: age at patient visit; gender; dyskinesia severity (before LCIG initiation); time from PD diagnosis to motor fluctuation onset (years); time from PD diagnosis to LCIG initiation (years); total LEDD without rescue medication with LCIG (at LCIG initiation) (mg); duration of LCIG treatment (months); monotherapy (at LCIG initiation); number of motor symptoms (before LCIG initiation); and number of non-motor symptoms (before LCIG initiation). [b] This analysis included the following additional independent variables: dyskinesia duration (before LCIG initiation) (hours); 'off' state time (before LCIG initiation) (hours). [c] 8 missing values were imputed. [d] 43 missing values were imputed. [e] 4 missing values were imputed. [f] 10 missing values were imputed. [g] 5 missing values were imputed.

Patient Variables with Significant Associations from Each Analysis

Conclusion: Greater LCIG-mediated improvements were observed for several patient characteristics (eg, longer baseline dyskinesia duration, longer time to motor fluctuation onset, longer baseline 'off' periods, earlier LCIG initiation, younger age, and greater number of motor symptoms at LCIG initiation). To better inform clinicians' decisions, further investigation into the impact of patient characteristics on LCIG efficacy is warranted.

Disclosure: This study was funded by AbbVie Inc. AbbVie Inc. participated in the study design; study research; collection, analysis, and interpretation of data; and writing, reviewing, and approving this abstract for submission.

EPR-011

Prediction of early neurological deterioration in Wilson's disease.

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Background and aims: Early neurological deterioration in Wilson's disease (WD) is one of the main challenges in disease management. It may happen even on anti-copper therapy, especially with d-penicillamine, however a lot of questions are open. Aim of our approach was to determine the frequency and risk factors of early neurological deterioration in WD.

Methods: We analyzed 61 drug-naive WD patients diagnosed between June 2012 and June 2017 in Institute of Psychiatry and Neurology, Warsaw, Poland. The early neurological deterioration was defined as change in Unified Wilson's Disease Rating Scale (UWDRS) scored baseline value and at 6 month follow-up. The baseline UWDRS scores, brain magnetic resonance imaging (MRI), laboratory results including serum neurofilament light chain (sNfL), duration of disease and type of treatment were analyzed as possible risk factors of early neurological deterioration.

Results: Early neurological deterioration was observed in 16.3% (10/61) of analyzed WD patients. The initial severity of neurological injury scored in UWDRS part II and III, brain semiquantitative MRI damage score, as well as pretreatment sNfL concentration, were significantly higher in patients who deteriorated within first six months of treatment. The duration of disease, type of treatment, and initial copper metabolism had no impact on risk on early neurological deterioration.

Conclusion: Severity of neurological symptoms scored in UWDRS, the brain MRI semiquantitative scale, as well as concentration of sNfL before treatment start can be used in combination as predictors of neurological deterioration in WD, which is still an unresolved problem for patient outcome in WD.

Disclosure: We have no financial interests relevant to the submitted publication.

EPR-012

MNCD: A New Tool for Classifying Parkinson´s Disease in Daily Clinical Practice.

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Background and aims: Parkinson´s disease (PD) is a clinically heterogeneous disorder in which symptoms and prognosis can be very different among patients. We propose a new simple classification to identify key symptoms and staging in PD.

Methods: 16 movement disorders specialists from Spain participated in this project. The classification was consensually approved after a discussion and review process from June to October, 2021. The TNM classification and the National Institutes of Health Stroke Scale (NIHSS) were considered as models in the design.

Results: The classification was named MNCD and included 4 major axes: 1) Motor symptoms; 2) Non-motor symptoms; 3) Cognition; 4) Dependency for activities of daily living (ADL) (Figure 1). Motor axis included 4 sub-axes: 1) Motor

fluctuations; 2) Dyskinesia; 3) Axial symptoms; 4) Tremor. Other 4 sub-axes were included in the Non-motor axis: 1) Neuropsychiatric symptoms; 2) Autonomic dysfunction; 3) Sleep disturbances and fatigue; 4) Pain and sensory disorders. According to the MNCD, 5 stages were considered, from stage 1 (no disabling motor or non-motor symptoms with normal cognition and independency for ADL) to 5 (dementia and dependency for basic ADL) (Tables 1 and 2; Figure 1).
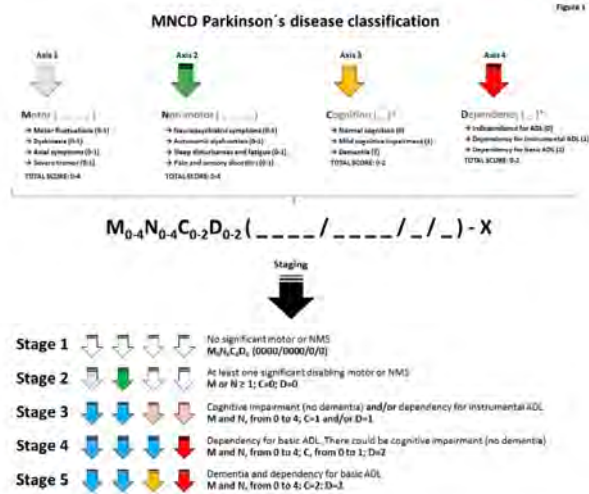
Figure 1. MNCD PD classification, showing the 4 major axis with their sub-axes and stages from 1 to 5. In Staging, an arrow with the same color as in the upper part indicates that there is a relevant symptomatology regarding the axis.

Stage 1
- The patient meets criteria of Parkinson's disease but neither significant disabling motor or non-motor symptoms and there is no cognitive impairment. The patient is functionally independent for activities of daily living.
- **MNCD classification is $M_0N_0C_0D_0$ (0000/0000/0/0).**

Stage 2
- The patient has at least one significant disabling motor or non-motor symptom. There is no cognitive impairment. The patient is functionally independent for instrumental and basic activities of daily living.
- **MNCD classification: M or N ≥ 1; C=0; D=0.**

Stage 3
- There is cognitive impairment (no dementia) and/or dependency for instrumental ADL.
- **MNCD classification: M and N, from 0 to 4; At least, C or D = 1.**

Stage 4
- The patient is functionally dependent for basic activities of daily living. There could be mild cognitive impairment but not dementia.
- **MNCD classification: M and N, from 0 to 4; C, from 0 to 1; D = 2.**

Stage 5
- The patient is functionally dependent for basic ADL and there is dementia.
- **MNCD classification: M and N, from 0 to 4; C = 2; D = 2.**

Table 1. Stages in PD according to the MNCD classification.

Example 1
- A 49 years old man 6 months from symptoms onset with stage 1 of H&Y and Unified Parkinson's Disease Rating Scale – part III score of 7 points, without cognitive impairment and any significant disabling motor or NMS and independent for ADL.
→ M0N0C0D0 (0000 / 0000 / 0 / 0) – 0.5.
→ Stage 1.

Example 2
- A 50 years old woman 2 years from symptoms onset with significant disabling resting tremor on the right part of the body but without axial symptoms, motor fluctuations, dyskinesia or any relevant NMS, with normal cognition and independent for ADL.
→ M1N0C0D0 (0001 / 0000 / 0 / 0) – 2.
→ Stage 2.

Example 3
- A 70 years old woman 6 years from symptoms onset with motor fluctuations, dyskinesia, FOG, depression, visual hallucinations, mild cognitive impairment and dependency for instrumental ADL.
→ M3N1C1D1 (1110 / 1000 / 1 / 1) – 6.
→ Stage 3.

Example 4
- A 79 years old man 4 years from symptoms onset with PIGD (postural instability gait difficulty) motor phenotype with FOG and falls but without motor complications, and severe RBD, pain and depression, without cognitive impairment but with loss of independence for basic ADL.
→ M1N3C0D2 (0010 / 1011 / 0 / 2) – 4.
→ Stage 4.

Example 5
- A 69 years old woman 20 years from symptoms onset with motor fluctuations without dyskinesia, FOG, falls, dysphagia, visual hallucinations with psychosis, orthostatic hypotension, severe insomnia, dementia, and dependency for ADL.
→ M2N3C2D2 (1010 / 1110 / 2 / 2) – 20.
→ Stage 5.

Table 2. Examples about the MNCD application.

Conclusion: A new simple classification of PD is proposed. The MNCD classification includes 4 major axes and 5 stages to identify key symptoms and monitor the evolution of the disease in patients with PD. It is necessary to apply this proof of concept in a properly designed study.
Disclosure: The authors have no conflicts of interest.

EPR-013

Sex-specific whole-brain network topologic organization in drug naïve Parkinson's disease patients

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Background and aims: Male sex is a prominent risk factor for developing Parkinson's disease (PD). Conversely, as the disease progresses female PD patients seem to be at higher risk to develop treatment-related motor complications. Compelling evidence suggests that a gender-specific pattern and functioning within the nigro-striatal dopaminergic pathway may underlie these differences. The aim of this study is to investigate the potential sex-difference effect on the whole-brain network topologic organization in a large cohort of drug-naïve PD patients using resting-state functional MRI (rs-fMRI).

Methods: 147 drug-naive PD patients (85/62 male/female) and 38 age- and sex-matched controls (20/18 male/female) were enrolled. Motor, non-motor and neuropsychological assessments as well as rs-fMRI were performed at baseline. Graph analysis and connectomics were used to assess global and local topological network properties and regional functional connectivity (FC) in female PD patients compared to males.

Results: At baseline, female PD patients showed a preserved global functional brain architecture compared to HC whereas widespread FC differences were found in male compared to HC. Male PD patients showed altered functional topological properties within the basal ganglia network compared to female PD patients. Regional decreased FC involving mainly striato-frontal, striato-temporal and limbic connections differentiated male from female PD patients.

Conclusion: Our findings revealed the presence of a disease-related, sex-specific functional architecture within the basal ganglia in a large cohort of early PD patients. We hypothesize that these findings may be related to the presence of different gender-specific nigrostriatal dopaminergic pathways and might be potentially used to predict disease progression over time.

Disclosure: Nothing to disclose.

EPR-014

Continuous Subcutaneous Foslevodopa/Foscarbidopa in Advanced Parkinson's Disease: Results From a 12-Month Phase 3 Study

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Background and aims: As Parkinson's disease (PD) progresses, the therapeutic window of oral levodopa narrows and motor complications become common. Foslevodopa/foscarbidopa (LDP/CDP) is a new soluble formulation of levodopa/carbidopa prodrugs delivered 24h/day as continuous subcutaneous infusion (CSCI) to control motor fluctuations in patients with advanced PD (aPD). Safety, tolerability, and efficacy of LDP/CDP were evaluated for up to 52 weeks in an outpatient setting.

Methods: This Phase 3, open-label, single-arm study (NCT03781167) included levodopa-responsive PD patients with a minimum of 2.5 hours of "Off" time/day. The primary endpoint is safety and tolerability. Efficacy assessments include change from baseline in hours of "On"

and "Off" time and presence of morning akinesia upon awaking (via PD diaries), activities of daily living (MDS-UPDRS part II), sleep (PDSS-2) and quality of life (PDQ-39, EQ-5D-5L).

Results: This analysis included 244 patients (59.8% male, 84.8% white, mean age of 64 years [Table 1]) from 56 sites. The most frequent adverse events were infusion site skin events, majority of which were non-serious, mild/moderate in severity and resolved (Table 2). Improvements in motor complications were observed as early as Week 1 and persisted through Week 52; at Week 52 the mean increase in "On" time without troublesome dyskinesia was 3.58 hours and decrease in "Off" time was 3.39 hours (Table 3). The percentage of patients with morning akinesia decreased from 77.7% to 19.4%.

Table 1. Select Patient Baseline Demographics and Disease Characteristics

Parameter	Patients, n (%) (N = 244)
Sex	
Male	146 (59.8)
Female	98 (40.2)
Age, years, mean ± SD	63.9 ± 9.18
< 65 years	119 (48.8)
≥ 65 years	125 (51.2)
Race	
White	207 (84.8)
Black or African American	1 (0.4)
Asian	34 (13.9)
American Indian or Alaska Native	1 (0.4)
Multiple	1 (0.4)
Weight, kg, mean ± SD	72.1 ± 17.37
BMI, kg/m², mean ± SD	24.95 ± 4.81
MMSE total score, mean ± SD	28.7 ± 1.72
MDS-UPDRS total score (part II), mean ± SD	15.8 ± 7.38
"Off" time[a], hours, (n = 236), mean ± SD	5.90 ± 2.24
"On" time without dyskinesia[a], hours, (n = 236), mean ± SD	6.51 ± 3.35
"On" time with non-troublesome dyskinesia[a], hours, (n = 236), mean ± SD	2.63 ± 2.55
"On" time with troublesome dyskinesia[a], hours, (n = 236), mean ± SD	0.96 ± 1.73

[a]Assessed using a 24-hour diary and were normalized as the (observed hours per day) × (16/waking hours). MMSE, Mini-Mental State Examination; MDS-UPDRS, Movement Disorder Society-Unified Parkinson's Disease Rating Scale; PD, Parkinson's disease; SD, standard deviation.

Table 2. Safety Summary

Safety Overview	Total, n (%) (N = 244)
Any TEAE	230 (94.3)
Any severe TEAE	62 (25.4)
Any serious TEAE	61 (25.0)
Any TEAE considered associated with study drug	224 (91.8)
Any TEAE leading to premature study drug discontinuation	62 (25.4)
Death[a]	3 (1.2)

Most Frequent (≥ 10%) Treatment-Emergent AEs by Preferred Term	Total, n (%) (N = 244)
Infusion site erythema	125 (51.2)
Infusion site nodule	68 (27.9)
Infusion site cellulitis	56 (23.0)
Infusion site oedema	47 (19.3)
Hallucination	41 (16.8)
Fall	39 (16.0)
Infusion site pain	38 (15.6)
Infusion site reaction	31 (12.7)
Anxiety	28 (11.5)
Infusion site abscess	26 (10.7)
Dizziness	25 (10.2)

[a]none of the events were considered by the investigator as reasonably possibly related to study drug. TEAE, Treatment-emergent adverse event; AE, adverse event; Coded using MedDRA, Medical Dictionary for Regulatory Activities v 24.0.

Conclusion: In this open-label trial, individualized, 24h/day, CSCI of LDP/CDP was generally safe, improved motor complications and morning akinesia, providing a potential efficacious and minimally invasive therapeutic alternative for aPD.

Disclosure: This study was funded by AbbVie. AbbVie participated in the study design; study research; collection, analysis, and interpretation of data; and writing, reviewing, and approving this abstract for submission.

EPR-015

Interactions between phenotype and demographic variables in a large PSP cohort

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Background and aims: Progressive Supranuclear Palsy (PSP) can present with Richardson's syndrome, or less common variant phenotypes. Demographic interactions with phenotype would affect the design of clinical trials for PSP. We therefore aimed to test whether sex and age of onset varied by phenotype.

Methods: The MDS 2017 criteria were used to phenotype PSP patients at the Cambridge Centre for Parkinson-plus. Using group-wise frequentist (logistic regression, ANOVA) and Bayesian analyses (as Bayes factors, BF), we assessed the relationship between phenotype, sex, age-of-onset and age-of-diagnosis.

Results: 295 patient records (male 56%, age 74.4±6.7, age of onset 68.3±7.1) were assessed, with either Richardson's syndrome (n=202) or variant PSP phenotypes (n=93 of which n=33 subcortical and n=60 cortical). People with PSP-frontal (PSP-F) were more likely to be male than people with PSP-RS (OR=3.99; p=0.03). Phenotypic group was unrelated to sex. Age of onset was unrelated to phenotypes (p=0.3, BF=0.1) or phenotypic subgroups (p=0.6, BF=0.2). Age of diagnosis was unrelated to phenotypes (p=0.7, BF=0.04) or subgroup (p=0.9, BF=0.06). There was no sex difference in age of onset (p=0.2, BF=0.3) or age of diagnosis (p=0.18, BF=0.3), with or without adjusting for phenotype. Survival at 60 months from diagnosis varied by age (p=0.005), but not by sex (p=0.16).

Presenting PSP Phenotype	N	Mean age of onset (years)	Mean age of diagnosis (years)	% Male
PSP (all)	295	68.31 ± 7.11	71.56 ± 6.86	56.27
PSP-RS	202	68.57 ± 7.17	71.57 ± 7.14	53.96
Subcortical Subgroup	33	66.04 ± 7.36	71.07 ± 6.33	60.61
PSP-P	13	65.45 ± 6.46	71.06 ± 5.72	76.92
PSP-PGF	12	66.72 ± 7.32	71.87 ± 6.81	33.33
PSP-PI	8	65.96 ± 9.53	69.90 ± 7.09	75.00
Cortical Subgroup	60	68.72 ± 6.65	71.77 ± 6.26	61.67
PSP-CBS	26	69.85 ± 7.91	72.89 ± 7.33	57.69
PSP-F	16	66.17 ± 6.09	69.01 ± 5.74	81.25
PSP-SL	18	69.35 ± 4.52	72.59 ± 4.24	50.00

PSP = Progressive supranuclear palsy, PSP-RS = Richardson's syndrome, PSP-P = Parkinsonium, PSP-PGF = Progressive gait freezing, PSP-PI = Postural instability, PSP-CBS = Corticobasal syndrome, PSP-F = Frontal, PSP-SL = Speech and language

Table 1: Demographic characteristics of each presenting PSP phenotype

A

Characteristic	OR[1]	95% CI[1]	p-value
Age of Diagnosis	1.03	0.99, 1.07	0.10
PSP phenotype			
PSP-RS	–	–	
PSP-CBS	1.13	0.49, 2.65	0.8
PSP-F	4.05	1.25, 18.1	0.034
PSP-P	2.63	0.76, 12.2	0.2
PSP-PGF	0.42	0.11, 1.40	0.2
PSP-PI	2.73	0.61, 19.1	0.2
PSP-SL	0.83	0.31, 2.22	0.7

[1] OR = Odds Ratio, CI = Confidence Interval

B

Characteristic	OR[1]	95% CI[1]	p-value
Age of Onset	1.03	1.00, 1.07	0.085
PSP Phenotype			
PSP-RS	–	–	
PSP-CBS	1.12	0.49, 2.63	0.8
PSP-F	3.99	1.23, 17.9	0.036
PSP-P	3.13	0.92, 14.4	0.093
PSP-PGF	0.44	0.11, 1.47	0.2
PSP-PI	2.80	0.62, 19.7	0.2
PSP-SL	0.83	0.31, 2.21	0.7

[1] OR = Odds Ratio, CI = Confidence Interval

Figure 1: A) Results of logistic regression for the effect of PSP phenotype on sex, after adjusting for age of diagnosis B) Results of logistic regression for the effect of PSP phenotype on sex, after adjusting for age of onset
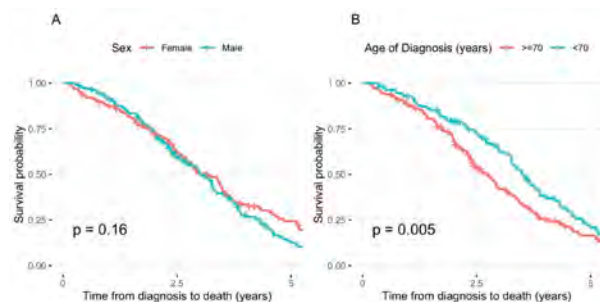
Figure 2: Kaplan-Meier survival curves A) No variation in survival by sex (60 months from diagnosis), log-rank test p=0.16 B) Significant variation in survival by age of diagnosis (60 months from diagnosis), log-rank test p=0.005

Conclusion: In contrast to PSP-RS, the PSP-F variant was more likely to be diagnosed in men. No other association was found between phenotype, age and sex. Further work is required to determine the sex-imbalance in PSP-F, whether from meaningful pathological differences or artefactual under-recognition of PSP-F in women.

Disclosure: Miss Kok, Dr Street and Professor Rowe report no disclosures of relevance to this presentation.

EPR-016

Unbiased phenotypical characterization of Essential and Dystonic tremor using time-series feature analysis

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Background and aims: Dystonic tremor (DT) is a potentially underrecognized clinical entity, sharing variable degrees of phenotypical features with essential tremor (ET), rendering clinical diagnosis subjective. Identifying the correct clinical diagnosis is important, as both aetiologies potentially require different treatment approaches. This study is aiming to establish a machine learning pipeline to adequately differentiate between accelerometer time-signal recordings from ET and DT patients.

Methods: Accelerometer recordings from a multi-centre cohort of 77 patients (27 DT, 13 Tremor associated with Dystonia (TaD), 37 ET), recorded according to centre-specific study protocols, have been combined into a single data set. Clinical diagnosis was based on current diagnostic criteria. Higher-order feature extraction was applied to perform supervised statistical learning against reference clinical diagnosis.

Results: Raw time-series signals from 40 DT/TaD and 37 ET patients were screened for movement artefacts, cleaned, aligned, harmonised and compared using different machine learning algorithms. Depending on centre, based on the extraction of >7,000 features from each recording, supervised statistical learning reached an optimal differentiation accuracy for ET vs. DT of up to 86.9% (Sevilla; 77.3% for Graz; 74.9% for UCL) for individual top features. We are establishing a way to increase overall classification accuracy by feature combination.

Conclusion: First analyses indicate that feature-based patient stratification is feasible to discern between DT and ET, depending on clinical diagnostic standards used. By applying tremor signal feature analysis in an unbiased manner, we aim to introduce common ground for improved diagnosis and guide therapeutic interventions.

Disclosure: Authors report no conflict of interest.

EPR-017

Long-term safety of continuous levodopa/carbidopa infusion with ND0612: Results from the ongoing BeyoND study

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Background and aims: Primary safety data from the BeyoND study (NCT02726386) showed that subcueaneous levodopa/carbidopa infusion with ND0612 is generally safe up to 1 year of treatment in people with Parkinson's disease (PD) experiencing motor fluctuations. The study has been extended to 102 months, and we report cumulative data beyond the 1st year of treatment.

Methods: PD patients (aged >30y) taking ≥4 levodopa doses/day and ≥1 other PD medication and experiencing ≥2 hours of OFF time/day were eligible for this ongoing study. Patients received open-label ND0612 for a regimen of either 16-hours/day or 24-hours/day.

Results: Of the 214 enrolled patients, 120 completed the first year and 114 continued into the extension period. As of December 2021, 58 patients were still in the study, with a treatment duration of up to 5.1 years. Cumulative safety data showed that 74.3% of patients had ≥1 drug-related treatment-emergent adverse event (TEAE). The most frequent TEAEs were Infusion Site Reactions (ISRs) (e.g., nodules, hematoma, infection, pain, eschar), which accounted for 532/690 related TEAEs and were generally reversible and manageable. The most common systemic TEAEs were fall (16.8%), urinary tract infection (14.0%), and nausea (10.7%). Only three TEAEs led to treatment discontinuation in ≥1% of patients over the whole study: infusion site nodule (6.1%), infusion site pain (3.3%) and infusion site haematoma (1.9%).

Conclusion: ND0612 infusion was safe, with generally mild to moderate local TEAEs that were reversible and manageable. Systemic safety was typical for PD patients treated with levodopa/carbidopa.

Disclosure: Funded by NeuroDerm.

Ageing and dementia & Sleep-wake disorders 1

EPR-018

Real-world treatment of pediatric narcolepsy with pitolisant

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Background and aims: Narcolepsy is a rare disease. First symptoms often occur during puberty or young adulthood, in up to 20% of cases even in the first 10 years of life. For children, approved medicines for the treatment of narcolepsy are scarce. Pitolisant (Wakix®) is an agent approved for the treatment of narcolepsy with and without cataplexy in adults. The aim of this real-world study is to investigate the efficacy and safety of pitolisant off-label treatment in children and adolescents with narcolepsy.

Methods: This study is a multicenter observational study of pediatric narcolepsy patients treated with pitolisant. Demographic and clinical characteristics, questionnaires, and sleep medicine and laboratory data were collected for this purpose.

Results: 56 children/adolescents (26 girls (46.4%), 30 boys (53.6%)) aged 6-18 years, with narcolepsy (Narcolepsy type 1=93%, type 2=7%), were treated with pitolisant. 17 (30.4%) children were drug naive; 35 (62.5%) children were previously treated with modafinil, methylphenidate, sodium oxybate, or venlafaxine. Reasons for switching to pitolisant were lack of efficacy (n=17, 30.4%) and side effects (n=8, 14.3%). 16 (28.6%) patients received pitolisant in addition to their ongoing medication. The mean pitolisant dose was 33.8 mg/d. The pediatric ESS score decreased from 19 to 13.5 (p<0.001) and the weekly cataplexy frequency improved from 7.78 at baseline to 5.08 (p<0.001). Side effects were mild and mostly short-term. Insomnia and nausea were reported most frequently (5.4% each).

Conclusion: The results suggest that pitolisant treatment in children and adolescents with narcolepsy is effective for excessive daytime sleepiness and cataplexy, and is generally well tolerated.

Disclosure: No funding for this study.

EPR-019

Inflammatory bowel disease and risk of dementia: a systematic review and meta-analysis

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Background and aims: Despite the growing evidence of potential shared pathogenic pathways between inflammatory bowel disease (IBD) and dementia, this relationship still remains uncertain. The aim of this meta-analysis was to investigate if IBD increases the risk of dementia.

Methods: We systematically searched PubMed, Web of Science, Embase, and Cochrane library to identify cross-sectional and longitudinal studies exploring the relationship between IBD and dementia until October 10, 2021, according to the updated Preferred Reporting Items for Systematic reviews and Meta-Analyses (PRISMA). Search terms were: "dementia", "cognitive impairment", "cognitive decline", "inflammatory bowel disease", "Crohn's disease", and "ulcerative colitis". The quality of included studies was assessed using the Newcastle-Ottawa Scale (NOS). Risk estimates were pooled using both fixed and random-effects models.

Results: Out of 189 relative studies, five studies (132,445 IBD patients, 2,202,027 non-IBD controls) were finally included. After IBD diagnosis (3 studies), the risk of developing dementia was significantly increased in IBD patients compared to controls (HR=1.25, 95% CI: 1.08-1.32, P=0.001), regardless of age, gender, and dementia or IBD subtype. Prior to IBD diagnosis (2 studies), the risk and comorbidity rate of dementia did not differ significantly between IBD patients and non-IBD controls (HR=0.87, 95% CI:0.62-1.22; 5% CI:0.44–1.03, respectively).

Conclusion: IBD patients have an increased risk of dementia only after IBD diagnosis. However, current evidence was insufficient to establish a causal relationship. Future studies are warranted to shed more light on the possible shared pathogenic mechanisms and development of new targeted treatment approaches.

Disclosure: Nothing to disclose.

EPR-020

Incipient Chronic Traumatic Encephalopathy in American Football players: NPS assessment and Brain HHG

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Background and aims: Chronic traumatic encephalopathy (CTE) is a degenerative disease caused by repetitive traumatic brain injury (TBI). Because CTE can be definitely diagnosed only post-mortem, it would be important to explore clinical and radiological correlates of CTE and TBI. In active American football players we assess: the neuropsychological profile - traumatic load relationship, the cerebral perfusion pattern, and whether this perfusion pattern correlates with neuropsychological performances.

Methods: In 20 American football players, we evaluated the traumatic load using the TraQ (Trauma Questionnaire), and cognitive performances on neuropsychological tests. Brain perfusion was estimated using arterial spin labeling MRI and compared to a group of 19 male age-matched healthy subjects.

Results: We found: 1) different cognitive performances between American football players stratified according to their field position, with worst results in type-1 field position players, and according to career length, with worst results in athletes with a career >7 years; 2) a statistically significant hypoperfusion in sensory-motor areas in American football players compared with healthy individuals without a sport-traumatic history; 2) and poorer neuropsychological performances in several tests, correlated with lower perfusion in specific brain areas.

This CBF evaluation, obtained with ASL MRI, shows red coloured areas as those characterised by higher CBF in HI (healthy individuals) with respect to AFP (American football players)

Conclusion: Our study pointed out diminished cognitive functions and the coexisting dysregulation of the cerebral local perfusion in the same cortical areas that resulted impaired. It could be hypothesized that functional impairment and structural damages induced by repetitive, low energy trauma are the two faces of the same medal. The observation of the hypoperfusion of the impaired areas highlights the importance of microcirculation in TBI.

Disclosure: I declare that all the participants to this study do not have conflicts of interest.

Stroop test performances of athletes with career duration >7 years or below/equal to 7 years.

EPR-021

Topographic characterization of thalamic strokes: contributions to sleep consolidation and spindle expression

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Background and aims: Thalamic vascular syndromes result in a wide variety of clinical outcomes dependent on the thalamic territory affected by the lesions. Paramedian stroke lesions cause a decrease in arousal and spindle rate, particularly in bilateral lesions. However, the contribution of each thalamic nucleus to the different sleep clinical outcomes is still unknown. We hypothesize that lesions to thalamic substructures have different effects on sleep-wake regulation and sleep oscillatory activity dependent upon the topography of the lesion.

Methods: 15 bilateral or unilateral thalamic stroke patients were included. Diffusion-weighted-images were used for categorization of sub-thalamic lesions. 15 age/gender matched controls were included in the analysis. All-night high-density EEG recordings were used to characterize sleep-wake architecture and expression of spindles in both, controls and thalamic patients. Sleepiness was determined using the Stanford Sleepiness Scale.

Results: Among the patients, sleepiness was increased in lesions encompassing the intralaminar (IL) or mediodorsal (MD) nuclei (p<0.001). Compared to controls, proportion of NREM1, wake episode duration and number of NREM2-NREM1 or NREM1-wake transitions were higher in IL/MD (p<0.01), but not in lateral lesions. Remarkably, a topographic decrease of individual spindles power was found in the frontal derivations (p<0.001). Topographically, frontal power was ipsilaterally or globally reduced, in unilateral or bilateral lesions, respectively. In contrast, posteriorly detected spindles were reduced equally in all lesions.

Conclusion: These results suggest that IL/MD lesions, but not lateral thalamic lesions, result in sleep fragmentation and reduced frontal spindles. Our work provides novel insights into thalamic sub-regions responsible for sleep-wake control and potentially identifies specific targets for sleep-related therapies.

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EPR-022

REM-sleep associated muscle activity in patients with narcolepsy and REM-sleep behaviour disorder

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Background and aims: To assess differences in extent and time course of REM sleep without atonia (RWA) in patients with REM sleep behaviour disorder (RBD) and narcolepsy and to define cut-off values of RWA differentiating RBD and narcolepsy patients from controls.

Methods: Polysomnographic (PSG) recordings of 16 RBD patients, 15 narcolepsy patients and 19 controls were retrospectively analyzed. EMG activity during REM sleep recorded from mentalis and tibialis anterior muscles was quantified in 3-sec miniepochs, irrespective of tonic or phasic EMG activity.

Results: EMG activity during REM sleep of both the mentalis and tibialis anterior muscles was significantly higher in RBD compared to both narcolepsy patients and controls. Narcolepsy patients also showed significantly higher EMG activity than controls. In RBD patients and in controls, RWA was significantly more pronounced in the second half of the night, while narcolepsy patients showed an even distribution of EMG activity between the first and second half of the night. Receiver operating characteristic (ROC) curves suggested a cutoff value of 17% RWA to correctly differentiate RBD patients from controls with 100% sensitivity and 94.7% specificity (AUC: 0.997). A cutoff value of 8.4% RWA correctly identified narcolepsy patients with 86.4% sensitivity and 68,4% specificity (AUC: 0,85).

Conclusion: Analysis of EMG activity during REM sleep can successfully differentiate RBD patients and narcolepsy patients from controls. High rates of RWA particularly in the second half of the night support a diagnosis of RBD, while moderately increased rates of RWA throughout the entire night might represent an additional diagnostic marker for narcolepsy

Disclosure: Nothing to disclose.

EPR-023

The effect of the microglia associated CD33 gene on neurological disease: A UKBIOBANK study.

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Background and aims: Microglial genes are increasingly recognised as risk factors for neurological diseases. The rs12459419-T minor allele variant of CD33 has previously been associated with protection against Alzheimer's disease (AD), and possibly Parkinson's disease (PD) and multiple sclerosis (MS). We investigated the association between CD33 and different neurological diseases, and its influence on brain structure and cognitive profile in healthy older adults.

Methods: Data was acquired from 392,373 participants within the UKBIOBANK study. Participant CD33 genotypes for rs12459419 were compared: CC (n=177,889), CT (n=172,459) and TT (n=42,025). Risk of AD (n=768), PD (n=1.639), motor neurone disease (MND; n=334), frontotemporal dementia (n=86) and multiple sclerosis (n=1.416) was calculated using the SNPstats web tool. A subgroup of healthy older adults underwent brain volumetric MRI and cognitive profile. These were compared across CD33 rs12459419 genotypes.

Results: The CD33 rs12459419-T variant was associated with protection against AD and MND (Figure 1) with a log-additive genetic model best fitting the data. No association with the other diseases of interest was found. Healthy older adults had between-group differences in caudate volumes (p=0.03); whereby pairwise comparisons indicated CT carriers were smaller than TT (p=0.04). There were negligible differences in numeric memory scores (p=0.04); with pairwise comparisons showing CT carriers had worse scores than CC (p=0.07).

Diagnosis	Odds ratio	95% CI	Significance
MS	0.94	(0.87 – 1.02)	P = 0.14
PD	0.98	(0.91 – 1.06)	P = 0.63
FTD	0.91	(0.66 – 1.26)	P = 0.58
MND	0.80	(0.68 – 0.95)	P = 0.01
AD	0.79	(0.71 – 0.89)	P < 0.001
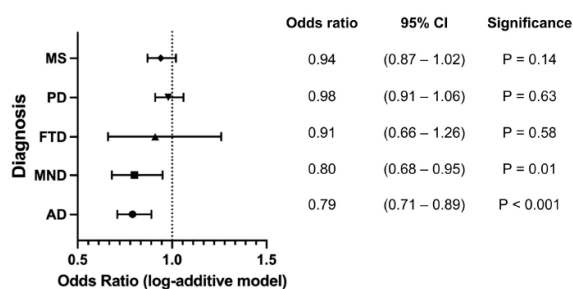
Odds ratio for neurological disease based on CD33 'T' status using a log additive model.

Conclusion: The CD33 rs12459419-T minor allele potentially protects against AD and MND, but not the other investigated neurological diseases. These findings within MND are novel, although microglia have previously been linked with MND pathogenesis, via both pro- and anti-inflammatory mechanisms.

Disclosure: Nothing to disclose.

EPR-024

Associations of daytime executive function and sleep measures in pediatric narcolepsy type 1

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Background and aims: Narcolepsy is a neurological sleep disorder characterized by excessive daytime sleepiness, fragmented night sleep, cataplexy, sleep paralysis, and hypnagogic hallucinations caused by loss of hypothalamic hypocretin producing neurons. Executive functions (EF) dysfunctions are frequently reported from narcolepsy populations, and are considered to be partially a result of sleepiness. How/if EF dysfunction is associated with objective sleep abnormalities in narcolepsy has not been reported from pediatric populations.

Methods: 56 youths (age 7–20, mean age 14.9, 57.1% females, 85.7% H1N1-vaccinated), with narcolepsy type 1 (NT1) according to International Classification of Sleep Disorders 3rd edition and admitted to our national narcolepsy experitice center participated. All patients answered on questionnaires including Behavior Rating Inventory of Executive Function (BRIEF), Epworth Sleepiness Scale (ESS), and had an overnight polysomnography (PSG) followed by multiple sleep latency test (MSLT).

Results: 37 youths (66.1%) had one or more BRIEF subscale in clinically relevant level, most frequently for working memory (in 51.8%). The BRIEF did not correlate significantly with mean sleep latency on MSLT, Sleep Stage Shift Index (SSS-I) awakening index (AI), or sleep efficiency (SE) on the PSG. The BRIEF subscales measuring inhibition problems (rho=0.348, p=0.009) and organizing materials (rho=0.379, p=0.004) was significantly associated with ESS severity after Bonferroni correction.

Conclusion: EF dysfunction related to inhibition and organizing measured by the BRIEF questionnaire was moderately correlated with subjective, but not objective, sleep measures. Our findings do not support that EF dysfunction in narcolepsy is mainly caused by daytime sleepiness or fragmented sleep.

Disclosure: Nothing to disclose.

EPR-025

Manual dexterity and anticipatory object manipulation correlate with cognitive performances of elderly adults

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Background and aims: Previous studies found that upper limb dexterity was impaired in patients with mild cognitive impairment and dementia. In this study, we evaluated whether traditional and novel sensor-based assessments of dexterity can also predict cognitive functioning in unselected elderly adults.

Methods: 91 elderly volunteers (75.0±5.7 years) performed tests of associative memory, executive functioning, verbal fluency as well the Quick Mild Cognitive Impairment (Qmci) screen. Upper limb motor functioning was assessed by measuring the hand grip strength, praxis as well as the nine-hole peg test (NHPT). Furthermore, we employed a novel test battery assessing anticipatory grip-force (GF) and torque control when lifting objects according to sensorimotor memories, size-, material-, shape-, and associative color-cues, and in repetitive movements and following perturbations. Multiple linear regression models with augmented variable back selection were fit to predict cognitive domain functions based on upper limb performance measures.
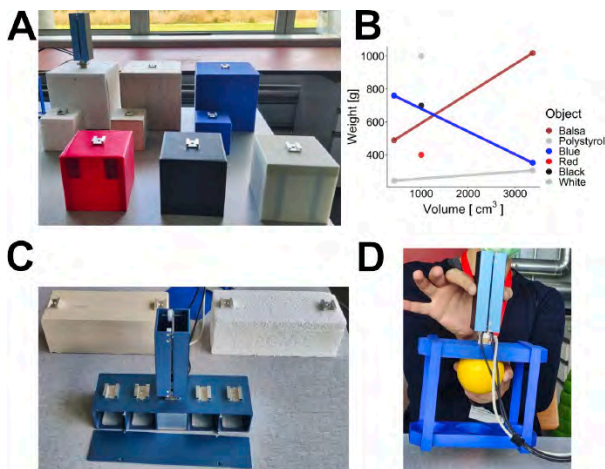
Figure 1: Experimental set up for the assessment of anticipatory torque control. A and B) Cubes of varying size, material, color and weight. C) Horizontal receptacle to assess torque control. D) Rectangle of anticipatory catching task.

Results: The NHPT time was significantly correlated with verbal fluency. Measures of sensorimotor and associative GF- and torque planning correlated with associative memory, verbal fluency and executive functioning. A combination of the grip strength, praxis, NHPT time and parameters of the novel battery of anticipatory kinetic force/torque control could account for 90% of the variance of the QMCI (adjusted R2 0.80).
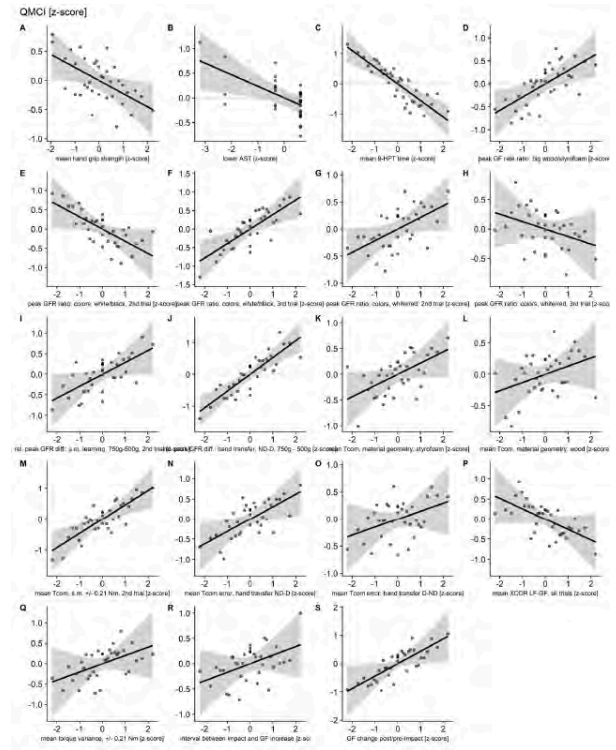
Figure 2: Partial effects plot with partial residuals of the multiple linear regression of model of QMCI (z-scored) with normalized predictors of upper limb functioning.

Conclusion: In summary, different subsets of specific aspects of anticipatory object manipulation planning were correlated with distinct cognitive domains. Therefore, the NHPT should be routinely administered in memory clinics, while sensor-based assessments could foster the understanding of the interplay between dexterity and cognition.

Autonomic nervous system diseases & Peripheral nerve disorders 1

EPR-026
Abstract withdrawn

EPR-027

Contribution of mendelian inheritance to Chronic Idiopathic Axonal Neuropathy

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Background and aims: To test the hypothesis that monogenic neuropathies may masquerade as Chronic Idiopathic Axonal Neuropathy (CIAP), we performed a genetic analysis of 234 probands with adult-onset CIAP selected from 594 consecutive patients with neuropathy referred over 10 years to our tertiary-care center for a sural nerve biopsy.

Methods: All probands were screend by flanking PCR and repeat-primed PCR for the biallelic AAGGG repeat expansion of the RFC1 gene associated with Cerebellar Ataxia, Neuropathy, Vestibular Arefexia Syndrome (CANVAS), and by a custom-designed next-generation sequencing (NGS) panel covering 24 genes associated with Charcot-Marie-Tooth disease (CMT)-related neuropathies.

Results: 43 (18%) probands were found to have a definite monogenic neuropathy. 34 patients had CANVAS (median age of onset 61 years, IQR 53–65; median duration of disease 48 months, IQR 24–72; 91% with a pure or prevalent sensory neuropathy); 7 had MME-related CMT2T, including 4 autosomal recessive cases (median age of onset 51 years, IQR 46-53; median duration of disease 54 months, IQR 48–120) and 3 autosomal dominant cases (median age of onset 70 years, IQR 51–76; median duration of disease 12 months, IQR 6–96); 2 patients had a variant transthyretin amyloid polyneuropathy (ATTRv-PN). 36 additional probands were carriers of as many heterozygous variants of uncertain significance in the following CMT2-related genes: LRSAM1 (n=14), GARS (n=10), MME (n=8), GDAP1 (n=3), HSPB1 (n=1).

Conclusion: Knowledge of new genes and availability of NGS may reveal a hitherto unsuspected contribution of mendelian inheritance to adult-onset CIAP.

Disclosure: Nothing to disclose.

EPR-028
Abstract Withdrawn

EPR-029

Association of cardiac autonomic responses with clinical features of myasthenia gravis.

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Background and aims: The aim of the study was to assess cardiac and autonomic function in patients with myasthenia gravis (MG) disease, and explore its relationship with disease status.

Methods: 37 patients with a MG were enrolled (aged 40.5 s±11.4) disease duration (7.4±6.8). Haemodynamic parameters, baroreflex sensitivity (BRS), spectral-indices of short-term heart rate (HRV) and blood pressure variability (BPV), were compared with age and gender matched controls (n=30). Cardiac autonomic function was assessed during response to standing (tilt) and deep breathing test (expiration/inspiration, ratio-E/I).

Results: HR and BP responses to the tilt test were similar in both groups. MG patients as compared to controls were characterized by significantly reduced HR response to deep breathing test (p<0.001), increased sympathovagal balance after tilt (delta LF/HF-RRI, p=0.034) and lower values of BRS (p=0.02) and haemodynamic parameters: cardiac index, index contractility, left ventricular work index, at rest and during tilt. There was no association between disease duration and haemodynamic, autonomic parameters. Disease severity as determined by MGFA (Myasthenia Gravis Foundation of America) corrected for age and sex, was an independent predictor of diminished vagal tone (E/I ratio), increased sympathetic response to tilt (delta LF/HF-RRI) as measured with HRV. Lower BRS was associated with greater disease severity and higher age. Hemodynamic parameters were predicted by age.
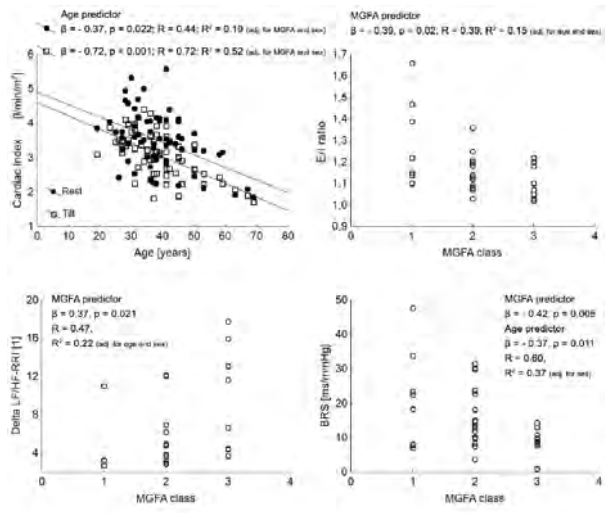
Table 1. Mean SD of resting and during tilt test haemodynamic and autonomic parameters for patients with myasthenia gravis (MG) and healthy controls (HC)

Group	MG	HC	MG	HC	MG	HC
	Rest		**70° tilt**		**Change after 70° tilt (delta)**	
Hemodynamic measures						
HR [1/min]	65.2±7.9	67.3±8.2	77.8±8.9	81.9±11.2	12.6±8.0	14.6±7.0
sBP [mmHg]	112.8±10.6	112.0±11.2	122.1±9.8	124.4±10.8	9.3±10.8	12.3±9.2
dBP [mmHg]	72.2±7.1	73.3±9.1	85.5±9.2	88.3±9.6	13.3±8.4	15.1±8.8
mBP[mmHg]	89.3±7.9	90.3±10.0	100.4±9.2	104.0±9.7	11.1±8.8	13.79.3±8.7
SI [ml/m²]	51.4±13.6	56.1±10.0	37.6±7.2	40.6±6.5	-13.8±8.4	-15.5±9.3
CI [l/min·m²]	3.3±0.8	3.7±0.8*	2.9±0.6	3.3±0.7**	-0.4±0.6	-0.4±0.7
TPRI [dyn*s*m2/cm⁵	2308.4±737.5	1968.8±510.6	2854.2±772.2	2602.1±782.9	545.8±412.9	631.1±661.7
LVWI [mmHg x L/min x m²]	3.8±0.8	4.5±0.9**	3.9±0.7	4.6±0.8***	0.0±0.8	0.1±0.9
IC [1000/s]	60.3±23.7	72.5±20.2*	43.8±15.0	52.0±13.9*	-16.5±12.7	-20.4±15.0
Heart rate variability (HRV)						
LFnu-RRI [ms²]	58.3±18.2	55.5±12.0	74.7±21.7	72.1±13.1*	16.5±16.7	16.2±15.1
Hfnu-RRI ms²]	41.7±18.2	44.5±12.0	25.3±21.7	34.4±39.3*	-16.5±16.7	-9.7±41.0
PSD-RRI [ms²]	3188.0±5406.4	1613.8±1298.0	1457.7±3074.4	1183.9±871.5	-1644.2±6054.4	-431.7±955.3
LF/HF-RRI [1]	2.2±1.9	1.5±0.9	6.8±6.0	3.7±2.5	4.6±4.9	2.2±2.4*
LF/HF [1]	1.5±1.3	1.2±0.5	4.5±4.2	2.6±1.7	3.0±3.5	1.5±1.6
Systolic and diastolic blood pressure variability						
LFnu-dBP [%]	43.3±10.3	46.3±9.4	51.9±11.9	52.2±14.2	8.6±10.9	6.5±11.0
Hfnu-dBP [%]	13.4±9.2	11.0±4.9	13.5±8.1	11.6±6.0	0.2±2.6	0.9±3.1
PSD-dBP [mmHg²]	9.6±7.0	7.7±5.4	7.1±4.2	6.1±3.9	-2.5±4.1	-1.7±2.3
LF/HF-dBP	4.5±2.5	5.0±2.2	5.1±2.8	5.6±4.0	0.5±1.5	0.5±2.6
LF/HF	1.5±1.3	1.2±0.5	4.5±4.2	2.6±1.7	3.0±3.5	1.5±1.6
LFnu-sBP [%]	39.4±10.8	39.3±8.7	49.7±13.0	48.1±12.3	10.4±10.2	8.7±10.6
Hfnu-sBP [%]	18.5±15.3	13.1±8.3	19.8±12.9	14.9±7.8	1.3±3.9	2.6±4.0
PSD-sBP [mmHg²]	17.3±18.2	12.1±10.0	11.9±9.2	8.7±6.1	-5.4±10.7	-3.5±4.7
LF/HF-sBP [1]	3.2±2.2	4.0±1.9	3.5±2.0	4.2±2.6	0.2±1.0	0.1±2.0
LF/HF [1]	1.3±1.2	1.0±0.5	4.3±4.0	2.5±1.6	3.0±3.4	1.5±1.6
BRS [ms/mmHg]	15.1±9.9	19.7±9.1				

HR - heart rate; sBP - systolic blood pressure; dBP - diastolic blood pressure; mBP - mean blood pressure; SI - stroke index; CI - cardiac index; TPR - total peripheral resistance; TPRI - total peripheral index, IC - index cardiac; LVWI - left ventricular work index; LF-RRI - low frequency R-R interval; HF-RRI - high-frequency R-R interval; PSD-RRI - power spectral density R-R interval; LF/HF - ratio between low and high band for heart rate and blood pressure variability; PSD-sBP - power spectral density of systolic blood pressure variability; LF-sBP - low frequency of systolic blood pressure variability; HF-sBP - high frequency of systolic blood pressure variability; PSD-dBP - power spectral density of diastolic blood pressure variability; LF-dBP - low frequency of diastolic blood pressure variability; HF-dBP - high frequency of diastolic blood pressure variability; BRS - baroreflex sensitivity; nu - normalised values; statistically significant differences between myasthenia gravis (MG) vs controls (HC) are indicated with *p < 0.05, **p < 0.01, ***p < 0.001.

Conclusion: Our results confirm autonomic dysfunction among MG patients with predominant parasympathetic involvement. Clinicians should consider evaluation of autonomic balance in MG patients with, or at risk for cardiovascular disease.

Disclosure: Nothing to disclose.

EPR-030

Sudomotor dysfunction in people with neuromyelitis optica spectrum disorders

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Background and aims: To determine the extent of sudomotor dysfunction in people with neuromyelitis optica spectrum disorder (pwNMOSD) and to compare findings with a historical cohort of people with relapsing remitting multiple sclerosis (pwRRMS).

Methods: We enrolled 48 pwNMOSD from four clinical centers. All participants completed the Composite Autonomic Symptom Score-31 (COMPASS-31) to determine sudomotor symptom burden. Sudomotor function was assessed using the quantitative sudomotor axon reflex test (QSART). The results were compared with a historical cohort of 35 pwRRMS matched for age, sex and disease duration.

Results: Sudomotor symptom burden, defined as secretomotor domain >0, was present in 26 (54%) of pwNMOSD. Sudomotor dysfunction measured with QSART was present in 25 (52.1%) of pwNMOSD, and 14 (29.2%) pwNMOSD had moderate to severe sudomotor dysfunction. No difference was observed between pwNMOSD and pwRRMS in any of the studied parameters. However, symptomatic sudomotor dysfunction was more frequent in pwNMOSD (n=8, 22.9%) compared to pwRRMS (n=1, 3%; p=0.028). In a multivariable logistic regression analysis, statistically significant predictors for symptomatic sudomotor failure were age and diagnosis of NMOSD.
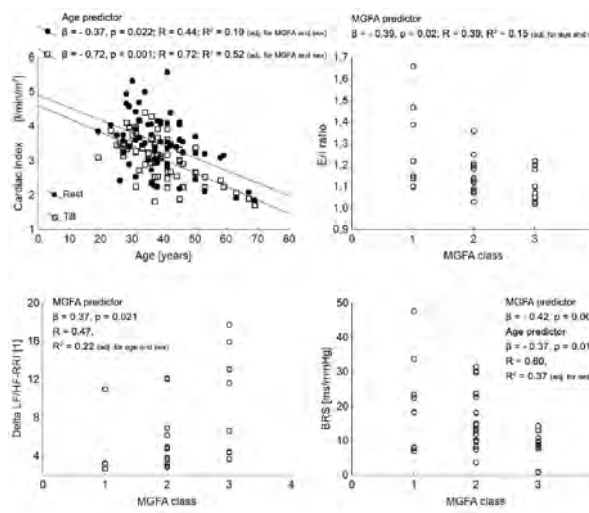
Frequency of pathological QSART for each tested site of the NMOSD cohort.
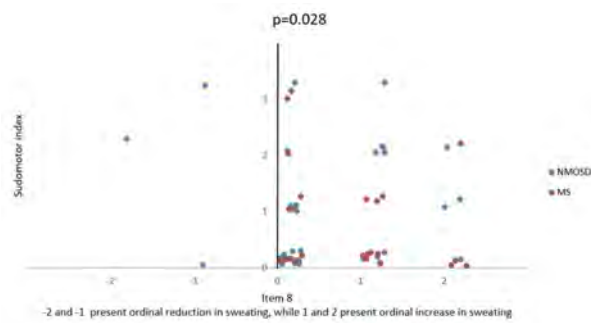
Results of the univariable and multivariable regression model for predicting symptomatic sudomotor failure.

Conclusion: Sudomotor dysfunction is common in pwNMOSD and more often symptomatic compared to pwRRMS.

Disclosure: MH: Participated as a clinical investigator and/or received consultation and/or speaker fees from: Biogen, Sanofi Genzyme, Merck, Bayer, Novartis, Pliva/Teva, Roche, Alvogen, Actelion, Alexion Pharmaceuticals, TG Pharmaceuticals.

EPR-031

COMPASS 31 bladder sub-scores correlate with uroflow parameters in patients with relapsing-remitting multiple sclerosis

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Background and aims: Bladder symptoms are common in patients with relapsing-remitting multiple sclerosis (RRMS) and require early detection. As uroflowmetry and bladder-sonography require equipment and expertise, the Composite-Autonomic-Symptom-Score-31 (COMPASS-31), a self-questionnaire, might facilitate detecting bladder symptoms. Therefore, this study evaluated whether abnormal COMPASS-31 bladder-scores predict abnormal residual urine-volume or uroflowmetry values in RRMS-patients.

Methods: In 70 RRMS-patients and 30 healthy participants, we determined voided urine-volume, maximum flow-rate, average flow-rate, flow-time, time to maximum flow by uroflowmetry (Solar-Uroflow™, MMS, Germany), and pre-voiding urine-volume and post-voiding residual urine-volume by bladder ultrasonography (Scanmaster™, MMS, Germany). The RRMS-patients completed the German COMPASS-31 version and were assigned to the group with or the group without abnormal COMPASS-31 bladder-scores. Parameters between the three groups of patients and controls were compared by the Kruskal-Wallis-test. Mann-Whitney-U-tests were used for post-hoc comparisons between two groups. The Spearman-test assessed correlations between COMPASS31 scores and voiding parameters. Significance was assumed for $p<0.05$.

Results: The COMPASS-31 identified 43 RRMS-patients with and 27 RRMS-patients without bladder symptoms. Average and maximal flow-rates were significantly lower in RRMS-patients with bladder symptoms than in RRMS-patients without bladder symptoms or healthy participants, both parameters negatively correlated with the COMPASS-31 bladder-scores. Post-voiding residual urine-volume was higher in both patient groups than in healthy participants.

Conclusion: In our RRMS-patients, increased COMPASS-31 bladder-scores were associated with altered Uroflow-rates while normal bladder-scores did not exclude increased residual urine-volume. Thus, the COMPASS-31 bladder-scores are valuable for screening for bladder dysfunction but should be complemented by uroflowmetry and sonographic assessments.

Disclosure: The authors have nothing to disclose.

EPR-032

Post-COVID19 syndrome dysautonomia: a tertiary referral centre experience

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Background and aims: Post-coronavirus disease 19 (COVID-19) syndrome remains poorly understood, with substantial health and economic implications. It is a multisystemic presentation, with prevalent autonomic symptoms. Understanding patient presentations and potential autonomic causes may help guide treatment strategies and recovery.

Methods: We conducted a retrospective review of all patients with a suspected or confirmed history of COVID-19 infection who underwent autonomic testing at our Autonomic unit between May 2020 and October 2021.

Results: There were 62 patients evaluated, 20 male and 42 female, with a mean age of 41.38 ±11.52). COVID-19 was confirmed by PCR in 15 patients (26%), and five (8%) required acute hospital intervention. Most common symptoms included palpitations (81%), light-headedness/ dizziness (62%), dyspnoea (48%), fatigue (46%), or cognitive symptoms (33%). Autonomic function testing showed normal blood pressure responses to pressor stimuli, a mean respiratory sinus arrhythmia of 18.89 b/m, and Valsalva ratio of 2.09. Postural tachycardia syndrome (PoTS) was diagnosed in 12 patients, autonomically mediated syncope (AMS) in 11, neurogenic orthostatic hypotension (NOH) in two, and initial orthostatic hypotension (IOH) in seven. Normal supine and upright plasma noradrenaline levels were measured in 34 patients (mean 283.38 pg/ml supine; 472.43 pg/ml tilted).

Conclusion: Abnormal testing was found in 32 cases (52%), the pathology is predominantly benign (PoTS and syncope). This helps to inform rehabilitation and recovery post infection. Patients with PoTS may need further phenotyping to exclude an underlying neuropathic pathology. NOH was found in two patients, one of whom had diabetes and one who had pre-existing OH.

Disclosure: Dr VI is supported by NIHR UCLH Biomedical Research Centre.

EPR-033

Initial orthostatic hypotension in patients with transient dizziness upon standing: a tertiary referral unit experience

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Background and aims: Initial orthostatic hypotension (IOH) is defined as a transient blood pressure (BP) decrease of >40 mmHg systolic and/or >20 mmHg diastolic within 15 seconds of standing, and associated with transient symptoms of cerebral hypoperfusion. Less clearly defined is whether IOH is a limited adrenergic dysfunction or if it is associated with widespread autonomic dysfunction. The aim of this study was to evaluate autonomic dysfunction in patients with history consistent with IOH.

Methods: We retrospectively evaluated patients with suspected diagnosis of IOH who underwent autonomic function tests (AFT) between May-August 2021. Following at least 5 minutes supine rest, beat-to-beat measurement of BP and heart rate (HR) during active standing was performed. Patients with an existing/likely diagnosis of classic or delayed orthostatic hypotension were excluded.

Results: 28 patients (10 M, 18 F) were included and IOH was confirmed in 75% of patients (7 M, 14 F, mean age 37 ± 17 years). 38% of patients presented additional autonomic dysfunction (postural tachycardia syndrome, autonomic-mediated syncope, inappropriate sinus tachycardia, and sympathetic/parasympathetic dysfunction). Average HR rise within 15 seconds of standing for patients with IOH was 36±15 b/m and compensatory HR rise during IOH fell with increasing age.
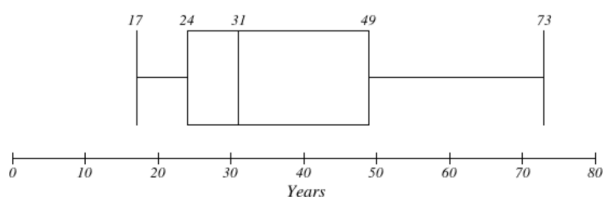
Figure 1: Box plot of ages for the 21 patients who demonstrated initial orthostatic hypotension during active standing.
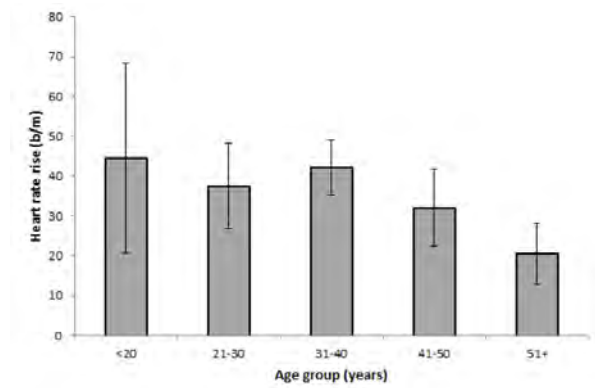
Figure 2: Average compensatory heart rate rise for patients who demonstrated initial orthostatic hypotension (IOH), categorised into age groups.

Conclusion: There was a high occurrence of IOH amongst patients with clinical history of transient dizziness upon standing. A third of these patients presented additional autonomic dysfunction. Continuous BP monitoring during active standing tests is required to confirm diagnosis of IOH and we advocate for this to be considered an integral part of the autonomic assessment.

Disclosure: Dr V. Iodice is supported by NIHR UCLH Biomedical Research Centre.

Headache 1

EPR-034

Eptinezumab for Migraine Prevention in Patients with 2–4 Prior Treatment Failures: DELIVER Subpopulation Analysis

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Background and aims: In DELIVER, eptinezumab treatment resulted in statistically significant reductions in monthly migraine days (MMDs) in patients with migraine and prior preventive treatment failures versus placebo. This exploratory analysis evaluated the preventive migraine efficacy of eptinezumab in selected subgroups of patients in DELIVER.

Methods: DELIVER (NCT04418765) is a phase 3b, multicenter, parallel-group, double-blind study that randomized patients to eptinezumab 100mg, 300mg, or placebo (administered intravenously every 12 weeks) for preventive migraine treatment. Eligible adults (18–75y) had episodic (EM) or chronic migraine (CM) and 2–4 documented unsuccessful treatments in the past 10y. The primary endpoint—change from baseline in MMDs over Weeks 1–12 (Wks1–12)—was analyzed in patient subgroups, including sex, disease classification, medication-overuse headache (MOH) diagnosis, and number of previous treatment failures.

Results: Across all subgroups, eptinezumab-treated patients demonstrated reductions from baseline in MMDs over Wks1–12. The advantages over placebo were numerically greater in patients with MOH versus the general population, in patients with CM versus EM, in patients with highfrequency versus low-frequency EM, and in patients with >2 prior preventive treatment failures versus <2 treatment failures. The 95% confidence intervals for mean differences from placebo in change from baseline did not cross 0 for any subgroups except men and patients with low-frequency EM (both had ≤40 patients per treatment arm).

Conclusion: Across all explored subgroups of adults with migraine and prior preventive treatment failures, greater reductions in MMDs over Wks1–12 were observed with eptinezumab versus placebo in patients with MOH, CM, and >2 documented treatment failures.

Disclosure: H. Lundbeck A/S, Copenhagen, Denmark.

EPR-035

Effectiveness of fremanezumab for preventive treatment of migraine: the observational PEARL study

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Background and aims: Fremanezumab, a humanised monoclonal antibody selectively targeting calcitonin gene-related peptide, is approved in Europe for migraine prevention in adults with ≥4 monthly migraine days (MMD). PEARL (EUPAS35111) is an ongoing observational study designed to generate real-world data on the effectiveness of fremanezumab in chronic and episodic migraine (CM/EM) patients. This interim analysis assessed key effectiveness endpoints.

Methods: PEARL is a 24-month, pan-European, prospective, Phase 4 study being conducted at approximately 90 sites across 11 European countries. The primary endpoint is proportion of patients reaching ≥50% reduction in MMD during the 6-month period after initiating fremanezumab. Secondary endpoints include mean change from baseline in MMD, Migraine Disability Assessment (MIDAS) scores, six-item Headache Impact Test (HIT-6) scores, and days of concomitant acute headache medication use at various timepoints (Months 1–24).

Results: This interim analysis included 389 patients (CM/EM, 77.1%/22.9%; female, 346[88.9%]; age, 44.9[12.00] years). In patients with complete data (n=181), 99(54.7%) reached ≥50% reduction in MMD during the 6-month period after initiating fremanezumab. Mean change from baseline in MMD was –8.0[7.24] at 6 months. Improved scores from baseline at 3 and 6 months, respectively, were reported by 47.1% and 55.8% of patients for MIDAS and 53.8% and 56.1% for HIT-6. Mean change from baseline in monthly days with acute medication use was –6.5(6.24) at 6 months. No drug-related serious adverse events have been reported.

Conclusion: Interim results of PEARL demonstrate the real-world effectiveness of fremanezumab for migraine prevention and reduction of migraine-related disability.

Disclosure: Funded by Teva Pharmaceuticals.

EPR-036

Final results from a real world evidence study on the treatment of migraine patients with Erenumab In GERMANY (SPECTRE)

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Background and aims: Migraine is among the most common neurological diseases world-wide. Erenumab, a calcitonin gene-related peptide (CGRP)-receptor antagonist, was the first anti-CGRP pathway treatment approved for migraine prevention. There still exists a need to better understand treatment with erenumab in clinical practice by headache specialists outside the setting of randomized controlled trials. The aim of the SPECTRE study was to elucidate patient profiles and treatment patterns for erenumab in Germany based on migraine characteristics and comorbidities.

Methods: This non-interventional study was conducted at 139 centers in Germany and enrolled 572 adult migraine patients receiving erenumab treatment. Patients were either new on treatment or had initiated treatment within 3 months of entering the study. Apart from a headache diary, the patient-reported-outcome questionnaires HIT-6 and TSQM were used to assess the impact of headaches on daily life and satisfaction of the patients with the treatment.

Results: Here the results of the final analysis of 572 migraine patients observed for 12 to 24 months will be presented. Previous interim analysis of 454 patients treated for 6 months showed that the majority of erenumab patients were women with chronic migraine, with a high proportion of psychiatric comorbidities. After 3 months of treatment with erenumab monthly migraine und headache days were reduced by 4.5 and 6.6 days, respectively. Furthermore, HIT-6 score was reduced after 3 months and treatment satisfaction remained high throughout 6 months.

Conclusion: SPECTRE will provide valuable insights into use of erenumab in clinical practice in Germany, help characterize prescription patterns and analyze the respective therapy response.

Disclosure: Dr. Charly Gaul received honoraria from Allergan Pharma, Bayer vital, Boehringer Ingelheim Pharma, Cerbotec , Desitin Arzneimittel , electroCore, Grünenthal, Hormosan Pharma, Lilly, Novartis, Ratiopharm, Sanofi, TEVA.

EPR-037

Comparison of efficacy and safety of anti-cgrp antibodies between over and under 65-year-old migraine patients

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Background and aims: Previous studies reported a positive effect of anti-CGRP monoclonal antibodies (mAbs) in migraine prevention, either in over and under 65-years aged patients. Aim of our study was to compare real-life efficacy and safety of mAbs between young and elder migraine patients.

Methods: 30 migraine patients treated with mAbs were enrolled, 15 over (O65) and 15 under (U65) 65 years old. Patients were matched for sex, monthly headache (MHD) and migraine (MMD) days at baseline. Between-group differences in MHD, MMD, Migraine Disability Assessment Test (MIDAS) score, number of days and pills of acute medication intake were assessed after 3 (M3) and 6 (M6) months of treatment. The presence of adverse events was also investigated.

Results: In each group, thirteen patients (87%) were women and nine patients (60%) had chronic migraine. Baseline mean MHD and MMD of both groups was 20 (SD 9.6). Mean age was 70 (65–76) and 45 (19–55) in O65 and U65 group, respectively. After 3 and 6 months of treatment, both groups had a reduction of MHD, MMD, MIDAS score, number of days and pills of acute medication intake, without statistically significant differences between the two groups (M3: $p=0.7$, $p=0.3$, $p=0.6$, $p=0.5$, $p=0.3$; M6: $p=0.1$, $p=0.4$, $p=0.4$, $p=0.3$, $p=0.9$). Also, a similar proportion of patients in each group complaint adverse events at M3 ($p=1.0$) and M6 ($p=1.0$).

Conclusion: Our real-life data showed that mAbs are as effective and safe in over as in under 65-year-old migraine patients.

Disclosure: Nothing to disclose.

EPR-038

Predictors of response to antiCGRP monoclonal antibodies: a multicenter, 24-week, cohort study on 864 migraine patients

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Background and aims: This study is aimed at investigating predictors of response ($\geq$50%) or super-response ($\geq$75%) to monoclonal antibodies (mAbs) targeting the Calcitonin Gene-Related Peptide (CGRP) in high-frequency episodic (HFEM) or chronic migraine (CM).

Methods: In this multicenter, cohort, real-life study, we considered all consecutive patients affected by HFEM or CM visited 21 Italian headache centers from 20.12.2018 to 30.06.2021 treated with erenumab, galcanezumab or fremanezumab for $\geq$24 weeks. Primary and secondary endpoints were $\geq$50% and $\geq$% response predictors at 24 weeks.

Results: 864 migraine patients (HFEM/CM, n= 208/656) received antiCGRP mAbs for $\geq$24 weeks. Unilateral pain (UP) + unilateral cranial autonomic symptoms (UAs) predicted $\geq$50% and $\geq$75% response in both HFEM (61.8% vs 28%, p=0.007; 72.2% vs 43.1%, p=0.005) and CM (60.4% vs 47.0%; p=0.017; 64.8% vs 50.7%; p=0.010). UP + allodynia, and UP + UAs + allodynia predicted $\geq$50% response (63.6% vs 50.4%, p=0.024; 70.1% vs 57.0; p=0.039) and $\geq$75% response (68.8% vs 53.6%; p=0.006; 75.0% vs 60.4; p=0.014) in CM. Multivariate analysis showed that UP + UAs predicted $\ddagger$0% and >=75% response in HFEM (OR: 4.23, CI 95%:1.57–11.4; p=0.004; OR: 3.44, CI 95%:1.42–8.31; p=0.006) and in CM (OR: 1.90, CI 95%:1.15–3.16; p=0.012; OR: 1.78, CI95%:1.14-2.80; p=0.012). In CM, UP + allodynia predicted $\geq$75% response (OR: 1.93, CI 95%:1.22–3.05; p=0.005), whereas obesity was a negative $\geq$50% response predictor (OR: 0.21, CI 95%:0.07–0.64; p=0.006).

Conclusion: Peripheral trigeminal sensitization symptoms (UP + UAs) alone, on association with central sensitization ones (allodynia) seem to predict $\geq$50% and $\geq$75% response to antiCGRP mAbs.

Disclosure: I have no disclosure.

EPR-039

Sleep restriction alters cortical inhibition in episodic migraine subgroups

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Background and aims: There is a well-known interaction between sleep and migraine which remains to be elucidated. Migraine patients having non-sleep related attacks (NSM) display increased pain sensitivity and polysomnography findings of relative sleep deficit compared to sleep related migraine (SM). Here, we investigated cortical inhibition after sleep restriction (SR) in these subgroups, as well as in migraine with (MA) and without aura (MwoA).

Methods: 29 controls and 46 interictal migraine patients (SM n=14, NSM n=32/MA n=19, MwoA n=27) underwent two sessions of transcranial magnetic stimulation (TMS) after two nights of either 8-hour sleep or 4-hour sleep in randomised order. Cortical silent period (CSP) was recorded from the abductor pollicis brevis muscle and analysed for interaction effects in random intercept models of CSP with sleep condition, group and their interaction as fixed effects.

Results: We detected a significantly larger decrease in CSP after SR in NSM than in controls (p=0.002; 95 % CI -34.7 to -7.9) and SM (p=0.007; 95 % CI -43.0 to -6.6). We also found a significantly larger decrease in CSP after SR in MA compared to controls (p=0.017; 95 % CI -35.2 to -3.5). Post hoc contrast revealed a significant effect of SR within the NSM (p=0.002) and MA group (p=0.030).

Conclusion: The larger decrease in CSP after SR in NSM and MA suggest these subgroups to be prone to sleep induced changes in central GABAergic systems.

Disclosure: Nothing to disclose.

EPR-040

An altered pontine-hypothalamic functional interplay could predict migraine disease progression over the years

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Background and aims: Little is known regarding the functional interaction between the pons and hypothalamus in migraine patients studied during the interictal phase. This study aimed to explore resting state (RS) effective connectivity (EC) abnormalities between these two regions in interictal migraine patients and investigate their value in predicting migraine progression over the years.

Methods: 90 episodic migraine patients and 72 controls underwent baseline RS functional magnetic resonance imaging. 23 patients underwent clinical evaluation after 4.5 years. RS EC of bilateral pons and hypothalamus was performed using SPM12 and dynamic causal modelling. RS EC differences between groups were investigated using parametric empirical bayes models. Linear regression models were used to identify imaging predictors of disease progression, as measured by changes in migraine frequency.

Results: At baseline, compared to controls, migraine patients had higher inhibitory EC within the left pons and from bilateral pons to the ipsilateral and contralateral hypothalamus. Migraine patients experienced also a lower inhibitory EC from the left hypothalamus to the left pons, as well as a lower excitatory EC from the right pons to the left pons. During the follow-up, 35% of patients reported a higher migraine attack frequency. Higher inhibitory RS EC from the left pons to bilateral hypothalamus predicted clinically worsening.

Conclusion: During the interictal phase, migraine patients experience a prominent inhibitory influence of the pons over the hypothalamus, while the inhibitory influence of the hypothalamus over the pons is reduced. A higher pontine-hypothalamic inhibitory activity may be a prognostic marker for migraine progression over the years.

Disclosure: The authors declare that they have no conflict of interest related to this study.

Miscellaneous

EPR-041

High density EEG signatures of connected vs disconnected consciousness during REM sleep

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Background and aims: A hallmark of rapid eye movement (REM) sleep is a "perceptual disconnection" from the physical environment, with the failure of external stimuli to be incorporated into the contents of consciousness (dreaming experiences). This study aims to characterize the neural correlates of connected (CC) vs disconnected consciousness (DC) during REM sleep.

Methods: We collected hdEEG from n=22 subjects (n=11 per condition) during REM sleep. A roving auditory oddball sequence was played for a total of six minutes. Participants were subsequently awakened and reported whether they were conscious or not before awakening, and if so, whether they heard the tones (connected) or not (disconnected).

Results: Topographical analysis of scalp oscillatory power across the whole session revealed decreased low-frequency 1–4 Hz poweh and increased high-beta 20–30 Hz power (p <0.05, SNPM corrected) during CC compared to DC. We also found a significant increase in negative amplitude of EEG responses to deviant tones (p=0.008, family-wise error corrected at the cluster level) at latency 258–284 ms in CC compared to DC. The negative amplitude of this component significantly increased the closer subjects approached to awakening (pFWE=0.003, cluster level) during CC compared to DC. Additional early (142–150 ms) and late (342–352 ms) positive components were found during CC in response to deviant tones (pFWE <0.006, cluster level), but the amplitude of these components did not show an interaction with time.
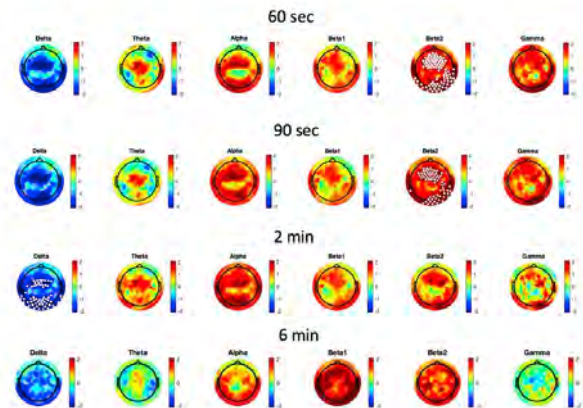
T-values showing differences in normalized percent power in each time window between connected and disconnected consciousness (white dots indicate p<0.05, SNPM corrected). Widespread decreases in 1–4 Hz and increases in 20–30 Hz power during CC
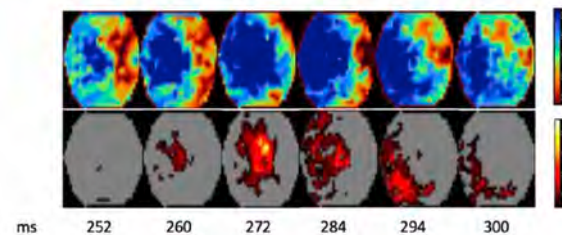
Mean (top) and t-values (bottom) of the contrast: DC Deviants – CC Deviants

Conclusion: Together this analysis suggests several promising electrophysiological signatures differentiating connected vs disconnected consciousness during REM sleep.

Disclosure: Nothing to disclose.

EPR-042

Caregivers' decision-making preferences for patients with disorders of consciousness in rehabilitation centers

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Background and aims: Shared decision making (SDM) is the gold standard in clinical practice, which is supposed to overcome the limits of a paternalistic approach. It consists of an exchange of information, a shared deliberation of values and a decision that both parties agree upon. Since SDM is a normative approach, it should be based on principles of medical ethics. In medical decision-making for patients with disorders of consciousness (DoC), SDM between the medical team and the patients' surrogate is demanded. In this study we aimed to investigate whether caregivers prefer to be included in SDM for their loved ones in the post-acute phase.

Methods: A survey on decision making styles, treatment decisions (life-saving/non-life saving procedures) and reasons for decision making addressed to family caregivers of patients with DoC was conducted at the admission of patients in post-acute rehabilitation facilities. Participants were recruited through consecutive sampling in two neurorehabilitation centers in Italy and Germany.

Results: Preliminary results with 30 participants showed that the majority of caregivers preferred to delegate decisions to clinicians in favour of a paternalistic approach to decision making.

Conclusion: The implementation of SDM is particularly challenging in the care for patients with DoC, due to the conjunction of many critical factors such as patient- and caregiver-related issues, e.g. (dealing with) uncertainty and emotional burden as well as contextual issues. We recommend promoting SDM through the development of specific European ethical guidelines for clinical practice of patients with DoC within EAN.

Disclosure: This work was supported by ERA PerMed JTC2019 "PerBrain".

EPR-043

Ultrasound assessment of cervical nerve root enlargement in polyneuropathy is not confounded by neuroforaminal stenoses

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Background and aims: Ultrasound can detect enlargement of the cervical nerve roots, which has been described both in – mainly demyelinating – polyneuropathies (PNP) and in compressive radiculopathies. This study investigates whether neuroforaminal stenosis by itself, as a common but often asympto-matic degenerative change, is associated with nerve root enlargement on ultrasound.

Methods: We retrospectively studied 182 patients (62 demyelinating, 71 axonal PNP; 49 without evidence of large-fiber PNP) who had undergone ultrasound of the cervical nerve roots C5 and C6 and magnetic resonance or computed tomography of the cervical spine that was reviewed with respect to neuroforaminal stenoses.

Results: No significant differences in cervical nerve root diameters were found between groups with vs. without neuroforaminal stenosis. Patients with demyelinating PNP had larger nerve roots than those with axonal/without PNP. The diagnostic performance of the discrimination of PNP subtypes based on ultrasound nerve root measurements did not differ significantly when including or excluding subjects with neuroforaminal stenoses.

Conclusion: The results suggest that neuroforaminal stenosis per se does not entail relevant cervical nerve root enlargement as detectable by nerve ultrasound. Ultrasound assessment of cervical nerve root size in polyneuropathy is unlikely to be confounded by common degenerative changes of the cervical spine. Conversely, ultrasound may be useful for differentiating asymptomatic from clinically relevant cervical compressive lesions.

Disclosure: No disclosures relevant to the abstract.

EPR-044

COVACiMS Study: SARS-CoV-2 vaccine effectiveness in patients with multiple sclerosis

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Background and aims: Some disease modifying treatments (DMT) used in multiple sclerosis (MS) treatment were associated with a greater risk of severe SARS-CoV-2 infection and may compromise seroconversion following infection and vaccination. We aim to evaluate the immunogenicity of COVID-19 vaccines, as measured by antibody and T-cell responses, in a real-world cohort of MS patients under different DMT.

Methods: Multicentre prospective cohort study of 500 MS patients vaccinated against COVID-19, with 3 study visits: 14–56 days, 3 months, and 9 months after completing vaccination. Demographic and clinical data including MS history and treatment, COVID-19 infection and vaccination will be collected. Analyses include lymphocyte counts and immunophenotyping, IgM and IgG anti-SARS-CoV-2-spike and -nucleocapside proteins, and SARS-CoV-2 spike and nucleocapside protein-specific T-cell responses. Recruitment is open until 15th March 2022. We present preliminary baseline data of 161 patients.

Results: 64.6% women, mean age 43.3 years. Mean time since diagnosis 9.4 years; mean EDSS was 2.4. Six patients (3.7%) had COVID-19 before vaccination, 84.5% had a complete mRNA vaccine scheme and 13.0% a mixt mRNA or adenovirus scheme; 73.9% had a boosted mRNA vaccine. 84.5% presented reactive T spots against total SARS-CoV-2 and spike protein.

Conclusion: The COVACiMS study will provide relevant information regarding the effectiveness of the SARS-CoV-2 vaccine according to DMT use in a Portuguese MS population. This data may support clinical decision making.

Disclosure: Data collection, statistical analysis and medical writing assistance is supported by Biogen. Merck and Roche support the study via a grant to GEEM (Portuguese MS Study Group).

EPR-045

Role of transcranial magnetic stimulation on recovery of post stroke aphasia

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Background and aims: Both hemispheres have role in post-stroke aphasia recovery but better recovery is expected with the restoration of function by the left hemisphere. Transcranial stimulation has been used to favor recruitment of left-hemispheric language networks, thus helps aphasia recovery. The aim of this study is to evaluate the effect of excitatory repetitive transcranial magnetic stimulation (rTMS) on recovery of post stroke aphasic patients.

Methods: 30 patients with post stroke chronic aphasia were included in the study. Aphasia severity was assessed using Aphasia Severity Rating Scale (ASRS). Speech deficits were assessed using Kasr Al-Aini Arabic Aphasia test (KAAT). Real rTMS was applied for 8 sessions (10 HZ) over the two parts of Broca's area: the anterior part (pars triangularis) and the posterior part (pars opercularis). All patients were evaluated before, after the end of treatment sessions and one month later.

Results: There was a significant improvement in the mean total score and mean scores of components of KAAT scale before, immediately after and after one month of rTMS ($p < 0.05$). Moreover, there was a significant improvement in mean scores of ASRS before, immediately after and after one month of rTMS ($p = 0.000$). There was a significant difference in mean scores of ASRS and KAAT before, immediately after the last session and after one month between small, medium and large brain infarcts ($p < 0.05$).
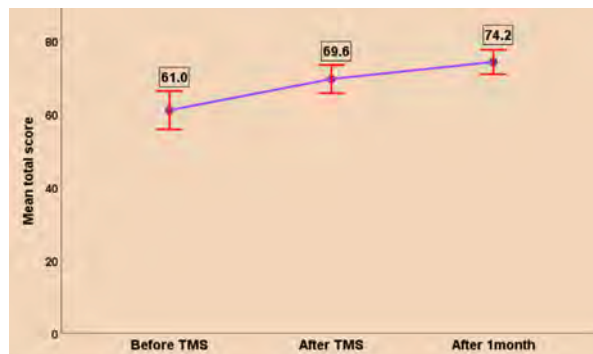
Fig. (1): Comparisons between means of total score of KAAT scale before, immediately after and after one month of rTMS in studied patients.
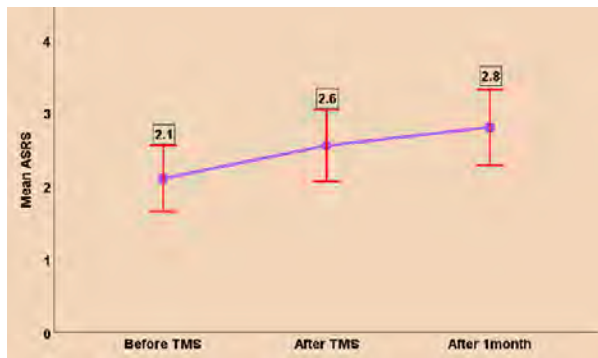
Fig. (2): Comparisons between mean scores of ASRS scale before, immediately after and after one month of rTMS in studied patients.

Conclusion: Excitatory rTMS is a beneficial adjuvant therapy that improves language skills in patients with chronic post-stroke non-fluent aphasia in short and long term.

Disclosure: The authors declare there was no conflict of interest.

EPR-046

Maurice Merleau-Ponty's phenomenology of perception and its relevance to modern cognitive science

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Background and aims: The aim of this poster/talk is to present Maurice Merleau-Ponty's philosophy of perception and delineate its contribution to modern neuropsychology.

Methods: Literature research.

Results: Merleau-Ponty (1908–1961) was a French philosopher. In an attempt at naturalizing phenomenology, he resorted to (neuro-)psychology, psychopathology and cognitive science. He focussed on perception, developing a theory of the lived body (corps propre). Utilizing clinical examples – the best known that of a patient suffering from visual agnosia after an occipital traumatic injury – Merleau-Ponty theorizes the body as a prenoetic means of actively perceiving the environment in a sensorimotor intentional arc. Overcoming the dualism of mind and body, Merleau-Ponty describes the ambiguity of the lived body: it is a perceivable object as well as a perceiving agent, thereby forming a nexus between the individual and his/her environment. This constellation informs the idea of a body schema induced by multisensory inputs and efference copies of intended movements as a prerequisite of the unity and coherence of our body in space that we perceive in health. Its disruption in neurological syndromes such as neglect, anosognosia, and somatoparaphrenia, as well as in experimentally inducible sensations, such as disembodiment and out-of-body experiences has been extensively investigated via morphological and functional imaging and psychophysical experiments.

Conclusion: Merleau-Ponty may be credited for two achievements: laying the conceptual foundation for many of the neuropsychological syndromes neurologists face, as well as clarifying that philosophy and neuroscience are not mutually exclusive, competing fields but rather inform and complement each other.

Disclosure: Nothing to disclose.

EPR-047

Acute glucocorticoid elevation after traumatic brain injury predicts reduces survival rate: a translational study

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P. Kostrukov [2], O. Kostyunina [2], M. Novikova [2],
A. Timokhova [3], M. Makhmudov [5], F. Rider [3],
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Background and aims: Glucocorticoid (GC) elevation in the acute period of traumatic brain injury (TBI) is an important link between the acute damage, late TBI complications and outcome. In addition, chronic stress can affect stress response associated with long-term disturbances of the hypothalamic-pituitary-adrenal (HPA) axis.

Methods: We asses acute cortisol level and survival rate in patients (n=63, mortality 13%) in 2-year longitudinal prospective study. We also measured the time course of corticosterone (CS) level in the blood and survival rate within three months after lateral fluid percussion TBI in rats (n=43, acute mortality 23%, chronic mortality 36%). Stress reactivity was assessed 3 months after TBI using forced swimming test. ROC-analysis was used for determining cut-off GC level. Survival rates were compared using Kaplan-Meier method.

Results: Both in clinical and experimental studies, acute GC levels were higher in subjects who died within follow-up period. Cortisol level in patients showed accuracy of 0.742 (AUC 0.815) in mortality prediction (Fig.1). For patients with acute cortisol level exceeding cut-off value of 600 nmol/l survival rate was significantly lower (Fig.2). In the experimental study, CS levels increased on day 3 after TBI and predicted mortality with accuracy of 0.882 (AUC 0.861). After forced swimming test performed 3 months after TBI, CS elevated in all rats, maximally in intact control group.
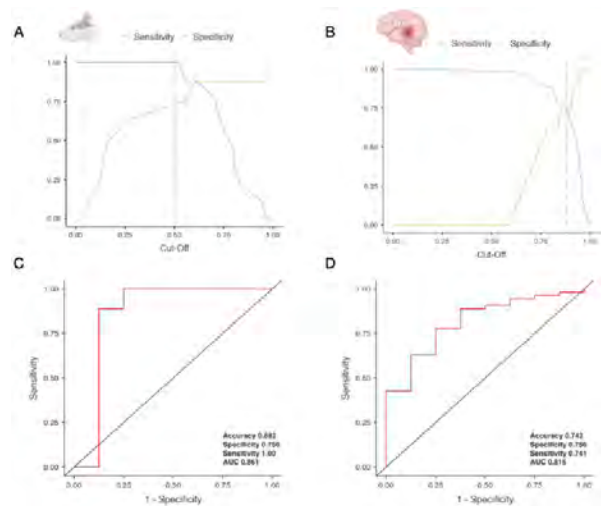
Figure 1. ROC-analysis and determining GCS cut-off level in the experimental (A, C) and clinical studies (B, D).
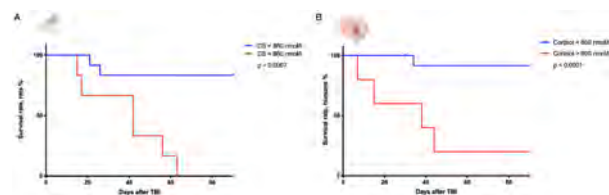
Figure 2. Survival rate in the experimental (A) and clinical studies (B) for selected GCS cut-off level.

Conclusion: Acute GC elevation predicts mortality within months after injury both in clinical and experimental settings. HPA axis function remains impaired in rats 3 months after surgical stress and TBI.

EPR-048

KCNT2-related epilepsies and developmental disorders

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Background and aims: The aim of our study is to explore the clinical and genotypic characteristics of a novel cohort of patients with pathogenic variants in KCNT2, which encodes for the alfa subunit of the potassium channel Slick and has recently been associated with a developmental and epileptic encephalopathy with 12 patients described in literature until now. We report the functional effects of the variants and describe a possible precision medicine strategy.

Methods: The patients have been collected through an international collaboration. All the variants included are classified as pathogenic or likely pathogenic according to the ACMG Classification. Functional tests were performed by recording the currents generated in HEK cells transfected with the variants of interest, through the patch-clamp technique in the whole-cell configuration.

Results: We describe eight previously unpublished patients, four females and four males (age range 1-14 years); four of them were diagnosed with epilepsy, West syndrome in two cases and focal epilepsy in the other two. The remaining four patients underwent genetic testing for developmental delay and/or autistic spectrum disorder; one patient presented a paroxysmal movement disorder. Four patients are carriers of gain-of-function (GOF) variants and four are carriers of loss-of-function (LOF) variants. Quinidine, which demonstrated the ability to reverse the GOF effects of one of the variants in vitro, was also clinically effective in the treatment of the patient carrying that variant.

Conclusion: Our data contribute to expanding the KCNT2-associated spectrum, supporting the role of both gain-of-function and loss-of-function variants, and provide novel insights for precision medicine strategies.

Disclosure: I have no actual or potential conflict of interest in relation to this abstract.

EPR-049

US and MRI guided assessment of the optic nerve sheath diameter in idiopathic intracranial hypertension

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Background and aims: The present study aims to assess and compare the possible role of the ultrasound (US) and magnetic resonance imaging (MRI) measurements of optic nerve sheath diameter (ONSD) in the diagnosis of idiopathic intracranial hypertension (IIH).

Methods: This study was carried out on 120 eyes of patients diagnosed with IIH and 80 eyes of healthy controls. The severity of papilledema in IIH patients were sub-classified into mild and moderate/severe group. US and MRI based evaluation of the ONSD was done 3 mm behind the globe.
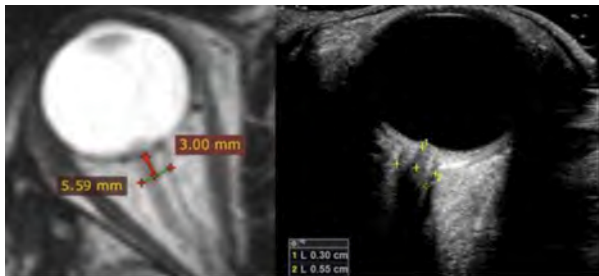
MRI and US guided evaluation of the ONSD.

Results: US guided ONSD was significantly higher in patients compared to controls and in mild papilledema group compared to the moderate/severe group ($p<0.00001$). The best ONSD cut-off value indicating IIH was 5.5mm with an area under the curve of 0.863 sensitivity 75% and specificity 92.5%. The ONSD was correlated to the grade of papilledema with 6.6mm as the best cutoff indicating moderate/severe papilledema with AUC of 0.782, sensitivity 76.7% and specificity 80.5%. The MRI guided ONSD were comparable to the US guided with significant positive correlation between both methods for evaluations ($r=0.75$, $p<0.001$).
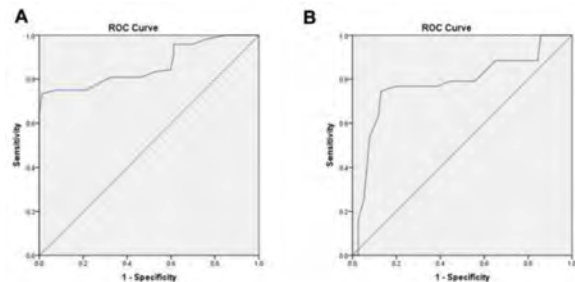
A) ROC curve of US guided ONSD for differentiating IIH patients from controls, B) ROC curve of US guided ONSD for differentiating mild versus moderate and severe papilledema groups.
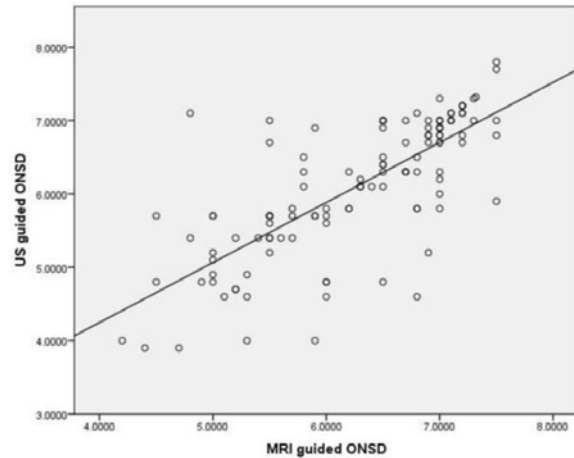
Correlation between the US and MRI guided ONSD evaluation

Conclusion: ONSD can serve as a reliable screening tool of raised ICP in IIH patients and indicator of the degree of papilledema. Stratifying the patients according to the grade of the papilledema may increase the sensitivity of the ONSD cutoff values. The US and MRI guided ONSD measurements were correlated; however the advantage of being a simple accessible low-cost bedside tool favors the US over the MRI.

Disclosure: The authors have nothing to diclose.

MS and related disorders 1

EPR-050

Efficacy of Ozanimod in Disease-Modifying Treatment Naive vs Experienced Patients With Relapsing Multiple Sclerosis

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Background and aims: The benefit of early intervention with ozanimod treatment was demonstrated in phase 3 trials (SUNBEAM–NCT02294058; RADIANCE–NCT02047734), where ozanimod was superior to interferon β-1a (IFN) on clinical and radiologic measures of disease activity in patients with relapsing multiple sclerosis (RMS). After switching from IFN to ozanimod in an ongoing open-label extension (DAYBREAK–NCT02576717), patients had numerically lower annualised relapse rates and decreases in lesion counts. This exploratory analysis assessed clinical and radiologic outcomes over 5–6 years among patients who were disease-modifying therapy (DMT)- naive or DMT-experienced before SUNBEAM/RADIANCE.

Methods: In SUNBEAM/RADIANCE ("parent trials"), adults with RMS received oral ozanimod 0.46 or 0.92 mg/d or intramuscular IFN 30 μg/wk for ≥12 (SUNBEAM) or 24 (RADIANCE) months. Upon completion, patients were eligible for open-label ozanimod 0.92 mg/d in DAYBREAK. This analysis assessed clinical and radiologic outcomes in patients who were DMT-naive or DMT-experienced at SUNBEAM/RADIANCE baseline, received IFN or ozanimod 0.92 mg in SUNBEAM/RADIANCE, and received ozanimod 0.92 mg in DAYBREAK (data cutoff: Feb 2021).

Results: Of 1501 patients who entered DAYBREAK from SUNBEAM/RADIANCE, 1073 (71.5%) were DMT-naive and 428 (28.5%) were DMT-experienced (predominantly glatiramer or an interferon) at parent trial baseline. Ozanimod treatment was associated with benefits in clinical and radiologic measures of disease activity, which was consistent between patients who were DMT-naive or DMT-experienced at parent trial baseline and was maintained over time in the OLE (Figures 1–3).
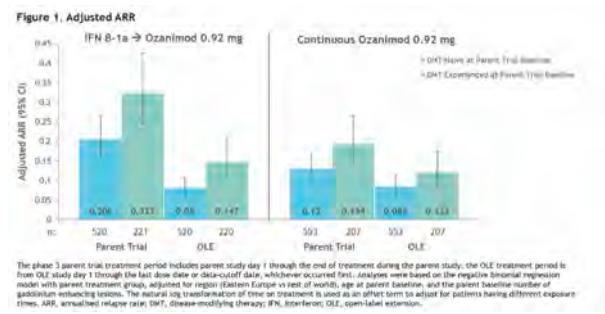
Figure 1
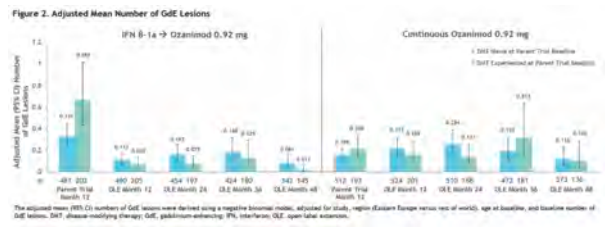
Figure 2

Figure 3

Conclusion: In patients with RMS, the benefit of early intervention with ozanimod was consistent regardless of prior DMT exposure and is maintained over time.

Disclosure: These studies were supported by Celgene International II.

EPR-051

Adipokine levels in multiple sclerosis patients of the same age: associations with clinical and radiological measures

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Background and aims: An imbalance of pro- and anti-inflammatory adipokines, white adipose tissue hormones, is suggested to play a crucial role in the immunopathology of multiple sclerosis (MS). However, correlations with MS phenotype remains to be elucidated. As age affects adipokine function and synthesis, we aimed to determine whether adipokine concentrations relate to disability measures and brain volumes in MS patients of the same age.

Methods: Serum adipokine levels (adiponectin, leptin, resistin) were measured using ELISA in 288 MS patients and 125 healthy controls (HC) from Project Y, a cross-sectional study of all people with MS born in the Netherlands in 1966, and age-matched HC. Adipokine levels were compared between MS patients and HC and correlated with 1) clinical measures like expanded disability status scale (EDSS), disease duration, treatment status and 2) brain volumes.

Results: Adiponectin concentrations were 1.2 fold higher in patients compared to HC, with highest concentrations in secondary progressive patients. Increased adiponectin levels were associated with longer disease duration in female progressive MS patients ($\beta=0.3$). Resistin and leptin levels did not differ between MS patients and HC, however, resistin levels were significantly reduced in patients using teriflunomide compared to patients using glatiramer acetate, dimethyl fumarate or ocrelizumab. Leptin levels significantly associated with EDSS ($\beta=0.4$) and strongly correlated with deep gray matter ($\beta=-0.7$) and cortical gray matter volume ($\beta=-0.5$) in primary progressive MS.

Conclusion: Adipokines are associated with clinical and radiological measures, indicating that adipokines are promising biomarkers for disease severity in MS.

EPR-052

Retinal layer thinning after optic neuritis as a predictor of future relapse remission in relapsing multiple sclerosis

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Background and aims: Remission of relapses is an important contributor to prognosis in relapsing multiple sclerosis (RMS). In MS-associated acute optic neuritis (MS-ON), retinal layer thinning measured by optical coherence tomography (OCT) is a reliable biomarker of neuroaxonal damage. However, prediction of non-ON relapse remission is challenging. We aimed to investigate whether retinal thinning after ON could predict relapse remission after subsequent non-ON relapses.

Methods: For this longitudinal observational study from the Vienna MS database (VMSD), we included MS patients with 1) an episode of acute ON, 2) available spectral-domain OCT scans within 12 months before ON onset (OCTbaseline), within 1 week after ON onset (OCTacute) and 3–6 months after ON (OCTfollow-up), and 3) at least one non-ON relapse after the ON episode. Subsequent non-ON relapses were classified as displaying either complete or incomplete remission.

Results: We analyzed 167 MS patients (mean age 36.5 years [SD 12.3], 71.3% female). In 61 patients (36.5%) ≥1relapse showed incomplete remission. In the multivariable analyses, incomplete remission of non-ON relapse was predicted by GCIPL thinning both from OCTbaseline to OCTfollow-up and from OCTacute to OCTfollow-up (odds ratio [OR] 2.4 per 5µm, $p<0.001$, respectively). Thinning of pRNFL was also associated with incomplete relapse remission when measured from OCTbaseline to OCTfollow-up (OR 1.9 per 10µm, $p<0.001$), but not when measured from OCTacute to OCTfollow-up.

Conclusion: Retinal layer thinning after optic neuritis may be useful as a predictor of future relapse remission in RMS, potentially informing treatment strategy.

EPR-053

Genetic variants in iron metabolism may contribute to the development and severity of progressive multiple sclerosis

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Background and aims: Slowly expanding lesions with a paramagnetic iron rim are crucial for the pathogenesis of progressive multiple sclerosis (MS) and the worsening of disability, but whether the elevated iron content is a primary or secondary phenomenon is still not clear. We investigated the contribution of genetic variants in iron metabolism to the susceptibility to progressive MS.

Methods: Starting from whole-genome data, we extracted 66,760 Single Nucleotide Polymorphisms (SNPs) located inside 319 genes deemed relevant for iron homeostasis or with known expression Quantitative-Trait-Loci (QTL) effect on these genes from public repositories. Then, we tested the association between the SNPs and the course of MS in 946 patients, comparing 250 patients with benign relapsing-remitting MS (disease duration ≥ 20 years, EDSS≤ 3.5) versus primary (n=409) and secondary (n=287) progressive MS patients [Fig. 1].
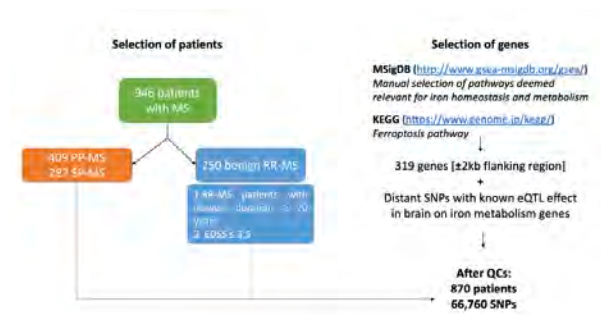
Study workflow.

Results: The top-ranked signal mapped to chromosome 14 in the Hypoxia-Inducible-Factor-1-alfa (HIF1A) gene, with the leading SNP (rs11621525_A) being protective towards the progressive course (p=5.62e-07;OR=0.53). Rs11621525 is known from literature to modulate the expression of HIF1A, through both expression- and methylation- QTL effects. Interestingly, the second-ranked signal mapped to chromosome 8 in the MYC gene (leading SNP=rs3891248_A;p=1.18e-05;OR=0.50), a central player in cell cycle and immune system regulation, whose activity is modulated by the interaction with HIF1-alfa. As a secondary analysis, rs3891248_AA was associated to reduced disease severity in the progressive MS patients

(n=649), assessed by the Age-Related Multiple Sclerosis Severity score (beta=-2.16; p=0.031).

Conclusion: Genetic variants in iron metabolism-related genes may contribute to the pathogenesis of progressive MS and impact on disease severity.

Disclosure: The authors report no relevant disclosures.

EPR-054

Processing speed in early-stage relapsing-remitting multiple sclerosis and its influence on treatment decision making

G. Saposnik [1], R. Gómez-Ballesteros [2], M. Borges [3], J. Martín-Martínez [4], J. Sotoca [5], A. Alonso [6], A. Caminero [7], L. Borrega [8], J. Sánchez-Menoyo [9], F. Barrero-Hernández [10], C. Calles [11], L. Brieva [12], M. Blasco-Quílez [13], J. Dotor García-Soto [3], M. Campo-Amigo [14], L. Navarro-Cantó [15], E. Agüera [16], M. Garcés-Redondo [17], O. Carmona [18], L. Gabaldón-Torres [19], L. Forero [20], M. Hervás [21], J. Maurino [2], T. Castillo-Triviño [22], S. Sainz de la Maza [23]

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Background and aims: The presence of cognitive impairment in patients recently diagnosed with RRMS has been a subject of debate. This study aimed to assess cognitive impairment in an early-stage RRMS population and its impact on therapeutic decision making.

Methods: A multicentre, non-interventional study was conducted. Adult patients with RRMS diagnosis, disease duration ≤3 years, and Expanded Disability Status Scale (EDSS) score between 0–5.5 were included. Participants were asked to choose their treatment preference in eight simulated MS case scenarios to assess status quo (SQ) bias and completed patient-reported measures to gather information on fatigue, mood/anxiety, quality of life, stigma, hopelessness, self-efficacy, patients' interest about their long-term prognosis (LTP), and symptom severity [SymptoMScreen (SyMS)]. SQ is the tendency to continue taking a previously selected but inferior therapeutic choice. Symbol Digit Modalities Test (SDMT) was selected to identify participants with cognitive impairment (cut-off score ≤49).

Results: A total of 189 patients were included (mean age: 36.1+/-9.4 years, 71.4% female, mean disease duration: 1.2 +/-0.8 years, median EDSS score: 1.0 [IQR=0.0-2.0]). Eighty-one patients (43.1%, n=81/188) had information processing speed problems. Higher baseline EDSS and number of T2 lesions were predictors of delayed processing speed (OR=1.57, 95% CI: 1.11-2.21, p=0.011; OR=1.50, 95% CI: 1.11-2.03, p<0.01, respectively). Among patients with cognitive impairment, SQ was associated with having discussed LTP (p=0.013) and higher SyMS score (p=0.035) after adjustment for co-variates.

Conclusion: Over 40% of early-stage RRMS patients experienced delays in cognitive processing affecting their decision-making ability. These results highlight the importance of early therapeutic interventions to preserve patients' cognitive performance.

EPR-055

Real world effectiveness of Natalizumab extended interval dosing in a French cohort

J. Pelle [1], A. Briant [2], C. Lebrun-Frenay [3], M. Cohen [3], L. Mondot [3], J. De Seze [4], K. Bigaut [4], N. Collongues [4], L. Kremer [4], D. Ricard [5], F. Bompaire [5], M. Sallansonnet-Froment [5], C. Ohlmann [5], J. Ciron [6], D. Biotti [6], B. Pignolet [6], J. Parienti [2], G. Defer [1]

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Background and aims: Patients with relapsing-remitting multiple sclerosis (RRMS) treated with Natalizumab (NTZ) extended interval dosing (EID) have lower risk of PML. Results of NOVA trial, despite not fulfilling the MR primary endpoint, suggest that patients stable on standard 4W interval dosing (SID) can switch to 6W EID with no clinically meaningful loss of efficacy. We conducted a French real-life retrospective multicentric case-control study evaluating the non-inferiority of this strategy.

Methods: RRMS patients previously treated with at least 11 NTZ infusions on SID over 12 months were included from 01/01/2010 to 01/05/2020. At baseline patients were assigned to the EID group if this standard period was followed by at most 9 infusions in the next 12 months or assigned to the SID group if they had an additional 12-month period of SID. Primary endpoint was the proportion of patients presenting no relapse 12-month after baseline. Secondary endpoints included annual relapse rate and disability progression. Statistical analysis was based on propensity score methods.

Results: The cohort included 303 patients (SID group n=156, EID group, n=147). Proportion of patients free from relapse was significantly non inferior in the EID group than the SID group (97% vs 92%, p<0,001), in the unadjusted and propensity score adjusted models. The annualized relapse rate was 0,083 +/- 0,300 in the SID group and 0,041 +/- 0,231 in the EID group (p=0,149). Disability progression was observed in 13% SID patients and 11% EID patients (p=0,610).

Conclusion: Our study confirms the non-inferiority of EID NTZ strategy on RRMS clinical activity.

Disclosure: This study was supported by Caen University Hospital's Research Center and funded by Biogen.

EPR-056

Dynamics of progression to wheelchair in SPMS and impact of siponimod: Subgroup analyses from the EXPAND study

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Background and aims: Worsening ambulation is a hallmark of secondary progressive multiple sclerosis (SPMS) leading to wheelchair dependence (EDSS score of ≥7.0), which is associated with poorer quality of life and increased healthcare costs.

Methods: The EXPAND core part (CP) was an event-driven, placebo-controlled study assessing the safety/efficacy of siponimod in patients with SPMS. Patients with 6-month confirmed disability progression during the CP were offered switch to open-label siponimod. This post-hoc analysis assessed time-to-sustained (until the end of the CP) progression to EDSS ≥7.0 using Cox proportional hazards models and Kaplan-Meier estimates in a modified full analysis set (mFAS) that excluded EDSS data following any switch to open-label siponimod during the CP. Extrapolation of observed data beyond the CP in the overall mFAS population and in pre-defined active/non-active SPMS (a/naSPMS) subgroups was performed based on multi-state Markov model estimates.

Results: In the EXPAND CP, siponimod reduced the risk of reaching sustained EDSS ≥7.0 by; 40% (HR [95% CI]:0.60 [0.41; 0.88] p=0.009) in the overall mFAS, 51% (0.49 [0.29; 0.81], p=0.005) in aSPMS and numerically by 22% (0.78 [0.42; 1.45], p=0.437) in naSPMS, versus placebo. Extrapolating beyond the CP, siponimod delayed the median time to wheelchair by; 5.8 years (15.3 versus 9.4 years, p=0.0134) in the overall mFAS, 7.9 years (15.5 versus 7.6 years, p=0.015) in aSPMS, and numerically by 3.0 years (15.5 versus 12.6 years, p=0.398) in naSPMS, versus placebo.

Conclusion: These results indicate that siponimod reduces risk of reaching wheelchair dependence in SPMS patients.

Disclosure: The study was supported by Novartis Pharma AG, Switzerland. The detailed author disclosures will be presented in the subsequent presentation.

EPR-057

Pregnancy outcomes in patients with multiple sclerosis treated with teriflunomide: post-marketing data from 2018-2021

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Background and aims: Teriflunomide is approved for the treatment of relapsing-remitting multiple sclerosis (MS). Although effective contraception is required, pregnancies have occurred in patients treated with teriflunomide. Here, we provide an update on outcomes of pregnancies in patients with MS who received teriflunomide in the post-marketing setting.

Methods: Outcomes from Sanofi's global pharmacovigilance database are summarized for new cases between 1 January 2018 and 31 July 2021, excluding known pregnancy registry cases, and for follow-up data on cases reported up to the previous data cut-off of 31 December 2017.

Results: Of 305 new confirmed teriflunomide-exposed pregnancy cases, 132 cases (reporting 133 pregnancies), were reported either prospectively or retrospectively and had known outcomes. Of these, there were 55 (41%) live births [1 was pre-term], 1 (1%) still birth, 46 (35%) spontaneous abortions, 29 (22%) induced abortions [including 1 unexposed termination of pregnancy for foetal anomaly]), and 2 (2%) ectopic pregnancies. Of 55 infants born alive, 7 (12.7%) had a reported major or minor birth defect with no specific pattern. Of 43 cases of maternal exposure to teriflunomide identified before the previous data cut-off that contained follow-up information on pregnancy outcomes, there were 34 (79%) live births (1 pre-term), 8 (19%) spontaneous abortions, and 1 (2%) ectopic pregnancy.

Conclusion: Reported cases from post-marketing experience did not reveal specific patterns or trends for abortion or birth defects, and do not change the overall assessment of outcomes of teriflunomide-exposed pregnancies.

Disclosure: Editorial support was provided by Richard Hogan, PhD, and Katie Crosslin, PhD of Elevate Medical Affairs, which was sponsored by Sanofi Genzyme.

EPR-058

The prognostic value of cerebrospinal fluid axonal damage biomarkers in Multiple Sclerosis patients: a prospective study

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Background and aims: There is a need for prognostic biomarkers in Multiple Sclerosis (MS) patients. We previously demonstrated that cerebrospinal fluid (CSF) Tau protein at diagnosis (T0), could predict worse prognosis after a mean follow-up of 2 years (T1). We aimed to confirm our results on a longer follow-up of 3.5 years (T2) and compare the prognostic value of CSF Tau and CSF neurofilaments light chain (NFL) in MS.

Methods: We analyzed CSF Tau and CSF NFL with ELISA at diagnosis (T0). EDSS, MSSS, and ARMS were obtained at T1 and T2. So far, 100 patients were evaluated at T1 and 75 patients were re-evaluated at T2.

Results: At T1, CSF Tau showed a higher correlation with MSSS and ARMSS compared to CSF NFL (Table). We confirm CSF TAU is a predictor of worse prognosis with both MSSS and ARMSS at T2, whereas CSF NFL is no longer statistically significant even after a correction for disease-modifying treatments (DMTs). Patients in high-efficacy DMTs at T2 presented higher CSF Tau levels (p=0.03) and higher CSF NFL levels (p=0.0001) at T0 compared with patients with low efficacy DMTs. A multivariate analysis accounting for radiological and clinical characteristics confirmed CSF Tau as the best predictor of MSSS (beta=0.367, p=0.001) and ARMSS (beta=0.38, p=0.02) at T2.

Table 1 Biomarker	MSSS T0 (N:100) Rho; p-value	ARMSS T0 (N:100) Rho; p-value	MSSS T2 (N:75) Rho; p-value	ARMSS T2 (N:75) Rho; p-value
CSF TAU (pg/ml)	Rho:0.37 ; p:0.0001	Rho:0.23 ; p:0.01	Rho:0.49; p<0.0001	Rho:0.35; p:0018
			Rho:0.37; p:0.001*	Rho:0.35; p:0.002*
CSF NFL (pg/ml)	Rho:0.23 ; p:0.02	Rho:0.20 ; p:0.04	Rho:0.17; p:0.1	Rho:0.16 ; p:0.1
			Rho:0.01; p:0.9*	Rho:0.08; p:0.4*

* with correction for DMTs (none/low efficacy versus high efficacy)

Conclusion: Our preliminary data confirm the usefulness of CSF axonal damage biomarkers performed at MS diagnosis for prognostic purposes. Patients with higher CSF axonal damage are more likely to develop a worse prognosis and to be treated with high efficacy DMTs.

Disclosure: No disclosures related to this study.

Neuro-oncology, Neuroimaging, & Clinical neurophysiology 1

EPR-059

Altered functional connectivity of the subthalamic nucleus in Parkinson's disease

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Background and aims: To investigate how the subthalamic nucleus (STN), the most frequently used deep brain stimulation (DBS) target for Parkinson's disease (PD), is functionally linked to other brain regions in different PD phenotypes using resting-state fMRI.

Methods: Clinical data and resting-state fMRI were acquired from 60 PD patients and 60 age- and sex-matched healthy control subjects within an ongoing longitudinal project. PD patients were divided into two groups: 19 patients eligible for DBS (PD-DBS) and 41 not candidate for DBS (PD-noDBS). Bilateral STN were selected as regions of interest and a seed-based connectivity analysis was assessed in PD groups and healthy controls.

Results: PD-DBS showed a decreased connectivity between bilateral STN and bilateral sensorimotor areas relative to both healthy controls and PD-noDBS patients. On the contrary, PD-DBS patients showed higher functional connectivity between bilateral STN and globus pallidus, putamen and thalamus bilaterally compared to healthy controls; similar patterns were found when PD-noDBS patients were compared to healthy controls (albeit with lower Z-scores connectivity levels than PD-DBS). We hypothesize that candidates for DBS showed an increased connectivity between STN and globus pallidus/thalamus, which in turn may provide a decreased connectivity with sensorimotor areas relative to patients not eligible for DBS.

Conclusion: Our results suggest that functional connectivity of deep nuclei varies among PD patients and confirm an important role of fMRI as a tool for selection of candidates for DBS. The idea that STN-DBS works by modulating and restoring functional connectivity between basal ganglia and sensorimotor areas is further corroborated.

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EPR-060

Metabolic-imaging of human glioblastoma explants: a new precision-medicine model to predict treatment response early

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Background and aims: Glioblastoma (GB) is the most severe form of brain cancer, with a 12–15 month median survival. Although cell therapies for GB are on the near horizon, surgical resection, temozolomide (TMZ) and radiotherapy (RT) remain the primary therapeutic options for GB, and no new small-molecule therapies have been introduced in recent years. This therapeutic standstill is partially because preclinical models of GB do not reflect the complexities of GB cell biology. Furthermore, the aggressive progression of GB makes it critical to identify patient-tailored therapeutic strategies early.

Methods: We developed a novel in-vitro 3D glioblastoma explants (GB-EXPs) model derived from patients' resected tumors maintaining cytoarchitecture seen in the tumors. We then performed metabolic-imaging by fluorescence lifetime imaging microscopy (FLIM) on live GB-EXPs to predict drug response, using TMZ as test-drug.
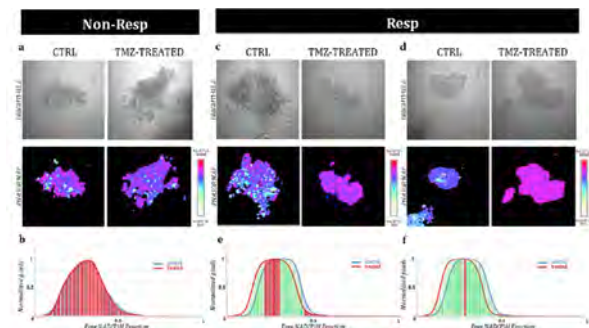
FLIM-based metabolic imaging on patien-derived glioblastoma explants

Results: The entire process was successfully completed within 1 week since surgery. A unique drug response sample stratification emerged, that was well reflected at the molecular level, highlighting new targets associated to TMZ treatment and identifying a molecular signature associated to survival.
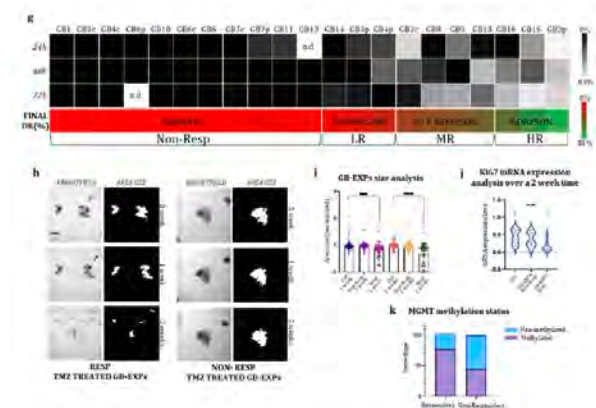
TMZ response stratification in GB patients

Conclusion: To the best of our knowledge, this is the first time that FLIM-based metabolic imaging is used on live glioblastoma explants to test anti-neoplastic drugs. FLIM-based readouts of drug response in GB explants could accelerate precision treatment of patients with GB and the identification of new anti-GB drugs.

Disclosure: No competing interests .

EPR-061

Striatal dopamine transporter imaging in Parkinson's disease drug-naïve patients: focus on sexual dysfunction

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Background and aims: Dopamine plays a key role in sexual behavior, but there are no dopaminergic imaging studies available establishing the relationship between nigrostriatal dopaminergic degeneration and sexual dysfunction (SD) in Parkinson's disease (PD).

Methods: We retrospectively analyzed clinical and 123I-FP-CIT SPECT data of 43 newly-diagnosed drug-naïve PD patients. Based on the sexual domain of the Non-Motor Symptoms Scale (NMSS), we identified patients with sexual concerns (WSC) reporting a score ≥ 1 due to hypoactive sexual desire and/or function, and patients without sexual concerns (NoSC), matched for disease duration (± 1 year) and UPDRS-III score (± 2 points). Uptake in the most and least affected putamen (maP, laP) and caudate (maC, laC), total putamen-to-caudate ratio, and total striatal binding ratio (tSBR) were assessed through semi-quantitative analysis.

Results: There were no significant differences between WSC and NoSC in demographic, motor and non-motor evaluation, and medical conditions. In WSC significantly lower uptake values in maP (p=0.004), laP (p=0.009), maC (p=0.016), laC (p=0.019), and tSBR (p=0.006) were found. Partial correlation analysis after Bonferroni correction revealed significant correlations between SD scores and the uptake in the maP (r=-0.544, p=0.0002), maC (r=-0.425, p=0.006), laP (r=-0.460, p=0.002), and the tSBR (r=-0.471, p=0.002). Furthermore, a logistic regression model with SD as categorical dependent variable, and after controlling for age, sex, and BDI score, demonstrated that only the maP and laP uptake and tSBR values were significantly associated with SD.

	WSC (n=23)	NoSC (n=20)	P-value
Age	67.13 (9.05)	63.40 (7.09)	0.144
Sex, M/F	17/6	11/9	0.219
Tremor dominant phenotype, n (%)	16 (69.6)	15 (75)	0.745
Right side of onset, n (%)	15 (65.2)	10 (50)	0.365
Disease duration, years	1.54 (0.91)	1.43 (0.74)	0.829
UPDRS-III score	11.78 (4.17)	11.45 (4.09)	0.794
Hoehn&Yahr stage			
- stage 1-1.5, n (%)	15 (65.2)	16 (80)	0.327
- stage 2-2.5, n (%)	8 (34.8)	4 (20)	0.327
RBD, n (%)	12 (52.2)	7 (35)	0.359
Hyposmia, n (%)	13 (56.5)	10 (50)	0.547
Gastrointestinal score NMSS	3.22 (3.69)	3.20 (5.79)	0.227
Urinary score NMSS	5.90 (8.17)	5.61 (8.40)	0.806
MMSE score	27.56 (1.94)	27.79 (1.82)	0.711
ACE-R score	89.69 (6.81)	91 (7.01)	0.625
BDI-II score	11.22 (8.78)	9.74 (8.99)	0.310
Zung anxiety scale score	36.28 (9.72)	33.41 (10.27)	0.296
Use of antidepressants, n (%)	4 (17.4)	3 (15)	1.0
Cardiovascular disease, n (%)	3 (13)	3 (15)	1.0
History of diabetes, n (%)	2 (8.7)	0	0.491
History of hypertension, n (%)	12 (52.1)	7 (35)	0.359
History of dyslipidemia, n (%)	1 (4.3)	3 (15)	0.323
Use of thiazides, n (%)	1 (4.3)	1 (5)	1.0
Use of beta-blockers, n (%)	2 (8.7)	2 (10)	1.0
maC uptake	2.34 (0.51)	2.79 (0.67)	0.016
maP uptake	1.44 (0.39)	1.81 (0.41)	0.004
laC uptake	2.56 (0.57)	3.04 (0.72)	0.019
laP uptake	1.68 (0.46)	2.08 (0.49)	0.009
tP/C	0.62 (0.11)	0.68 (0.09)	0.078
tSBR	2.01 (0.44)	2.43 (0.53)	0.006

Group comparisons between WSC and NoSC of demographic and clinical characteristics, neuropsychiatric measures, medical conditions, concurrent therapy, and 123I-FP-CIT SPECT data.

Conclusion: This is the first study reporting the relationship between specific patterns of dopaminergic nigrostriatal denervation and SD in PD.

Disclosure: Nothing to disclose.

EPR-062

CNS complications of immune checkpoint inhibitors are not associated with increased serum cytokine levels

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Background and aims: Biomarkers that allow an early diagnosis of CNS immune-related adverse effects (CNS-iAE) of immune-checkpoint inhibitors (ICI) are lacking. High titers of some citokines have been related to systemic-iAE. We aimed to compare cytokine levels of CNS-iAE patients with patients on ICI treatment without iAE.

Methods: Archive serum of samples obtained in the initial diagnostic-workup of patients with CNS-iAE attended in our centre between 2017–2021 were retrospectively analysed. Serum samples of control patients were collected at baseline, and after 2 and 6 weeks of ICI beginning. We analysed TIM3, IL1b, IL6, IL8, IL10, IL12, IL17, IL18, IFNg, TNFa.

Results: Of 1,092 patients under ICI, 8 patients (0.7%) had CNS-iAE. Serum samples of 7 patients were recovered, 2 women (28.6%) with median age (IQR) of 63.4 (54.5–70.7) years-old, and median (IQR) time from ICI until symptoms of 29 (18–174) days. 5 patients (71.4%) fulfilled Graus criteria for possible autoimmune encephalitis, 1 presented an ICI-related encephalopathy and other a meningoencephalitis. Controls included 12 patients, without significative differences in age or gender. IL17 was lower in CNS-iAE group than in controls at baseline (p=0.013), 2 (p=0.022) and 6 weeks (p=0.017). IL18 was lower in CNS-iAE than in controls at 2 (p=0.036) and 6 weeks (p=0.036). There was a non-significant trend of lower levels of IL6 in CNS-iAE. Remaining cytocines were similar among both groups.
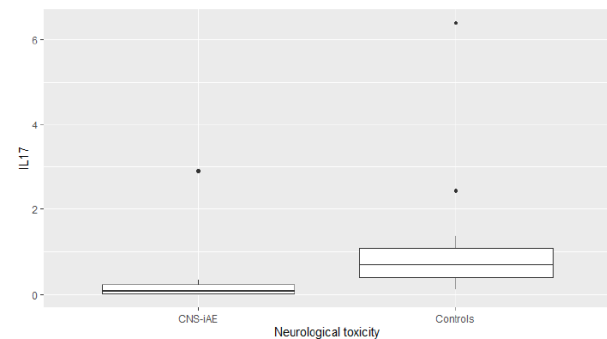
IL17 levels of the CNS toxicity of ICI vs control group after 6 weeks of ICI beginning
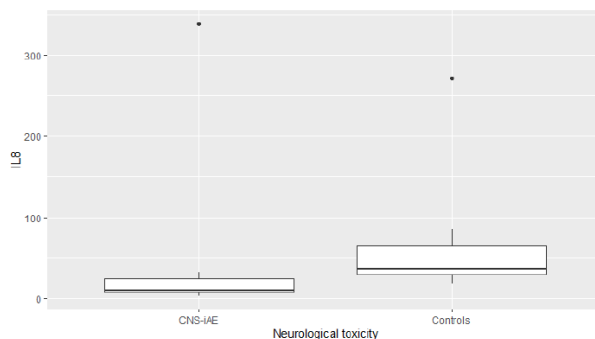
L8 levels of the CNS toxicity of ICI vs control group after 6 weeks of ICI beginning
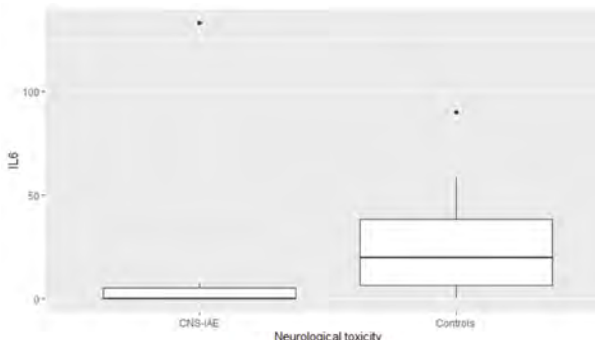
IL6 levels of the CNS toxicity of ICI vs control group after 6 weeks of ICI beginning

Conclusion: In our study, CNS-iAEs were not associated with a higher serum cytokine level than in patients without iAEs. Due to our limitations, further investigations are warranted to confirm our findings.

Disclosure: There are not relevant conflicts of interest to disclose.

EPR-063

Diagnostic accuracy of edited 2HG spectroscopy for IDH-mutant prediction in a clinical setting: initial results

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Background and aims: Isocitrate dehydrogenase (IDH) mutation is a strong prognostic factor in diffuse brain gliomas. IDH mutation results in intratumor D-2-hydroxyglutarate (2HG) accumulation. Edited magnetic resonance spectroscopy (MRS) has shown high diagnostic value in the detection of 2HG oncometabolite in research settings. Therefore, incorporation of this technique into clinical practice is advisable, even though challenging, especially in terms of data quality. In this study, we explored the diagnostic performance of edited 2HG spectroscopy in a clinical setting.

Methods: We prospectively examined 13 patients (8 females, 48.6±14 years of age) with possible low-grade gliomas on a 3T Siemens MRI system at the Pitié-Salpêtrière hospital. The spectroscopic volume of interest was positioned in the lesion by using a 3D FLAIR image. MR spectra were acquired using a Mescher–Garwood point-resolved spectroscopy (MEGA-PRESS) sequence and analyzed with LCModel. Automated immunohistochemical analysis (IHC) and Sanger sequencing results on surgical samples were used as gold standard and were available for 11 out of 13 patients.

Results: 2HG was detected in 6 out of 9 IDH-mutant gliomas (Fig. 1), resulting in 67% sensitivity and 40% negative predictive value. 2HG was not measured in the two IDH-wild type glioblastomas, confirming the 100% specificity and positive predictive value of MEGA-PRESS in the prediction of IDH-mutation. 2 patients had IDH1 mutations other than R132H, and therefore were not detected by IHC analysis, while they both showed 2HG resonance (Fig. 2).

Figure 1. This table summarize clinical details of the subjects, results of 2HG MRS and final histological diagnosis.
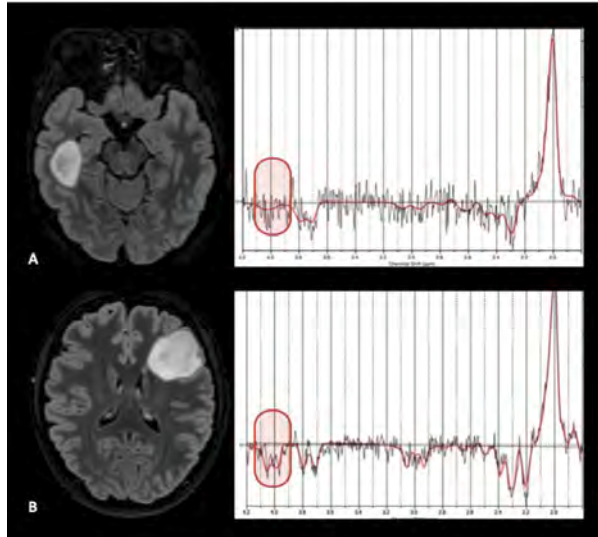
Figure 2. 3D FLAIR in axial plane and their corresponding edited MRS spectra of the two gliomas with minor IDH mutations. (A): patient n. 10 and (B) patient n. 2 of the Figure 1

Conclusion: Our preliminary results confirm the reliability of this edited MRS in the non-invasive detection of IDH-mutation and encourages its integration into clinical workflows.

Disclosure: Nothing to disclose.

EPR-064

Irreversible neurotoxicity after CAR-T cells treatment

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Background and aims: Chimeric antigenic receptor T cells therapy was approved as 3rd line treatment of relapsing B-cell lymphoma but have side effects, such as neurotoxicity.

Methods: Here, we report a case of atypical neurotoxicity due to the injection of antiCD19 CAR-T cells.

Results: 74 years, male psychologist, with normal baseline neurological examination (except for a MOCA score of 27/30) and vascular leukopathy on brain MRI received an antiCD19 CART-cells infusion for relapsed diffuse B cell lymphoma. Initial adverse events were a cytokine release syndrome (CRS) grade 2 (day 0) and neurotoxicity (ICANS) grade 3–4 from day 3 with complete remission by day 9 after Tocilizumab and dexamethasone treatment. The brain MRI showed bilateral hyper signals with diffusion restriction that also resolved after treatment. However, a new neurological degradation occurs at day 21 as confusion with clinical-paraclinical discordance: no new brain MRI changes, while an inflammatory syndrome remained (CSF IL-6: 37, 4 pg/mL, CSF neopterin: 87.7 nmol/L, blood IL-6: 142 pg/ml). Any other alternative diagnostics (inflammatory, infectious …) have been eliminated. Conventional treatments (methylprednisone, anakinra) showed no improvement, the patient deceased three months later. Lastly, the CSF biomarkers: beta-1amyloid-42: 207pg/mL, tau: 974pg/mL and pTau: 130.1pg/mL and the left parieto-temporal hypo metabolism on the PET CT confirmed a pre-existent Alzheimer disease (AD) as suggested by the discreet initial cognitive impairment.
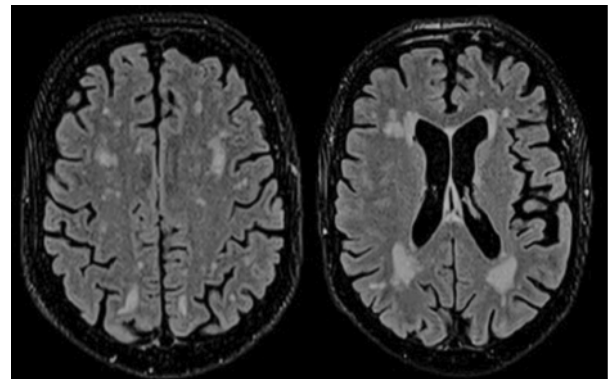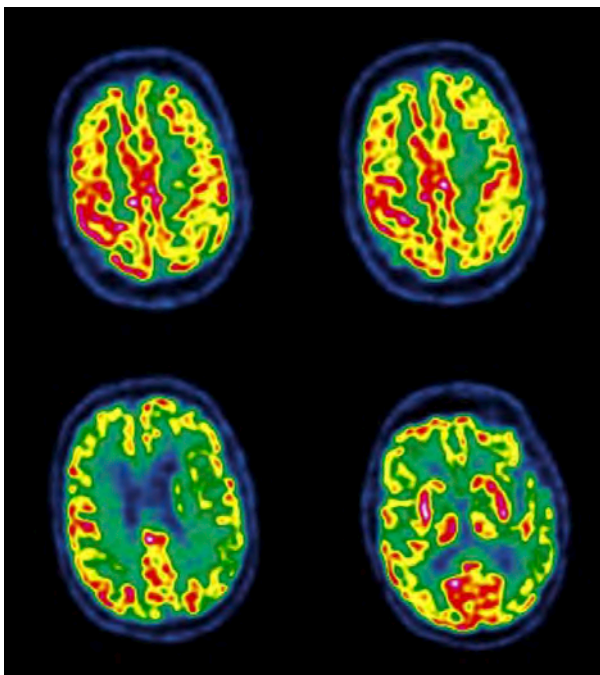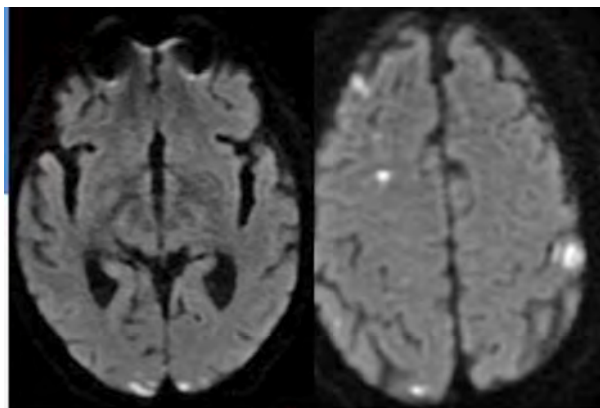
Conclusion: Our case brings a solid argument for an increased risk of severe and irreversible neurotoxicity of CAR-T in case of pre-existing neurodegenerative disease. That confirms the importance of a full pre-therapeutic neurologic assessment.

Disclosure: No conflict of interest.

EPR-065

Description of routine electroencephalogram features in the Alzheimer's disease continuum in Down syndrome

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Background and aims: Down syndrome (DS) is a genetically determined form of Alzheimer's disease (AD). AD is an independent risk factor for epilepsy, especially in DS. Late-onset myoclonic epilepsy in DS (LOMEDS) related to symptomatic AD has been described, but there are conflicting results in the literature concerning electroencephalogram (EEG) findings. We aimed to characterize the EEG findings in adults with DS across the AD continuum.

Methods: We conducted a cross-sectional study in adults with DS from January 2015 to December 2021. All participants were assessed by neurologists and neuropsychologists and classified into asymptomatic -aDS, prodromal -pAD- and dementia AD -dAD- patients. We also administered a structured questionnaire about epilepsy (including the age of onset, seizure semiology, and risk factors). We obtained a routine EEG using the international system 10/20 for electrode placement.

Results: We obtained 517 EEG recordings from 400 subjects (45.7% female), mean age 42.6 ± 11.1 years. Background activity (Hz) significantly decreased along the AD continuum and in those patients with epilepsy independent of the cognitive category. Interictal epileptiform discharges (IED) increased along the AD continuum (7.8% in aDS, 23.9% in pAD, and 30.6% in dAD). In those patients with LOMEDS, we found IED in 47.5% of patients and generalized spike and polyspike-waves in 37.5%.
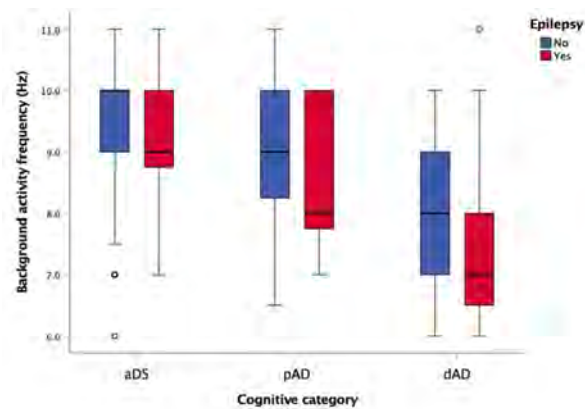
Boxplot representing background activity frequency (in Hertz) according to cognitive category and epilepsy diagnosis. aDS: Down syndrome without cognitive impairment, pAD: prodromal Alzheimer's disease in Down syndrome, dAD: dementia Alzheimer's disease
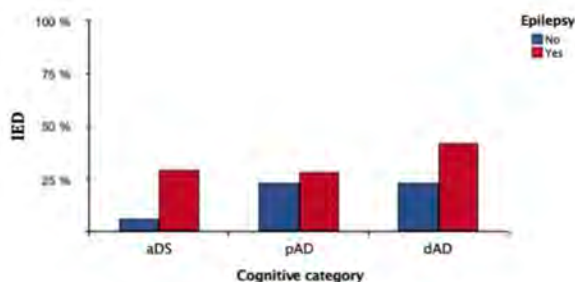
Bar graph representing percentage of interictal epileptiform discharges according to cognitive category and epilepsy diagnosis. aDS: Down syndrome without cognitive impairment, pAD: prodromal Alzheimer's disease in Down syndrome, dAD: dementia Alzheimer's

Conclusion: A significant percentage of subjects with DS show anomalies in EEG, including epileptiform discharges, especially in symptomatic AD patients and those with LOMEDS. However, the diagnostic performance of routine EEG is reduced and the acquisition of longer recordings including sleep could be of interest.

Disclosure: The authors declare that there are no competing interests.

EPR-066

Guiding differentiation of non-acute MOGAD from AQP4-NMOSD and RRMS using clinical and MRI measures

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Background and aims: MRI and clinical features of myelin-oligodendrocyte-glycoprotein-antibody-associated disease (MOGAD) may overlap with those of aquaporin4-antibody-positive neuromyelitis optica spectrum disorder (AQP4-NMOSD) and relapsing remitting multiple sclerosis

(RRMS) posing diagnostic challenges, especially in non-acute phases.

Methods: Data from 16 MAGNIMS centres were retrospectively collected. Inclusion criteria were: diagnosis of MOGAD/AQP4-NMOSD/RRMS, MRI ≥6 months from relapse, EDSS on the day of MRI. Brain white matter lesions, cortical and cord lesions were identified. Random-forest models were constructed to classify patients; a leave one out cross-validation procedure assessed the performance of the models.

Results: 1162 MOGAD (99F, mean age: 41 [±14] years, median EDSS: 2 [0-7.5]), 162 AQP4-NMOSD (132F, age: 51 [±14] years, EDSS: 3.5 [0-8]), 189 RRMS (132F, age: 40 [±10] years, EDSS: 2 [0-8]) patients and 152 healthy controls (91F) were studied. In young patients (<34 years), with low disability (EDSS<3), the absence of Dawson's fingers, temporal lobe lesions and longitudinally extensive transverse myelitis (LETM) favoured MOGAD over the other two diseases (accuracy/sensitivity/specificity: 76%/81%/84%, p<0.001) (Figure 1). In these non-acute patients, a number of brain lesions <6 predicted MOGAD versus RRMS (accuracy/sensitivity/specificity: 83%/82%/83%, p<0.001). An EDSS <3 and the absence of LETM predicted MOGAD versus AQP4-NMOSD (accuracy/sensitivity/specificity: 76%/89%/62%, p<0.001).
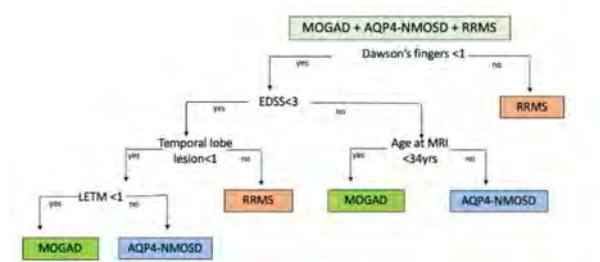
Visual representation of the best set of discriminators between myelin oligodendrocyte glycoprotein antibody associated disease (MOGAD), aquaporin-4-antibody-positive neuromyelitis optica spectrum disorder (AQP4-NMOSD) and relapsing-remitting MS (RRMS).

Conclusion: Non-acute MOGAD patients showed distinctive clinical and MRI features when compared to AQP4-NMOSD and RRMS. A careful inspection of the morphology of lesions with clinical information, can guide further analyses towards diagnosis of MOGAD.

Disclosure: R. Cortese was awarded a MAGNIMS-ECTRIMS fellowship in 2019.

MS and related disorders 2

EPR-067

Personalized extended interval dosing of natalizumab up to 9 weeks in relapsing remitting multiple sclerosis (NEXT-MS)

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Background and aims: Natalizumab is an effective therapy for relapsing remitting multiple sclerosis (RRMS). As natalizumab serum concentrations vary widely between patients, extended interval dosing (EID) based on individual trough concentrations could be efficacious. Our aim was to study feasibility and to validate the efficacy of personalized EID based on natalizumab trough concentrations.

Methods: In this ongoing investigator-initiated multicenter prospective study (NEXT-MS), adult patients with RRMS are included in three groups: standard interval dosing (SID) of four weeks, personalized EID with an aim trough concentration of 10 µg/mL (EID10), and a subgroup of personalized EID with an aim of 5 µg/mL (EID5). The primary outcome is MRI activity (new/enlarging T2 lesions). Planned follow-up (FU) is two years with annual brain MRI scans and clinical monitoring.

Results: In the interim analysis of October 2021, 295 participants were included. Median FU was 45.1 weeks (IQR 28.0 to 59.3). In the SID group (n=51), one participant (6.7%) had one new T2 hyperintense lesion during FU. In the EID10 group (n=190), median treatment interval was 5 weeks (IQR 5–6). One participant (3.7%) had one new T2 hyperintense lesion during FU. In the EID5 subgroup (n=54), median treatment interval was 6 weeks (IQR 5–7). There were no signs of radiological disease activity during FU. None of the participants experienced a relapse.

Natalizumab concentrations in the personalized EID groups. Number of infusions after start of EID is displayed on the x-axis. The y-axis indicates natalizumab trough concentrations in µg/mL.

Conclusion: MS disease activity is adequately controlled with personalized EID of natalizumab. A lower aim of natalizumab trough concentration (5 µg/mL) is likely sufficient as well, enabling 78% of patients to extend the natalizumab treatment interval ≥6 weeks.

Disclosure: On behalf of the NEXT-MS study group; T. Rispens received funding for research from Genmab; B.M.J. Uitdehaag and J. Killestein report personal fees from Genzyme, Biogen Idec, Teva Pharmaceutical Industries, Merck Serono, Roche, Novartis.

Natalizumab treatment intervals in the personalized EID groups. Percentage of participants in each study group (EID5 in blue; EID10 in red) is displayed on the x-axis. The y-axis indicates the natalizumab

EPR-068

Integrating Expanded Disability Status Scale with ambulation, visual and cognitive tests, improves dosability assessment

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Background and aims: The Expanded Disability Status Scale (EDSS) is usually calculated through a neurological examination with self-reported performance. This may lead to incorrect assessment of several Functional Scores (FS), prominently visual and cerebral FSs, and ambulation. Aim of our study was to estimate the difference between EDSS scores obtained during routine visits, or after specific visual, cognitive and ambulation tests.

Methods: We enrolled 330 Multiple Sclerosis (MS) patients that underwent a routine visit with EDSS calculation. Then, patients underwent a visual evaluation using the Landolt's C-target digital eye optotype table, ambulation evaluation with an odometer, and neurocognitive assessment with the Brief International Cognitive assessment for MS (BICAMS). We calculated a new integrated EDSS (iEDSS) using the refined values of the FS. EDSS and iEDSS were compared in terms of absolute values and in terms of change caused by the addition of recalculated FSs.

Results: FSs were all significantly higher after additional evaluations: ambulation score (+0.909, CI 0.732, 1.086; $p<0.001$), visual FS (+1.174; I.C. +1.034, +1.314: $p<0.001$), cerebral FS (+0.658; CI 0.558, 0.755; $p<0.001$). Mean iEDSS was higher than EDSS (+0.658; CI +0.558, +0.755, $p<0.001$). Addition of visual acuity tests worsened the EDSS score in 31% of cases, cognitive tests in 10%, ambulation measurement in 35%, all three measurements in 59% of cases.
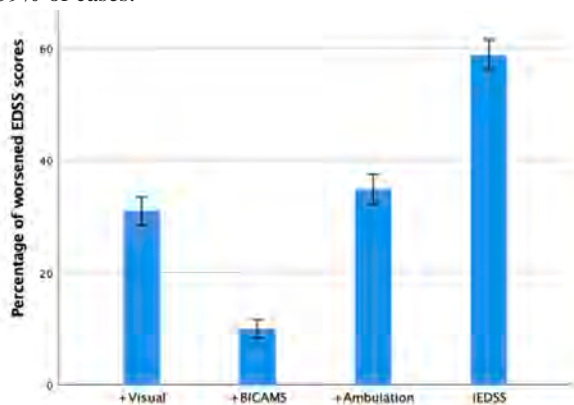
Percentage of worsened EDSS scores

Conclusion: Accurate measurement of visual, cognitive and ambulation results in a better calculated EDSS in almost two-thirds of cases. This should lead to a more thorough evaluation of critical patients, i.e. patients in the transition or progressive phase.

EPR-069

Cortical lesion load at the diagnosis predict conversion to secondary progressive multiple sclerosis

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Background and aims: Cortical pathology is a major driver of multiple sclerosis (MS) disability accumulation, being evident since early phases. We investigated the predictive value of cortical lesions (CLs) at the diagnosis on onset of secondary progressive MS (SPMS) and long-term disability accumulation.

Methods: We evaluated 199 relapsing-remitting MS (RRMS) patients. All patients underwent at the diagnosis and after two years (T2) a 1.5T MRI, inclusive of cortical lesion number (CLn) assessment with Double Inversion Recovery sequences, and regular clinical follow-up, including assessment of Expanded Disability Status Scale (EDSS) and conversion to SPMS.

Results: After a mean follow-up of 17.0 ± 3.2 years, 39 (19.6%) patients had a diagnosis of SPMS, 54 (27.1%) and 28 (14.0%) reached an EDSS ≥4.0 or ≥6.0, respectively. Patients with SPMS had increased baseline CLn (6.28 ± 3.7 vs 1.2 ± 2.3, p<0.001), CL volume (657.7 ± 404.2 vs 114.7 ± 236.5, p<0.001) and new CLn at T2 (2.18 ± 1.79 vs 0.21 ± 0.7, p<0.001). Cox Regression confirmed that a higher CLn (>3, HR 16.15 [CI 4.36-59.85], p<0.001, Figure 1), and presence of spinal cord lesions (HR 2.63 [CI 1.19-5.83], p=0.0171) were significantly associated with SPMS conversion. Accumulation of new CLs in the first two years predicted earlier conversion to SPMS (HR 1.35 [CI 1.13-1.16], p=0.001), as well as the earlier reachment of EDSS≥4 (HR 1.28 [CI 1.09-1.51], p=0.002) and EDSS≥6 (HR 1.39 [CI 1.12-1.73], p=0.003). ROC analysis estimated optimal cut-off of 3 CLs according to risk of developing SPMS.
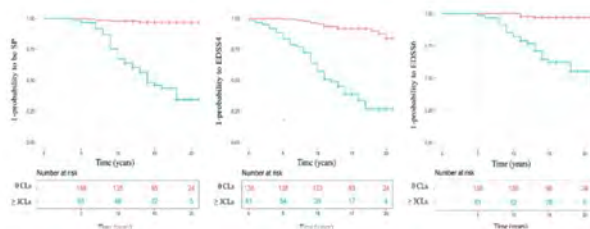
Patients with 3 or more CLs at the time of diagnosis had a significantly increased risk of entering in MS progressive phase and developing significant disability

Conclusion: The early assessment of focal cortical damage is a prognostic marker of developing SPMS and disability accumulation, with implications for clinical practice.

Disclosure: All authors: no disclosures relevant to the manuscript.

EPR-070

REMODEL I/II Trials: Efficacy, Safety, and Tolerability of Remibrutinib in Patients With Relapsing Multiple Sclerosis

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Background and aims: Inhibition of Bruton's Tyrosine Kinase (BTK), a cytoplasmic tyrosine kinase and member of the TEC kinase family, results in reduced activation of B cells and innate immune cells. This offers an alternative mechanism to modulate immune regulatory networks and related neuroinflammation via inhibiting B cells and myeloid cells. Remibrutinib is a potent, highly selective, covalent BTK inhibitor with a short plasma half-life, and a promising pharmacological and safety profile. Here, we summarise the design of the REMODEL I/II Phase 3 trials, which aim to evaluate the efficacy, safety, and tolerability of remibrutinib versus teriflunomide in patients with relapsing multiple sclerosis (RMS).

Methods: REMODEL I/II are identical randomised, double-blind, double-dummy, active comparator-controlled, parallel-group, event-driven, multicentre studies. Patients aged 18–55 years having at least one/two relapses within the previous one/two years, or one active Gadoliniumenhancing lesion in the 12 months prior to screening, with an EDSS of 0.0–5.5 will be enrolled. The studies consist of an initial double-blind core part (Adaptive design, up to 30 months) followed by an open-label extension (up to 5 years). The primary endpoint is annualised relapse rate. Key secondary/exploratory endpoints are listed in the Table 1.

Primary endpoint	ARR of confirmed relapses	
Key secondary endpoints	1.	Time to 3mCDP on EDSS, based on the pooled data of the two studies
	2.	Time to 6mCDP on EDSS, based on the pooled data of the two studies
	3.	Number of new or enlarging T2 lesions on MRI per year (annualised T2 lesion rate), based on the MRI cohort data
	4.	Total number of Gd+ T1 lesion per MRI scan, based on the MRI cohort data
	5.	NfL concentration in serum
	6.	Percentage of participants with NEDA-3, as assessed by absence of confirmed MS relapses, 6mCDP and new/enlarging T2 lesions on MRI, based on the pooled MRI cohort data of the two studies
Key exploratory endpoint	1.	Annualised rate of BVL, based on percentage brain volume change from baseline
	2.	Change from baseline in cortical grey matter volume, hemispheric white matter volume and thalamus volume
	3.	Slowly expanding lesions in MRI

3mCDP, 3-month confirmed disability progression; 6mCDP, 6-month CDP; ARR, annualised relapse rate; BVL, brain volume loss; EDSS, Expanded Disability Status Scale; Gd+, gadolinium-enhancing; MS, multiple sclerosis; MRI, magnetic resonance imaging; NEDA, no evidence of disease activity; NfL, neurofilament light chain.

Table 1: Phase 3 REMODEL I/II study endpoints

Results: Both studies are currently recruiting participants (n=800/study). A planned futility interim analysis will be based on pooled 6-month MRI data (new/newly enlarging T2 lesions) from a subset of 200 participants.

Conclusion: The REMODEL I/II studies will investigate the efficacy, safety, and tolerability of remibrutinib versus teriflunomide to support regulatory approval worldwide as a potential new oral treatment for patients with this disabling disease.

Disclosure: The study was supported by Novartis Pharma AG, Switzerland. The detailed author disclosures will be presented in the subsequent presentation.

EPR-071
Abstract withdrawn

EPR-072
Autoimmune Screening Panel in Patients with Multiple Sclerosis – A Vienna MS Database Study

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Background and aims: Autoimmune screening panel (ASP) is routinely ordered as a part of diagnostic work-up in people with suspected multiple sclerosis (MS). However, data on prevalence and significance of ASP seropositivity in MS is scarce.

Methods: In this retrospective study, we investigated patients who were diagnosed with MS (pwMS) between 2014 and 2021 and had a blood sample drawn for ASP. Autoantibody titers were defined as either negative, or mildly ($\leq$1:160), moderately ($\leq$1:640) and strongly ($\geq$ 1:1280) positive.

Results: We analyzed 212 pwMS (median age 29 [IQR 25–36] years, 67.0% female). Ten (4.7%) patients had red flags for presence of systemic autoimmune disease (joint pain [n=4], dermatitis [n=3], sicca syndrome, bronchial asthma/rheumatic fever in childhood [n=1, each]). Antinuclear antibodies (ANA) were positive in 24/210 (11.4%) with 18 (8.6%), 5 (2.4%), and 1 (0.5%) having mildly, moderately, and strongly positive ANA titers, respectively. Positive autoantibodies were found as follows: anti-Ro (5/211; 2.4%), IgM against cardiolipin (4/205; 2.0%), anti-centromere B (2/211; 0.9%), anti-dsDNA (1/208; 0.5%) and anti-La (1/211; 0.5%). Antibodies against smooth muscles were mildly positive in 11/166 (6.6%) patients. None of pwMS was positive for other autoantibodies (anti-SCL70, anti-SM, anti-u1RNP, anti-Jo1, c-ANCA, p-ANCA). Further evaluation following positive results led to diagnosis of rheumatoid arthritis (n=2) and Sjögren's syndrome (n=1), all of them presenting with red flags (ASP PPV 8.8%, NPV 96.1%).

Conclusion: Rate of ASP seropositivity in pwMS is low and within the range expected in the general population. Performance of ASP without clinical suspicion of systemic autoimmune disease seems unwarranted.

Disclosure: Nothing to disclose.

EPR-073

Humoral and cellular immunity in convalescent and vaccinated COVID-19 people with multiple sclerosis: effects of DMTs

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Background and aims: To determine anti-SARS-Cov2 antibodies and T-cell immunity in convalescent people with multiple sclerosis (pwMS) and/or pwMS vaccinated against Covid-19, depending on the disease modifying therapy, and in comparison to healthy controls (HC).

Methods: 75 participants were enrolled: Group 1–29 (38.7%) COVID-19 convalescent participants; Group 2–4 (45.3%) COVID-19 vaccinated; Group 3–12 (16.0%) COVID-19 convalescent participants who were later vaccinated against COVID-19. Cellular immunity was evaluated by determination of number of CD4+ and CD8+ cells secreting TNFα, IFNγ, and IL2 after stimulation with SARS-CoV-2 peptides.
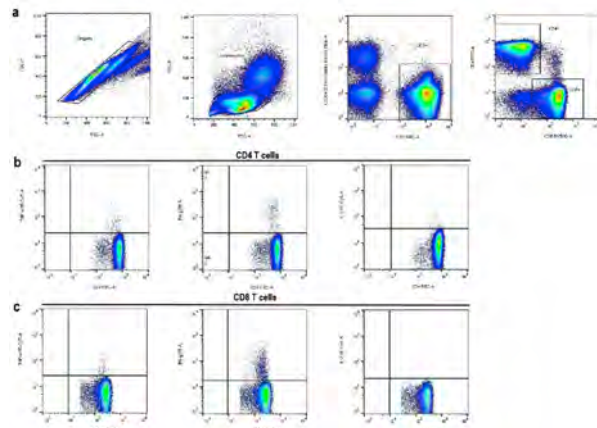
Gating strategy to detect SARS-CoV-2 reactive CD4+ and CD8+ T cells after in vitro stimulation for 8 hours with surface glycoprotein, matrix and nucleoprotein overlapping peptide pools. Representative gating of a single live CD4 and CD8 T cells.

Results: pwMS treated with ocrelizumab were less likely to develop humoral immunity after COVID-19 recovery or vaccination. No difference was observed in the cellular immunity in all studied parameters between pwMS treated with ocrelizumab compared to HC or pwMS who were treatment naïve or on first line therapies. These findings were consistent in convalescent, vaccinated, and convalescent+vaccinated participants. COVID-19 vaccinated convalescent pwMS on ocrelizumab compared to COVID-19 convalescent HC who were vaccinated did not show statistically difference in the rate of seroconversion nor titers of SARS-CoV-2 antibodies.
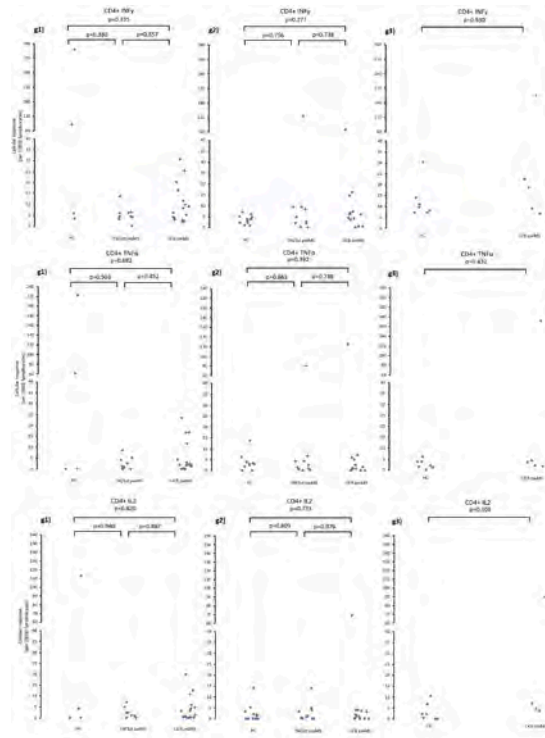
Number of CD4+ TNFα, IFNγ and IL2 cells in three groups of participants.
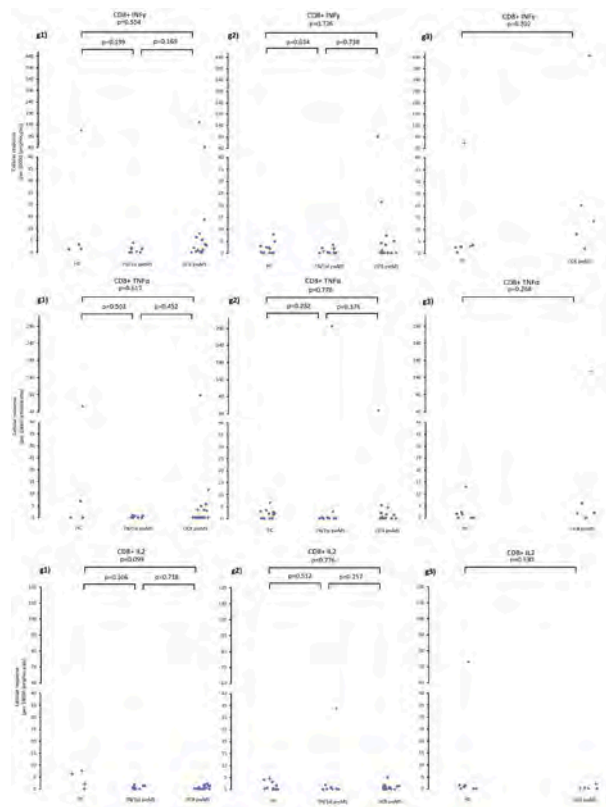
Number of CD8+ TNFα, IFNγ and IL2 cells in three groups of participants.

Conclusion: Presence of cellular immunity in pwMS on B-cell depleting therapies is reassuring, as at least partial protection from more severe COVID-19 outcomes can be expected.

Disclosure: Participated as a clinical investigator and/or received consultation and/or speaker fees from: Biogen, Sanofi Genzyme, Merck, Bayer, Novartis, Pliva/Teva, Roche, Alvogen, Actelion, Alexion Pharmaceuticals, TG Pharmaceuticals.

EPR-074

Structural Brain Changes Associated with Fatigue in People with Multiple Sclerosis

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Background and aims: Fatigue is a perceived physical and/or cognitive exhaustion, which occurs in up to 95% of people with multiple sclerosis (pwMS). Previous studies suggest an association between fatigue and MS-related changes in brain structure. The aim of the present study was therefore to investigate potential macro-/microstructural MRI-correlates of fatigue in pwMS.

Methods: Clinical, neuropsychological and MRI-data were collected from 90 pwMS (56% female; mean age=39+/-11 years; EDSS median=1.0 (IQR=2.8)). Fatigue was measured using the Fatigue Scale for Motor and Cognitive Functions, providing a total, cognitive, and motor fatigue score. Global and subcortical brain-volumes, total lesion load and lesion patterns associated with fatigue using "lesion probability mapping" were explored. Fractional anisotropy (FA) of white matter tracts was assessed.

Results: The strongest correlation was found between fatigue and the caudate nucleus volume (r=-0.36). Total lesion load did not correlate with fatigue, but lesions in the right anterior thalamic radiation were associated with cognitive fatigue (p<0.05). Furthermore, fatigue was negatively associated with FA in the right anterior thalamic radiation (r=-0.23) and the right and left corticospinal tracts (right: r=-0.24; left: r=-0.25). A final hierarchical regression analysis showed that the caudate nucleus volume was a significant predictor of cognitive (β=-0.19) and motor fatigue (β=-0.22), independent from demographics, neuropsychological, clinical and MRI-(brain-volume, lesion load, FA) data.

Conclusion: Our findings highlight the relevance of the caudate nucleus volume for fatigue. In addition, focal lesions in fronto-thalamic white matter tracts were associated with cognitive-fatigue. Regarding microstructural MRI-correlates, initial analyses reveal associations between fatigue and FA in cortico-striato-thalamo-cortical tracts.

Disclosure: Nothing to disclose.

EPR-075

Safety/efficacy of evobrutinib, a Bruton's tyrosine kinase inhibitor, 2.5 years into Phase II MS open-label extension

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Background and aims: Evobrutinib, a Bruton's tyrosine kinase inhibitor, was well tolerated and effective in a double-blind, randomised Phase II trial in patients with relapsing multiple sclerosis (pwRMS; NCT02975349).
Objective: report evobrutinib safety and efficacy data 2.5 years into an open-label extension (OLE).
Methods: In the 48-week (W) double-blind period (DBP), pwRMS (n=267) received placebo (switched to evobrutinib 25mg once-daily, W24), evobrutinib 25mg once-daily, 75mg once-daily, or 75mg twice-daily, or open-label dimethyl fumarate (DMF; 240mg twice-daily). At W48 patients could enter the OLE (DMF: 4–8W washout); evobrutinib 75mg once-daily (median ~48W) then 75mg twice-daily. We report the latest available OLE data.
Results: Of 267 DBP patients, 213 (80%) entered the OLE; 164 (61%) completed ≥132W OLE treatment. Treatment-emergent adverse events (TEAEs) were reported by 165/213 patients (77.5%); 59 (27.7%) had a treatment-related TEAE (six were serious; Table). Severe/opportunistic infections (≥Grade 3) were reported by 9/213 patients (4.2%);three (not treatment related; Covid pneumonia [n=2]) were fatal. Most patients had normal IgG (91%), IgA (88%) and IgM (82%) levels (OLE W120). Mean CD19+ B cells levels were 0.218×10^6cells/mL (OLE baseline) and 0.122×10^6cells/mL (OLE W96). ALT/AST elevations only occurred in patients previously receiving DMF/evobrutinib 25mg, and within 12W of OLE initiation. Amylase/lipase increases occurred in 6 (2.8%)/24 (11.3%) patients, without clinical signs and symptoms. ARR, for patients receiving 75mg twice-daily in the DBP, was 0.12 (95%CI 0.07–0.20 [all available OLE data]).

Table: Overall TEAEs during OLE

Conclusion: Evobrutinib safety and efficacy data over 2.5 years shows acceptable tolerability, no new safety signals and maintained efficacy in pwRMS.
Disclosure: Study was sponsored by EMD Serono Research & Development Institute, Inc., Billerica, MA, USA, an affiliate of Merck KGaA (CrossRef Funder ID: 10.13039/100004755), detailed author disclosures will be included in the presentation.

Muscle and neuromuscular junction disorder 1

EPR-076

Clinical characteristics and long-term outcome of patients with idiopathic inflammatory myopathies

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Background and aims: Identify risk factors associated to poor long-term outcome in idiopathic inflammatory myopathies in our area.

Methods: We conducted a single-centre retrospective study of patients diagnosed of idiopathic myositis after muscle biopsy between January 2011 and August 2021. We analysed demographic (gender, age, years of follow-up) and clinical variables (serum creatine kinase [CK] elevation, clinical phenotype, comorbid connective tissue disease or cancer, and final diagnosis). We analysed the relationship between clinical variables and death.

Results: 37 patients met the inclusion criteria. 24 (64.9%) were female, aged (standard deviation [SD]) 64.5 (14.4) years old. There were 9 patients with dermatomyositis, 3 inclusion body myositis, 4 necrotizing myositis, 12 overlap syndromes, and 9 polymyositis. 19 (51.3%) patients presented 10 different myositis specific autoantibodies in serum. As shown in Table 1, 10 patients had died at the time we conducted this study, and they did so 2.7 (SD, 2.4) years after diagnosis. Serum CK elevation and myocardiopathy were associated to the probability of death (p<0.05). Interstitial lung disease (ILD) was associated to the probability of death, in a non-significant manner (p=0.054). Presence of myocardiopathy was associated with a higher risk of death (relative risk, 3.375; 95% CI, 1.127-10.103), and so was presence of ILD (relative risk, 2.314; 95% CI, 1.025–5.223).

	Alive (n=27)	Deceased (n=10)	p value
Gender (%, female)	17 (63%)	7 (70%)	0.690
Age (SD)	63,3 (15.0)	67,6 (13.0)	0.391
Years of follow-up (SD)	4,6 (1.9)	2,7 (2.4)	0.266
Serum CK elevation	**8,4 (7.9)**	**26,4 (55.1)**	**0.004**
Clinical Phenotype			
Degree of muscle affection	6 absent / mild	4 absent / mild	0.506
	5 moderate	2 moderate	
	16 severe	4 severe	
Skin (%)	11 (40.7%)	5 (50%)	0.255
Interstitial lung disease (%)	7 (25.9%)	6 (60%)	0.054
Myocardiopathy (%)	**4 (14.8%)**	**5 (50%)**	**0.027**
Connective tissue disease (%)	6 (22.2%)	1 (10%)	0.399
Cancer (%)	3 (11.1%)	3 (30%)	0.166
Final diagnosis (%)			
Dermatomyositis	7 (25.9%)	2 (20%)	0.548
Inclusion body myositis	2 (7.4%)	1 (10%)	
Necrotizing myopathy	4 (14.8%)	0	
Overlap syndrome	7 (25.9%)	5 (50%)	
Polymyositis	7 (25.9%)	2 (20%)	

Annotation.
- *Serum CK elevation:* multiplier for the upper limit of normality for CK levels, adjusted by gender and ethnicity. European Federation of Neurological Sciences upper limits of normality: Black females: 414. Non-black females: 217. Black males: 801. Non-black males: 336.
- *Degrees of muscle affection.* Mild: myalgias, cramps or undue fatigue. Moderate: weakness of either shoulder or pelvic girdle. Severe: tetraparesis.

Conclusion: Idiopathic inflammatory myopathies present high morbidity and mortality, affecting mostly women in their fifties and sixties. The elevation of CK, and the presence of cardiac or pulmonary affection, increase the risk of death due to myositis.

Disclosure: There are no conflicts of interest regarding this research.

EPR-077

Zilucoplan prevented functional impairment induced by AChR+ myasthenia gravis patient sera in an in vitro NMJ model

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Background and aims: Myasthenia gravis (MG) is a rare autoimmune disease driven by autoantibodies targeting components of the neuromuscular junction (NMJ). Most autoantibodies target the nicotinic acetylcholine receptor (AChR), impairing neurotransmission through three mechanisms: AChR blockade, antigenic modulation, and complement activation. To dissect the pathogenic mechanisms of autoantibodies in MG, an in vitro NMJ model was established. This platform was used to examine the impact of anti-AChR autoantibodies on complement activation and neurotransmission, and examine the effect of zilucoplan, a peptide inhibitor of complement C5 under clinical development for AChR-seropositive (AChR+) generalised MG.

Methods: A microfluidic platform (NeuroMuscleTM) was employed to connect 3D co-cultures of neurospheres derived from human induced pluripotent cells and primary human skeletal fibres. Functional connectivity was assessed with glutamate stimulation of neurospheres and subsequent calcium transients in GCaMP6-transduced muscle fibres. In vitro NMJs were incubated with MG patient sera in the absence or presence of zilucoplan, followed by evaluation of C5a/sC5b9 products, C5b9 deposition, and functionality.

Results: AChR antagonists confirmed functional connections of NMJ co-cultures developed in the NeuroMuscleTM platform. Sera from AChR+ MG patients, as compared to healthy controls, induced C5b9 deposition, a 5–6-fold increase in complement C5 split products, and reduced calcium transients from $100.0\pm3.1\%$ to $18.8\pm3.0\%$. Furthermore, treatment with zilucoplan prevented complement activation and NMJ functional impairment.

Conclusion: These data provide a mechanistic rationale for the clinical response observed in AChR+ gMG patients treated with C5 inhibitors and highlight how an in vitro human NMJ platform may functionally dissect pathogenic autoantibodies and support drug discovery.

Disclosure: BS, JW, CS, DV: current UCB Pharma employees with equity ownership. MW, JY: employees of UCB Pharma with no disclosures. MG, SMG, BP, DM: employees of Ananda Devices. MM: CEO, founder and shareholder of Ananda Devices.

EPR-078

Effectiveness of early treatment initiation with corticosteroids in Ocular Myasthenia Gravis

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Background and aims: To present the outcome of patients with Ocular Myasthenia Gravis (OMG) managed in our center.

Methods: A total of 37 patients [median age 58.0 years, 11 females] with OMG were subdivided into 16 patients who had received early and high doses of corticosteroids (subgroup A) and 21 patients initially treated conservatively and after >6 months switched to the intense approach (subgroup B) (table 1). Classical scales for quantitative assessment of symptoms were employed to define the degree of deterioration and the efficacy of treatment.

Table 1. Clinical and laboratory features in total and two subgroups of ocular MG patients

	Total	Subgroup A	Subgroup B	P-value#
No of cases	37	16	21	
Current age,yrs*	58 (24.5)	53.5 (25.5)	60 (19.5)	0.914
Age at onset, yrs*	46 (26)	50 (32.5)	46 (16)	0.416
Female sex, no (%)	11 (29.7)	5 (26.3)	6 (25)	0.862
Duration from diagnosis, yrs*	4.0 (10.25)	3.0 (2.9)	8.0 (12.5)	**0.014**
Duration of our monitoring, yrs*	3 (4.5)	3 (2.9)	4 (5.5)	0.976
Auto-antibodies, no (%)AChR	24 (64.9)	11 (68.8)	13 (61.9)	0.736
MuSK	3 (8.1)	1 (6.3)	2 (9.5)	
AChR+MuSK	1 (2.7)	0 (0)	1 (4.8)	
Seronegative	9 (24.3)	4 (25)	5 (23.8)	
Thymus pathology, no (%)	7 (18.9)	2 (12.5)	5 (23.8)	0.668
Hyperplasia	4 (10.8)	1 (6.3)	3 (14.3)	
Thymoma	3 (8.1)	1 (6.3)	2 (9.5)	

*values expressed as median (interquartile range); #comparison between subgroups with different management approaches; no= number and (%) percentage of patients in the specified groups or otherwise indicated

Table 1

Results: In subgroup A, only 7.7% of patients with OMG and a minimum 2-year follow-up experienced generalization. On the contrary, in subgroup B the disease became generalized in 75.0%, a percentage close to that expected by the natural course of MG in the Caucasian population. Postintervention Status was significantly better in subgroup A (table 2). Quantitative MG score at the worst point was significantly higher in subgroup B [median QMG 9 vs 4 (p<0.001)]. Three double seronegative OMG patients in subgroup B who progressed to generalized MG developed treatment refractoriness, as opposed to subgroup A. Persistent ocular symptoms were found in 18.8% of patients in subgroup A and 52.4% in subgroup B (p=0.037). None of the patients suffered a serious side effects related to steroids leading to treatment discontinuation (table 2).

Table 2. Treatment data, disease course and clinical outcome of Ocular MG patients

	Total, no 37	Subgroup A, no 16	Subgroup B, no 21	P-value*
Thymectomy, , no of pts(%):	9 (24.3)	2 (12.5)	7 (33.3)	0.143
Immunosuppressants, no of pts(%): none	0	0	0	0.03
steroids alone	21 (56.8)	13 (81.3)	8 (38.1)	
1 or 2 more drugs	15 (40.5)	3 (18.8)	12 (57.1)	
3 or more drugs	1 (2.7)	0	1 (4.8)	
Relapses # no of pts (%)	9 (24.3)	2 (12.5)	7 (33.3)	0.143
no of episodes	23	6	17	0.162
Postintervention Status, no of pts (%): CSR	1 (2.7)	0	1 (4.8)	**0.025**
PR	13 (35.1)	10 (62.5)	3 (14.3)	
MM1	7 (18.9)	44 (25)	3 (14.3)	
MM2	0	0	0	
MM3	8 (21.6)	1 (6.3)	7 (33.3)	
Change in status, no of pts (%):ǂ				0.657
U	32 (86.5)	14 (87.5)	18 (85.7)	
W/E	5 (13.5)	2 (12.5)	3 (14.3)	
Refractory no of pts (%)	3	0	3	
Ocular → Generalized, ¥no of pts (%)	37 → 16 (43.2)	16 → 1 (6.3)	21 → 15 (71.4)	**0.000**
MG-QOL15 at recent visit#	4 (4)	3 (2)	4 (10)	0.137

* comparison between the subgroups; ¥ only ocular myasthenia cases with disease duration of at least two years were considered; # values expressed as median (interquartile range)

Table 2

Conclusion: Our suggested approach consisting of early and adequate immunotherapy in OMG patients significantly reduced the risk of generalization, allowed better control of generalized symptoms when present and resulted in less residual ocular symptoms.

Disclosure: Nothing to disclose.

EPR-079

Swallowing Function in Children with Later-Onset Spinal Muscular Atrophy Treated with Nusinersen: CHERISH-SHINE Results

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Background and aims: Swallowing and feeding issues commonly occur among individuals with later-onset spinal muscular atrophy (SMA). Tube feeding is often required among those with SMA Type II. Limited data are available on bulbar function among later-onset SMA patients treated with nusinersen.

Methods: CHERISH was a randomized, sham-procedure-controlled study for non-ambulatory participants most likely to develop SMA Type II/III. Participants were eligible to enroll in the ongoing SHINE open-label extension. Swallowing function was assessed in SHINE using the Parent Assessment of Swallowing Ability (PASA) questionnaire. Item-level PASA scores were examined for the overall cohort (n=119) and by age at first nusinersen dose.

Results: As of the 27th August 2019 datacut the PASA was administered a median of 4 times over 1 year starting at a median of 2.7 years after treatment initiation. At the last PASA assessment, median age was 8.0 (range:6.0–12.9) years with a median time on nusinersen of 3.7 years. For items on general feeding, drinking liquids, and eating solid foods, participants were consistently rated over time as never to rarely experiencing difficulties, with no notable differences by age at first nusinersen dose. On the parental assessment of swallowing concerns, parents generally and consistently disagreed with having such concerns. Three participants were reported to be tube fed on >=1 PASA assessments; of these participants, one was often, one was sometimes, and one was no longer tube fed at their last assessment.

Conclusion: All later-onset SMA participants treated with nusinersen maintained the ability to swallow at their last visit.

Disclosure: This study was sponsored by Biogen (Cambridge, MA, USA) .

EPR-080

Analysis of Juvenile Onset Pompe Disease patients included in the Spanish Pompe Registry

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Background and aims: Late Onset Pompe patients (LOPD) is the main phenotype on Pompe disease that start with symptoms from the age of two years to late in the adulthood, Because of the heterogeneity of the disease, it has been described the Juvenile Onset Pompe Disease (JOPD) subgroup, who become symptomatic between 2 and 18 years old.

Methods: We described the demographic and clinical features of all JOPD patients and their progression (using six-minute walking test -6MWT-, forced vital capacity -FVC- and Creatin Kinase -CK- values and comparing it with the other LOPD patients) registered at the Spanish Pompe Registry (SPR), with 121 patients registered in Spain.

Results: We identified 28 JOPD patients (18.8%) in the SPR, with 16 males (57%), median age of symptoms onset was 8.5 years. The most frequent mutation was c.32-13T>G in 19 patients (68%). HyperCKemia was the most common

reason for diagnosis in 17 (61%) patients. 19 patients (68%) developed muscle symptoms, being lower limbs weakness the most predominant (13). 9 (34.6%) developed respiratory symptoms, 2 (7%) of them before 18 years. All JOPD received Enzyme Replacement Therapy. JOPD patients showed significantly baseline higher CK values compared to LOPD (p<0.001) but tended to decline over time, without any significant difference of the progression of CVF and 6MWT (Mann-Whitney).
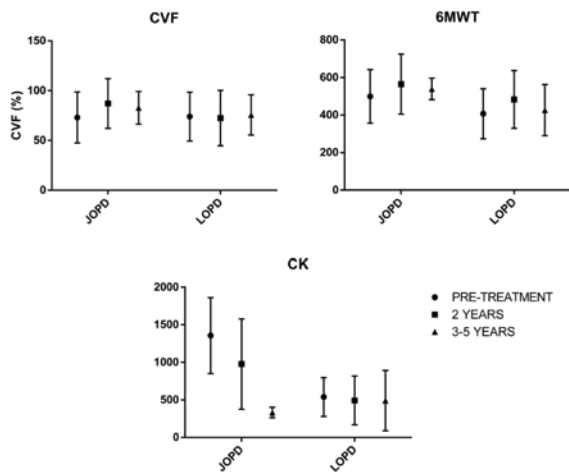
Conclusion: Most of the JOPD patients in the SPR were diagnosed because of hyperckemia, and lower limbs muscle weakness before 18 years old. We have not identified differences in the progression of the disease between JOPD patients and LOPD patients.

Disclosure: This study was sponsorized by Sanofi Genzyme.

EPR-081

Does small fiber neuropathy contribute to chronic muscle pain in patients with myotonic dystrophy?

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Background and aims: Chronic myalgia is common in myotonic dystrophies (DM), the pathophysiology is however unclear. We aim to investigate whether small fiber neuropathy contributes to chronic pain in DM patients.

Methods: We included DM1 and DM2 patients (18-65 years) with myalgia. Exclusion criteria were diabetes mellitus or polyneuropathy. Patients completed three pain questionnaires, neurological examination, nerve conduction study, quantitative sensory testing (QST) and skin biopsy. QST data were compared with 30 gender- and age-matched healthy controls.

Results: We recruited 32 DM2 and 21 DM1 patients. DM2 patients, in comparison to DM1, showed higher pain related disability (p=0.026), higher pain interference (p=0.012), described pain more often as radiating (78% vs 25%, p<0.001) and suffered more of chronic constant pain (38% vs 25%) rather than pain attacks as in DM1 (55% vs 25%). In QST, we found multiple differences between DM1 and DM2 and between DM and controls. DM2 patients were characterized by a loss in cold, warm, mechanical and vibration sensitivity, while DM1 patients showed signs of mechanical hyperalgesia (lower mechanical pain threshold, higher mechanical pain sensitivity). Both DM patient groups showed increased pressure pain sensitivity. IENFD was reduced in 63% of DM1 patients and in 50% of DM2. this correlated with age (p=0.050) but, interestingly, not with QST data.

Conclusion: This study shows the presence of loss in detection sensitivity and gain in pain sensitivity in patients with myotonic dystrophy, as well as reduced IENFD. Ongoing analyses will further examine how these abnormalities correlate with the severity and quality of pain.

Disclosure: This study received a grant by FöFoLe, LMU.

EPR-082

Blood Neurofilament light chain as potential biomarker of neurological involvement in Myotonic Dystrophy type 1

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Background and aims: Central Nervous System (CNS) involvement in Myotonic Dystrophy type 1 (DM1) encompasses intellectual disability, characteristic of congenital and infantile cases, and frontotemporal behavioural and cognitive changes frequently seen in adult-onset forms. Diagnostic biomarkers to assess either the severity of brain involvement or treatment response are still needed in DM1. Recently, blood neurofilament light chain (NfL) levels were recognized as a sensitive biomarker of disease severity and/or treatment response in distinct CNS disorders.

Methods: We conducted a pilot study on 40 DM1 patients and 22 age-matched controls to measure serum NfL using an ultrasensitive immunoassay (Simoa platform, Quanterix). Neuropsychological, neuroimaging, demographic and other DM1-related diagnostic parameters (MIRS, nCTG, disease form and duration) were also collected. For statistical analysis, we used the Mann-Whitney U Test to compare Nfl between controls and patients and the Spearman correlation to evaluate correlations between Nfl and other collected variables.

Results: 40 patients were enrolled, with a mean age of 47,7 (±10,8) years and a male majority (25/40, 62,5%). Their cognitive profile consisted of a mild to moderate frontotemporal impairment in line with previous studies. Mean serum NfL levels resulted significantly higher in DM1 (25,32 pg/ml, ±28,12) vs age-matched controls (6,2 pg/ml, ±0,48). In the DM1 group, Nfl levels positively correlated only with patients' age, while no correlations were found with cognitive, neuroimaging data, nor with other collected parameters.

Mean ± SEM CTR 6.235 ± 0.4809 N=22
Mean ± SEM of DM 25.32 ± 4.446 N=40
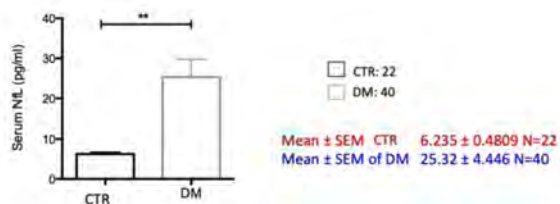
Conclusion: Results support a role for serum NfL as a potential biomarker of CNS damage in DM1. Studies on larger DM1 cohorts are needed to definitively address this issue.

Disclosure: This study was not sponsored. The authors report no conflict of interests.

EPR-083

Clinical score for early diagnosis of myotonic dystrophy type 2

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Background and aims: Myotonic dystrophy type 2 (DM2) is a rare, multisystemic, autosomal dominant disease with highly variable clinical presentation. DM2 is considered to be highly under-diagnosed. The aim of this study was to determine which symptoms, signs and diagnostic findings in patients referred to neurological outpatient units are the most indicative to arouse suspicion of DM2. We tried to make a useful and easy-to-administer clinical scoring system for early diagnosis of DM2 - DM2 Early Diagnosis Score (DM2-EDS).

Methods: 291 patients with a clinical suspicion of DM2 were included: 69 were genetically confirmed to have DM2 and 222 patients were DM2 negative. Relevant history, neurological, and para-clinical data were obtained from the electronic medical records.

Results: Following parameters appeared as significant predictors of DM2 diagnosis: cataracts (beta=0.410, p<0.001), myotonia on needle EMG (beta=0.298, p<0.001), hand tremor (beta=0.211, p=0.001), positive family history (beta=0.171, p=0.012), and calf hypertrophy (beta=0.120, p=0.043). In the final DM2-EDS, presence of these symptoms was associated with following values: cataracts 3.4, myotonia 2.5, tremor 1.7, family history 1.4, and calf hypertrophy 1.0. Cut-off value of 3.25 of maximum 10 points had sensitivity of 84% and specificity of 81% to diagnose DM2, while cut-off value of 4.6 points had sensitivity of 81% and specificity of 95% in early diagnosis of DM2.

Conclusion: Significant predictors of DM2 diagnosis in neurology outpatient unit were identified. We made an easy-to-administer DM2-EDS score for early diagnosis of DM2.

Disclosure: Authors have no conflict of interest to declare.

Neurogenetics, Neuroepidemiology, & Neurological manifestation of systemic diseases 1

EPR-084

Quality assurance for next-generation sequencing diagnostics of rare neurological disease in European Reference Network

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Background and aims: In the last decade, next-generation sequencing-based approaches have transformed genetic diagnostics in patients with rare neurological disorders (RND). However, there is a concurrently growing need to harmonize the technical, interpretative and reporting standards and to offer a quality assurance mechanism to institutions using these approaches. For this reason, the European Reference Network for Rare Neurological Diseases (ERN-RND), in collaboration with EMQN CIC, has established an external quality assessment scheme for NGS-based approaches in diagnostics for RNDs.

Methods: In 2021, a pilot run of the scheme was performed and DNA samples of three cases were sent out to 29 laboratories. The results were marked for genotyping, interpretation and clerical accuracy. In addition, we have analysed the differences in the selected genes, sequencing quality parameters, adherence to standards in variant interpretation and clinical guidance provision.

Results: Altogether, 25 ERN-RND laboratories returned the scheme reports. A majority of participants (56%) reported using exome sequencing, and virtual gene panels were commonly employed, albeit with highly variable gene content. Although the majority of participants returned a report with a correct molecular diagnosis, large variability in the data analysis, variant interpretation and reporting approaches was observed.

Conclusion: The initial experience of the scheme demonstrates a good overall quality of participating laboratories and widespread use of comprehensive genomic approaches to diagnose RND patients, but with a large variety in the data analysis, interpretation and reporting. These results present grounds for further harmonisation, development of guidelines and support further provision of external quality assessment in this field.

Disclosure: No disclosures are reported.

EPR-085

Vitamin B12 deficiency-related neurological manifestations: 5 years of experience in a Portuguese tertiary center

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Background and aims: Vitamin B12 (vitB12) plays a major role in cellular metabolism with an important influence on the nervous system. Almost 40% of the patients diagnosed with vitB12 deficiency show neurological manifestations, such myelopathy, peripheric neuropathy, optic neuritis or neuropsychiatric symptoms, for example cognitive deterioration.

Methods: Clinical, laboratorial and imagological characterization of patients with neurological manifestations related to vitB12 deficiency (<187 pg/ml). We designed a retrospective and observational study and included patients followed at Neurology Department between January 2016 and May 2021.

Results: Overall, 72 patients (54.2% female) were included with a mean age of diagnosis of 70.9 ± 14.1 years. The most common neurological manifestation associated with vitB12 deficiency was cognitive deterioration (70.8%) followed by peripheral neuropathy (15.3%) and myelopathy (12.5%). Patients with cognitive impairment had a mean MMSE score of 21.4 ± 5.5 points. 90.8% and 87.7% of patients had hemoglobin and MCV values within the reference values, respectively. 58.2% of the cranioencephalic CT scans revealed signs of atrophy. There was significant statistically difference between the value of serum vitB12 and different neurological manifestations. Post-hoc tests indicated a difference in the mean value of vitB12 measure between patients with myelopathy versus peripheral neuropathy or neuropsychiatric manifestations. There was no significant statistically correlation between the vitB12 value and the hemoglobin value.

Conclusion: VitB12 deficiency can present itself in the form of different neurological syndromes, even in the absence of appreciable hematological alterations. Since it is a reversible and preventable cause of neurological impairment, early diagnostic suspicion and treatment are essential for better outcome.

Disclosure: In the interest of transparency, disclose all relationships/activities/interests related to your manuscript.

EPR-086

Natural history of Adrenomyeloneuropathy in an Italian cohort of 44 adult males

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Background and aims: Adrenomyeloneuropathy (AMN) is the most frequent adult-onset form of adrenoleukodystrophy (ALD), a rare X-linked disease caused by ABCD1 mutations, and characterized by progressive myelopathy and adrenal failure. Here, we describe the clinical features and evolution of a large Italian cohort of AMN patients.

Methods: We reviewed information of 44 genetically-diagnosed AMN patients out of 59 adult ALD subjects followed at Carlo Besta Neurological Institute from Jan 2004 to Dec 2021.

Results: Patients usually presented with spastic-ataxic gait associated with impotence and bladder dysfunction in their late twenties (mean age 29, range 14–69). Skin hyperpigmentation and alopecia were common extra-neurological findings. First brain MRI was unremarkable (pure AMN, pAMN, n=32) or revealed lobar white matter (WM) abnormalities (adrenoleukomyeloneuropathy, ALMN, n=12). In five cases, psychiatric symptoms preceded by years the neurological onset. After a mean follow-up of 16 years (range 4–34), symptoms variably worsened, three pAMN patients developed central demyelination and 11 patients died (one pAMN, two pAMN who developed central demyelination, and eight ALMN; median survival time 18 years).

Conclusion: In AMN, overt psychiatric symptoms may be the only clinical manifestation over a long time frame. The presence of lobar WM involvement at first MRI may be the most relevant poor prognostic risk factor. Surprisingly, the percentage of pAMN patients developing central demyelination is much lower than previously reported in other countries over a comparable observational period (9% versus 19% or 63%). This may be due to genetic, epigenetic or environmental protective factors worth to be investigated.

Disclosure: The authors have no disclosures to declare.

EPR-087

Exome sequencing in the diagnosis of neuromuscular diseases: a single Centre experience

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Background and aims: Focused exome sequencing and whole-exome sequencing (WES) are valuable research tools for the identification of molecular defects of suspected genetic diseases. The aim of our study was to evaluate the effectiveness of these methods in achieving a diagnosis in CMT disease, myopathies and hyperCKemia.

Methods: We prospectively enrolled n=40 consecutive patients from a single tertiary referral Centre. After excluding PMP22 duplication/deletion in CMT1 cases, SPG4 and SPG7 mutations if spasticity was present, and biallelic RFC1 expansion in case of sensory axonal polyneuropathy, respectively, n=16 patients underwent focused exome sequencing and n=24 underwent WES. Likely pathogenic / pathogenic mutations, according to ACMG guidelines, were confirmed by Sanger sequencing.

Results: n=40 index patients included: CMT1 (n=2), CMT2 /intermediate CMT (n=16), distal hereditary motor neuropathy (n=4), hereditary sensory neuropathy (n=2), hyperCKemia (n=5), myopathy (n=11). Mean age at genetic testing was 53±15 years. A molecular diagnosis was achieved in 12/40 (30%) of subjects: LITAF (n=1), MPZ (n=1), NEFL (n=1), AARS1 (n=1), SIGMAR1 (n=1), TRPV4 (n=1), GJB1 (n=1), RNF170 (n=1), GNE (n=2), LMNA (n=1), RYR1 (n=1), ANO5 (n=1). WES helped to make diagnosis of CMT due to GJB1 pathogenic mutation (p.Tyr151Cys) in a patient previously diagnosed with chronic inflammatory demyelinating polyneuropathy. Also, two patients with GNE homozygous mutations were reclassified as affected by GNE myopathy.

Conclusion: A genetic diagnosis was reached in the 30% of cases and this proportion was in agreement with previous data. Exome sequencing proved as valuable research tool in achieving a molecular diagnosis of neuromuscular diseases in a clinical scenario.

Disclosure: Nothing to disclose.

EPR-088

A causal role for the GRN p.E393A mutation in frontotemporal lobar degeneration

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Background and aims: Heterozygous loss-of-function (LOF) mutations in the progranulin gene (GRN) cause frontotemporal lobar degeneration (FTLD) with an autosomal dominant pattern of inheritance. Here, we present the genetic and phenotypic characteristics of carriers of a novel pathogenic GRN mutation.

Methods: We analyzed potential pathogenicity of rare GRN missense variants observed in a cohort of Belgian FTD patients by measuring serum progranulin, and evaluating clinical data i.e., symptoms, biomarkers, and neuropathology.

Results: We observed p.E393A in the last codon of exon 10, affecting exon splicing, resulting in a frameshift and nonsense-mediated mRNA decay of the mutant transcript. This led to decreased serum progranulin levels, comparable with known LOF mutations, indicating that p.E393A is pathogenic. Inclusion and screening of relatives procured two other affected carriers. Diagnoses were non-fluent variant PPA (nfv-PPA) or unspecified dementia. Common symptoms were executive dysfunction, language, and memory impairment. Brain MRI showed pronounced asymmetry in 2/3 carriers. Neuropathological examination indicated FTLD-TDP type A with concomitant Alzheimer's disease pathology.
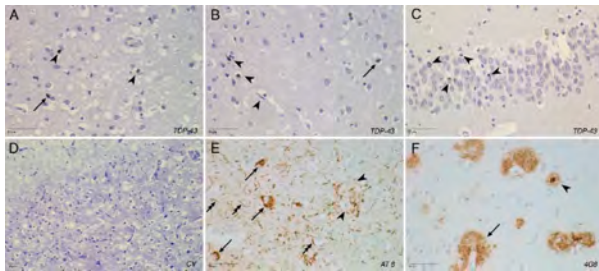
Neuropathological examination of GRN p.E393A index patient demonstrates FTLD-TDP type A pathology with concomitant Alzheimer's disease pathology
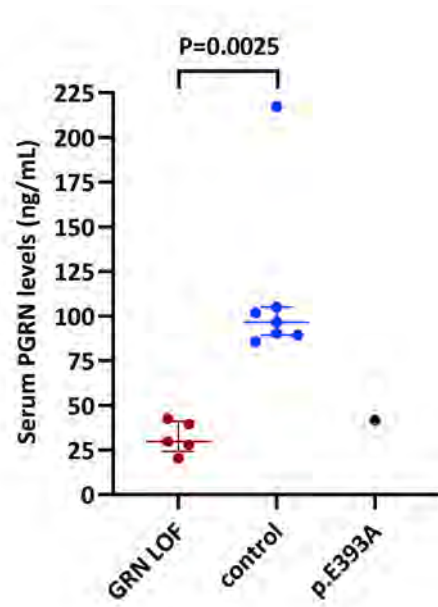
Figure. Scatterplot for serum PGRN levels measured in carriers of GRN p.E393A and LOF mutations and control individuals
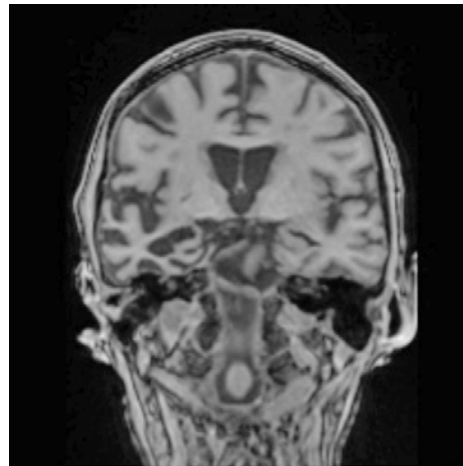
Figure. Structural brain MRI of index patient The patient had a diagnosis of unspecified dementia with pronounced memory impairment, disorientation and executive dysfunction. On this coronal view, extensive cortical atrophy can be seen, most evidently so

Conclusion: We identified a novel pathogenic GRN mutation p.E393A /p.E393fs in a Belgian pedigree, leading to reduced serum progranulin levels and cognitive decline. The phenotype is characterized by executive dysfunction, language, and memory impairment with pronounced asymmetry on MRI. Neuropathology in the index carrier with nfv-PPA revealed FTLD-TDP type A, with concomitant Alzheimer's disease pathology.

Disclosure: Nothing to disclose.

EPR-089

A common calpain-3 variant explains a significant number of LGMD R1 calpain3-related cases in Eastern and Central Europe

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J. Zídková [5], L. Fajkusová [5], S. Limborska [3],
A.J. Van der Kooi [6], E. Brusse [7], L. Leonardis [8], A. Maver [9],
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Clinical presentation

Graph of rs201892814 minor allele frequency distribution, overlaying a modern-day map of Europe

Splicing analysis of the c.1746-20 C>G variant. A. Schematic representation of the splicing patterns B. Electrophoresis image of the various transcription products in affected patient and control

Background and aims: A significant number of patients showing reduction of calpain-3 in the western blot and a phenotype corresponding to autosomal recessive calpainopathy have only a single pathogenic CAPN3 variant identified. The investigated intronic CAPN3 variant c.1746-20C>G occurs in the Central and Eastern Europe with a frequency of >1% and currently there are conflicting interpretations on its pathogenicity.

Methods: We collected clinical data on 14 patients carrying the CAPN3 c.1746-20C>G variant in trans position with another CAPN3 pathogenic/likely pathogenic variant. RT PCR and RNA-Seq were performed. The allelic frequency of the c.1746-20C>G variant was calculated from population studies in Russia, Latvia and Poland.

Results: The patients compound heterozygous for the CAPN3 c.1746-20C>G variant present a phenotype consistent with calpainopathy of mild/medium severity. We report five unaffected individuals homozygous for c.1746-20C>G and three affected, prevalently showing a late-onset, mild calapinopathy phenotype. Molecular studies showed that different splicing isoforms are produced in the muscle. We hypothesize that c.1746-20C>G is a hypomorphic variant with a specific reduction of RNA and protein expression and only individuals having a higher ratio of abnormal isoforms are affected. The variant is most frequent in the North/West regions of Russia and may originate from that area.

Conclusion: Reclassification of the CAPN3 variant c.1746-20C>G from variant with a conflicting interpretation of pathogenicity to hypomorphic variant explains a large number of unidentified cases of LGMD R1 calpain3-related in Eastern and Central Europe. The very high frequency of the variant c.1746-20C>G may result in the pseudo-dominant inheritance.

Disclosure: The work was supported by European Regional Development Fund, Estonian Research Council, the Russian Foundation for Basic, and the Ministry of Health of the Czech Republic.

EPR-090

Age at migration and phenotype differences in Multiple Sclerosis: a multicenter study in Italy

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M. Buccafusca [10], D. Landi [11], M. Di Gregorio [12],
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Background and aims: Previous studies considering migrant individuals with Multiple Sclerosis (MS) indicate that phenotype differences across Countries may be driven by genetic and cross-cultural characteristics. We investigated if age at migration could contribute to phenotype differences between individuals with MS living in Italy but born abroad.

Methods: The MigIt study included 1,360 individuals with MS (458 foreign-born and 902 age- and sex-matched native-born Italian patients). Age disease onset, symptoms at onset and MRI parameters at diagnosis were analyzed comparing people migrating within or after 15 years of age using logistic regression models setting two-sided with alpha level set at 0.05.

Results: 50, out of the 458 individuals with MS born aboard migrated to Italy within the age of 15. Italian individuals had less frequently a progressive onset (OR 0.73; CI 0.54–0.98; p≤0.03) and higher disability (OR. 0.46; CI 0.29–0.73; p=0.001). A complete diagnostic work-up was performed more frequently among patients migrating before age 15 compared to the others (OR 1.55; CI 0.83–2.90; p=0.1). Patients who migrated earlier showed an inverse association with higher age at disease onset (above or not 28 years old) (OR 0.50; CI 0.27–0.94; p=0.027), a progressive disease course since onset (OR 0.34; CI 0.12–0.98; p=0.036).

Conclusion: The present study confirm how age at migration in people with MS can represent a disease modifying factor of phenotype characteristics. This observation strengthen the need to consider the effects of population as well as cross-cultural differences, in the management of individuals with MS belonging to different geographical areas.

Disclosure: Dr Ragonese received research funding by Almirall and Roche; he also received travel grants and honoraria for speaking by: Biogen, Genzyme Sanofi, Merck, Novartis, Roche.

EPR-091

Optical Genome Mapping Enables Accurate Detection And Quantification of RFC1 Repeat Expansion in CANVAS

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Background and aims: CANVAS is a late-onset ataxia caused by a biallelic intronic (AAGGG)n repeat expansion in RFC1 gene on chromosome 4. While many patients have more than 1,000 repeat long expansions, as low as 250 repeats are sufficient to cause the disease. Southern Blotting (SB) is currently the only technique able to detect and estimate the size of large biallelic expansions in RFC1. However, its implementation is limited by the large amount of DNA needed and its time and cost constraints. Optical Genome Mapping (OGM) is a novel technique which is able to detect large scale structural variations by labelling ultra-high molecular weight DNA molecules at specific sequence motifs. Aim of this study was to validate OGM as a tool to detect and quantify RFC1 repeat expansions.

Methods: 9 CANVAS cases and 54 controls underwent OGM. RFC1 expansion size of 9 patients (n alleles=18) as detected by SB and OGM was compared.

Results: OGM correctly identified all biallelic repeat expansions larger than 250 repeats in all CANVAS patients but not in controls. OGM showed high concordance with SB repeat expansion quantifications (R=0.96), with improved resolution in discriminating two expanded alleles in cases where SB resolution allowed only to detect only a single homozygous expansion.

Conclusion: The study shows that OGM could accurately quantify the size of biallelic repeat expansions and appears to be a promising high-throughput tool for genetic diagnosis in CANVAS, as well as other large repeat expansion disorders.

Disclosure: Nothing to disclose.
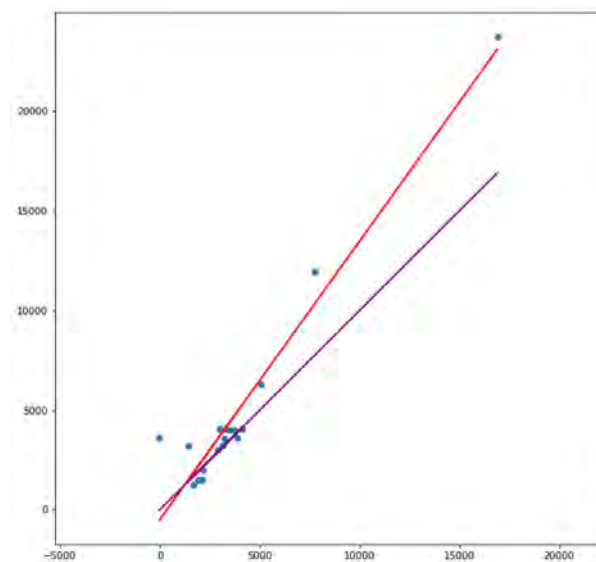
Neuroimmunology 1

EPR-092

Autoimmune new-onset refractory status epileptics (A-NORSE): electroclinical features and response to treatment

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Background and aims: The aim of this study was to characterize the clinical features and outcome of a cohort of patients with new-onset status epilepticus of presumed autoimmune origin (A-NORSE).

Methods: Retrospective study of patients meeting the 2018 ILAE definition of NORSE who were tested for onconeural and/or neuronal surface antibodies, with final evidence of an immune-mediated etiology (satisfying the 2016 Criteria for autoimmune encephalitis).

Results: Between 2009–2017, 878 patients were tested for the presence of onconeural and/or neuronal surface Abs. Twelve of these patients (9 male; median age 54,5; range 24–81) satisfied the inclusion criteria. An autoimmune etiology was suspected based on: (1) Brain MRI features consistent with encephalitis (9: 75%); (2) cerebrospinal fluid (CSF) evidence of inflammation (5; 42%); (3) detection of neuronal antibodies (4; 33%); (4) response to immunotherapy (5; 42%). Antibody positivity included: NMDAR (2), CASPR-2 and Ma2 in 1 patient each. A-NORSE anticipated the diagnosis of cancer in one patient (thymoma). In 10 patients 18-fluorodeoxyglucose PET (FDG-PET) and/or full-body computed tomography (CT) failed to detect a neoplasia. Immunotherapy was given in most of the patients (8; 67%): steroid bolus (6); intravenous immunoglobulin (6); plasma exchange, and rituximab (1 patient each). Long-term outcome was available for 11 patients: 5/7 treated with immunotherapy (71%) were seizure-free, as opposed to only 1/4 (25%) of the patients that were not treated with immunotherapy.

Brain MRI features
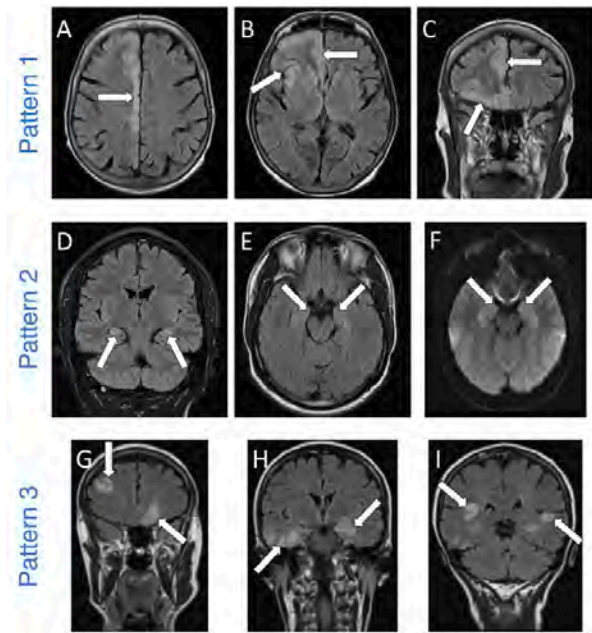
Clinicoradiological features

Conclusion: NORSE is an increasingly recognized manifestation of autoimmune encephalitis. Adequate recognition of this entity is mandatory since aggressive immunotherapy could lead to status resolution and recovery.

Disclosure: The authors report no disclosures relevant to the study.
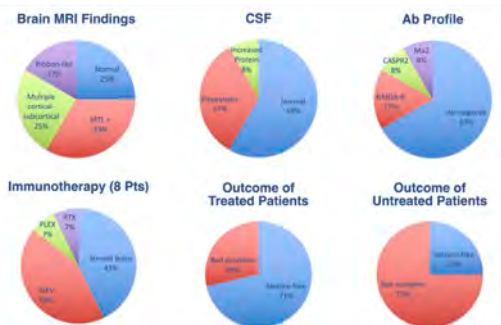
EPR-093

Peripheral neuropathy and MOG-IgG: a clinical and neuropathological retrospective study

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Background and aims: Myelin oligodendrocyte glycoprotein antibodies (MOG-Abs) may rarely be associated with peripheral nervous system involvement. We aimed to test MOG-Abs in patients with undetermined peripheral neuropathy (PN).

Methods: Consecutive patients with available sural nerve biopsy and paired serum sample were retrospectively identified (January, 1st 2016-November, 1st 2021) and tested for MOG-Abs with live cell-based assay (CBA). Patients with antibody titre ≥1:160 (secondary H+L antibody) and selective MOG-IgG presence (IgG-Fc predominance) were considered MOG-IgG positive. All positive samples were analysed with immunohistochemistry and CBAs for antibodies against Neurofascin-155 and Contactin-1. Clinical and neuropathological data were collected through clinical reports.

Results: Among 163 patients, 5 (3%) resulted positive for predominantly IgG MOG-Abs (median titer 1:320, range 1:160–1:5120), none showed other concomitant antibodies. Median age was 74 years-old (range 55–81), median disease duration was 60 months (range 1–167), 60% of patients were female. Of these, 4/5 cases had clinical features suggestive of acute (n=1) or chronic (n=3) inflammatory demyelinating neuropathy, 2/5 fulfilled the criteria of combined central and peripheral demyelination (CCPD) whilst 3/5 had isolated PNS involvement. Neuropathological findings showed mixed axonal-demyelinating features in 2/5, predominant demyelination in 3/5 cases. Other neuropathological hallmarks included paranodal demyelination (n=3), myelin outfoldings (n=4), slight inflammatory infiltrates (n=3), onion bulbs (n=3), clusters of regeneration (n=4).
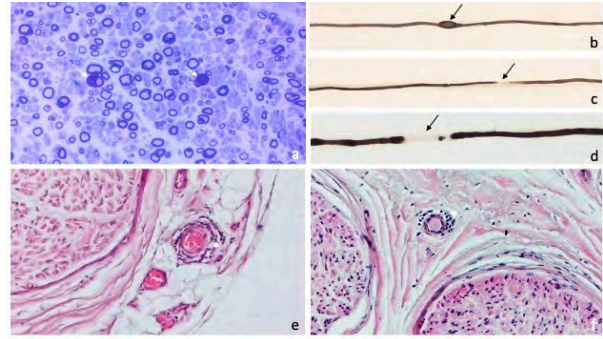
Representative neuropathological findings of sural nerve biopsy of MOG-IgG positive patients (A,B: outfolding of myelin; C,D: paranodal demyelination; E;F: Slight epineurial perivascular infiltrates of inflammatory cells).
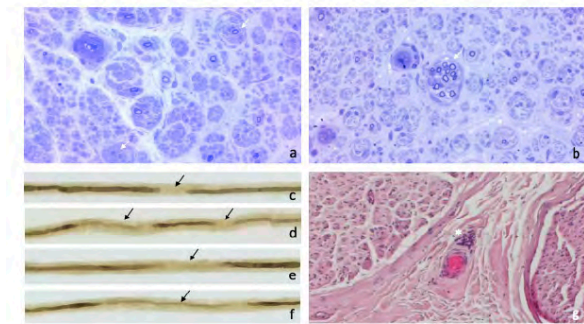
Sural nerve biopsy findings in case #4 (A: onion bulbs; B: clusters of regeneration; C,D,E,F: paranodal and segmental demyelination at different stages; G: small perivascular inflammatory infiltrate).

Conclusion: MOG-IgG can be detected in patients with isolated PN or CCPD. Clinical and neuropathological features are suggestive for demyelination and slight inflammation. Further studies should include larger cohorts of patients to elucidate the utility of MOG-Abs testing in PN.

PD: Parkinson Disease; Hyp: Hypertension; HCC: hepatocellular carcinoma; cryo*: cryoglobulinemia; HypH: hyperhomochysteinemia; DM: Diabetes Mellitus; IvIG: intravenous immunoglobulins; OP: oral prednisolone.

EPR-094

Serum NfL predicts NEDA-status in a 6-year longitudinal cohort of MS patients

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Background and aims: We aimed to determine the ability of serum neurofilament light chain (sNfL), an emerging blood marker of axonal damage, to dissect distinct measures of disease severity and predict future "No evidence of disease activity" (NEDA) status at six-year follow-up (FU) in a cohort of patients with relapsing-remitting multiple sclerosis (MS).

Methods: 153 patients were included with a median FU time of six years (IQR 4-7). Serum was collected at baseline and FU; sNfL levels were measured by single molecule array.

Results: Patients experiencing Expanded Disability Status Scale (EDSS) progression or new persistent T1-lesions at FU showed increased sNfL levels already at baseline compared to stable patients or patients suffering only from inflammatory activity (defined as relapses, new T2 hyperintense or gadolinium-enhancing lesions). We observed a strong association of baseline sNfL with development of persistent T1 lesions at FU, confirmed by linear regression analysis. Thus, we incorporated absence of persistent T1 lesions to the NEDA-3 concept (NEDA-3T1). sNfL significantly improved the prediction of NEDA-3T1 status (0.697 95% CI 0.616–0.770 vs. 0.819 95% CI 0.747–0.878, p<0.001) compared to a cumulative risk score summarizing factors differentiating patients with and without NEDA-3T1 status. Patients with sNfL values ≤8.6 pg/ml showed a 76% risk reduction for evidence of disease activity or development of persistent T1 lesions (EDAT1) at FU (Hazard ratio 0.244, 95% CI 0.142–0.419, p<0.001) compared to patients with sNfL values >8.6 pg/ml.

Conclusion: Baseline sNfL values predicted NEDA-3T1-status at six-year follow-up.

Disclosure: S. B. has received honoraria from Biogen Idec, Bristol Meyer Squibbs, Merck, Novartis, Roche, Sanofi Genzyme and TEVA. His research is funded by Deutsche Forschungsgemeinschaft (DFG) and Hertie foundation.

EPR-095

B cell subsets dynamic during pregnancy and early post partum in women with MS

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Background and aims: Objective: To investigate the dynamic of B cell subsets in pregnant women with Multiple Sclerosis (MS) during pregnancy and post-partum. Background: Reduction of inflammation during MS pregnancy and postpartum inflammatory rebound are usually thought to involve T cell immunomodulation. Nevertheless, B cell dynamics have been poorly explored during pregnancy and post-partum.

Methods: We designed a monocentric non interventional study (BABIES study) enrolling untreated pregnant MS women within 8 weeks±5 days from the last menstrual period. Clinical and immunological data are collected at baseline (T1), 20th (T2), 32nd (T3) gestational week,2 weeks (T4), 3(T5) and 6(T6) months from delivery. B cell subpopulations were analyzed by multi-parametric flow cytometry in freshly isolated PBMCs.

Results: Preliminary results on 6 women followed up at least until T3 show that absolute number and percentage of circulating CD19+ B cells decrease during pregnancy. Among subpopulations, CD24+CD38+ naive transitional immature B cells and CD27+ memory cells drop, CD27- mature naïve B cells increase. CD27+ memory cells also reorganize as the IgG/IgA switched memory cells increase while the less differentiated IgM cells decrease. Consistently, antibodies producing CD27hiCD38hi plasmablasts are rapidly and dramatically augmented in peripheral blood of pregnant women. All these changes are rapidly reverted after delivery.

Conclusion: In MS women pregnancy induces specific B cell depletion and reorganization with a dramatic reassortment in subpopulation composition; such immunological adaptations are rapidly reverted after delivery. If B cell dynamic during pregnancy and post-partum is associated with disease remission and rebound has to be elucidated.

Disclosure: Nothing to disclose.

EPR-096

A novel cell-based assay detects antibodies against alpha3-nAchR exclusively in autoimmune autonomic ganglionopathy

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Background and aims: Autoantibodies against alpha-3 nicotinic acetylcholine receptors (alpha3-nAChR), usually measured by radioimmunoprecipitation assay (RIPA), are detected in autoimmune autonomic ganglionopathy (AAG) patients, but also in patients with other neurological diseases, albeit in lower levels. Our aim is to develop a sensitive and specific method for the selective detection of the potentially pathogenic alpha3-nAChR antibodies, seemingly present only in AAG patients.

Methods: The detection of the autoantibodies against the cell-exposed alpha3-nAChR domain was performed by a live cell-based assay (CBA), which was developed for this purpose with alpha3-nAChR transfected cells. The study included sera from 55 patients suspected of autonomic failure, 13 patients diagnosed with autonomic failure, positive for alpha3-nAChR antibodies by RIPA, 52 patients with Ca2+-channel or Hu antibodies and 2628 control patients with various neuroimmune diseases.

Results: RIPA detected alpha3-nAChR antibodies in 25 patient sera. 15/25 were also positive by CBA. Remarkably, all CBA-positive patients had AAG, while all CBA-negative had other neurological diseases. RIPA antibody levels of the CBA-negative sera were low, even though our CBA could detect equally low antibody levels. No serum bound to control cells, and none of the 2,628 control sera was found alpha3-CBA-positive.

Conclusion: This study showed that in contrast to the established, but moderately disease-specific RIPA for alpha3-nAChR antibodies, our CBA seems AAG-specific, while at least equally sensitive with the RIPA.

EPR-097

Efgartigimod improved quality-of-life in gMG: a randomised, double-blinded, placebo-controlled, phase 3 trial (ADAPT)

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Background and aims: ADAPT trial (NTC03669588) supported FDA approval of efgartigimod alfa-fcab in generalized myasthenia gravis (gMG). Here, we describe 2 important health-related qualify-of-life (HRQoL) outcomes in ADAPT.

Methods: ADAPT enrolled 167 adults with gMG (Myasthenia Gravis Foundation of America class II-IV and Myasthenia Gravis Activities of Daily Living [MG-ADL] score ≥ 5). Patients were randomized to 10-mg/kg efgartigimod (n=84) or placebo (n=83), administered as 4 weekly infusions per cycle. Subsequent cycles were administered per clinical status ≥ 8 weeks after prior cycle initiation. Efficacy was assessed weekly for 8 weeks after each cycle initiation, then every 2 weeks for ≤ 26 weeks. HRQoL outcomes included MG-QoL15r, a disease-specific measure, and EuroQoL 5-Dimensions 5-Levels (EQ-5D-5L), including visual analogue scale (VAS), as generic health status measures. We analyzed MG-QoL15r and EQ-5D-5L scores in AChR-Ab seropositive, modified intention-to-treat population (patients with baseline and ≥ 1 post-baseline MG-ADL scores: n=65, efgartigimod; n=64, placebo) -from baseline through week 8 of cycle 1. Mixed model for repeated measures was fitted for change from baseline; least squares mean difference and p-values were calculated at each visit.

Results: HRQoL was poor at baseline. Significant improvements in MG-QoL15r scores were seen with efgartigimod compared to placebo at weeks 1–8 (Figure 1). Improvements were also observed across all 5 EQ-5D-5L domains with efgartigimod. EQ-VAS change from baseline showed significant improvements at weeks 1–6 (Figure 2).
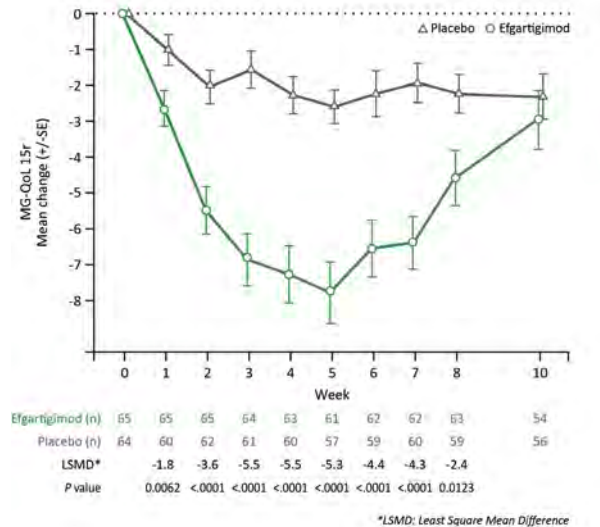
Figure 1: MG-QoL15r Mean Change From Baseline During Cycle 1 in the AChR-Antibody Seropositive Population (Modified Intent-to-Treat Analysis Set)
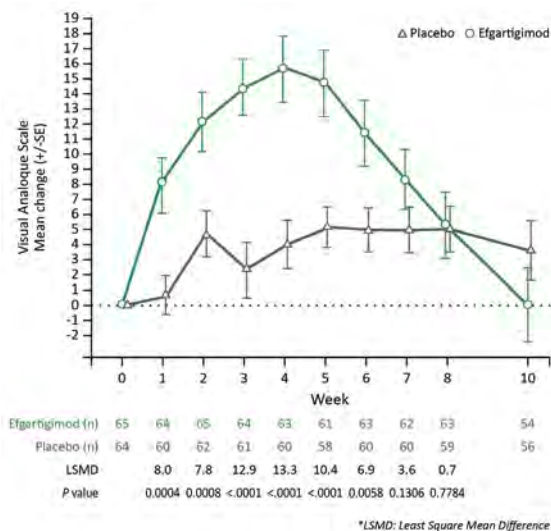
Figure 2: Visual Analogue Scale Mean Change From Baseline During Cycle 1 in the AChR-Antibody Seropositive Population (Modified Intent-to-Treat Analysis Set)

Conclusion: In patients with AChR-Ab−positive gMG, efgartigimod treatment resulted in significant and rapid HRQoL improvements, with sustained impact on MG symptoms, for up to 8 weeks after the first infusion.

Disclosure: This study was sponsored by argenx SE, the manufacturer of efgartigimod alfa-fcab which is FDA-approved for use in gMG. Tam M. Nguyen-Cao, PhD, CMPP of Claritas Scientific LLC provided medical writing support (funded by argenx).

EPR-098

Neurofilament light chain levels in anti-NMDAR encephalitis and primary psychiatric psychosis

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Background and aims: We aimed to assess the performance of neurofilament light chain (NfL) testing in anti-NMDAR encephalitis (NMDARe) and its differential diagnosis.

Methods: NfL were determined with Single molecule array in patients with NMDARe, pFEP, herpes simplex encephalitis (HSE), and healthy subjects (HC). Receiver operating characteristic (ROC) analyses were performed to assess the prediction accuracy of serum NfL (sNfL) levels for NMDARe and pFEP.

Results: 118 patients with NMDARe (33 with isolated psychosis), 45 pFEP, 36 HSE, and 36 HC were studied. NMDARe patients with seizures/status epilepticus, ICU admission, CSF pleocytosis (>20 WBC/µL), and without early immunotherapy were more likely to have higher sNfL than NMDARe without these features. NfL levels at diagnosis of NMDARe did not correlate with outcome at 1 year follow-up assessed with the modified Ranking Scale. NMDARe patients had significantly higher NfL than pFEP and HC, and lower than HSE patients. ROC analysis of sNfL levels between NMDARe with isolated psychosis and pFEP provided an AUC of 0.93 (95% CI 0.87-0.99) and a sNfL cutoff ≥15 pg/mL to distinguish these disorders. 43/45 (96%) pFEP had sNfL<15pg/mL whereas 5/33 (15%) NMDARe with isolated psychosis were below this cutoff. None of the HSE and 35/36 (97%) HC had sNfL<15pg/mL.
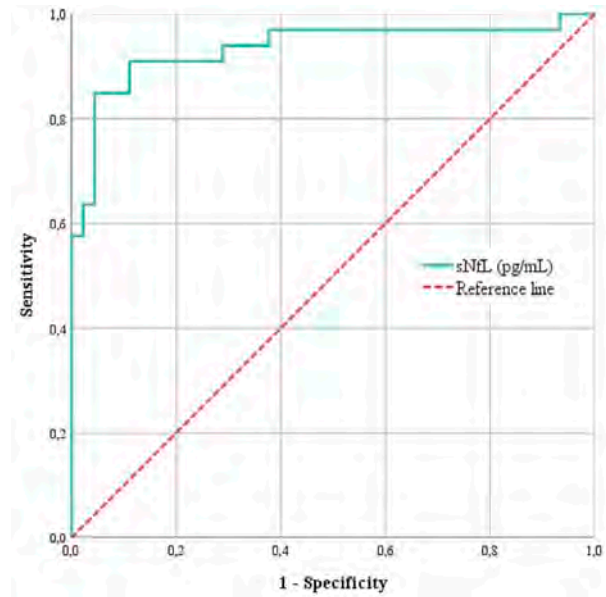
ROC curve for sNFL between NMDARe and pFEP
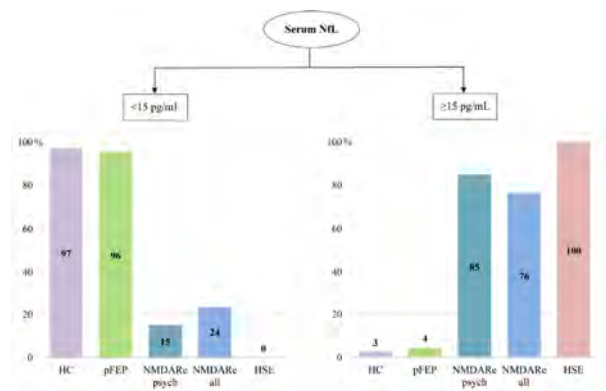
Distribution of patients according to stablished cutoff value for sNfL

Conclusion: NfL measured at diagnosis of NMDARe associated with several features of disease severity but not with long-term outcome. sNfL cutoff≥15pg/mL correctly classified 96% of pFEP and 85% of NMDARe with isolated psychosis. Patients with FEP of unclear etiology and sNfL≥15pg/mL should undergo CSF NMDAR-antibody testing.

Disclosure: No disclosures related to the current study.

Figure 1. Group comparisons

EPR-099

Real-world application of the updated diagnostic criteria for paraneoplastic neurological syndromes

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Background and aims: Paraneoplastic neurological syndromes (PNS) are remote effects of cancer that can affect any part of the nervous system. Diagnostic criteria for PNS have been updated in 2021. In this study we aimed to compare the updated PNS-Care score to the previous diagnostic criteria.

Methods: We retrospectively applied the 2004 (2004–PNSc) and the updated diagnostic criteria (2021-PNSc) to a cohort of patients with suspected PNS admitted to our Institution from 2012 to 2020. High-risk (HR) and intermediate-risk (IR) clinical phenotypes were defined according to 2021-PNSc. The K index of Cohen was employed to calculate concordance between the two criteria.

Results: 68 patients were included. 47 patients (69%) had a HR phenotype (progressive cerebellar syndrome, 23; limbic encephalitis [LE], 21; Lambert-Eaton myasthenic syndrome [LEMS], 2; LE and LEMS, 1). Twenty-one patients (31%) were diagnosed with IR phenotype (autoimmune encephalitis, 18; stiff-person syndrome, 2; Morvan syndrome, 1). Cancer was diagnosed in 30/68 patients (44%), most frequently small cell lung cancer, followed by thymoma and ovarian cancer. In HR patients there was good concordance between "definite" PNS (2004-PNSc) and "definite" plus "probable" PNS according to 2021-PNSc (K index: 0,872); concordance was lower when only "definite" categories were compared (K index: 0,578). Among IR patients, the PNS-Care score identified 6/21 (29%) as "definite" or "probable" PNS. PNS-Care score had 91,6% sensitivity and 95,7% specificity in diagnosing patients with PNS.

Serological and oncological association in patients with high-risk phenotypes.
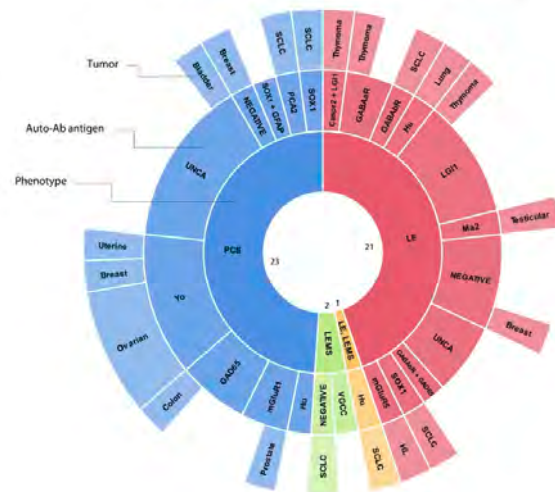
Score distributions in high-risk phenotype patients

Fig. 2 fehlt leider

Conclusion: There is good concordance between the 2004-PNSc and 2021-PNSc in patients with HR phenotypes. The PNS-Care score has a high sensitivity and specificity in diagnosing PNS.

Disclosure: Nothing to disclose.
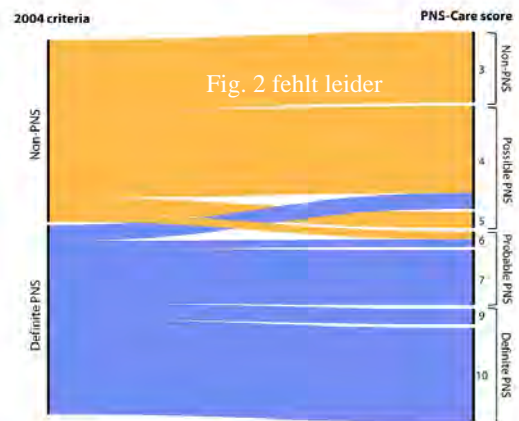
Serological and oncological association in patients with intermediate-risk phenotypes.

ePresentations

Sunday, June 26, 2022
Movement disorders 2

EPR-100

Investigating cortical function with TMS-EEG to explain motor impairment in patients with Parkinson's Disease

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Background and aims: A novel brain-stimulation technique which combines MRI-navigated TMS with high-density EEG (TMS-EEG) has emerged as a powerful tool to non-invasively probe brain circuits. Indeed, a previous TMS-EEG study unveiled the change of motor cortical network excitability in patients with Parkinson's disease (PD). This study aimed at characterizing the TMS-evoked potentials (TEP) obtained by targeting occipital and premotor cortex in PD patients and to evaluate their association with dyskinesia.

Methods: In 14 PD patients clinically assessed with the Unified Parkinson Disease Rating Scale (UPDRS), we measured the TEPS obtained by targeting the premotor and occipital cortices. An integrated neuronavigation system which employs the individual structural MRI of each patient was used to estimate and monitor the maximum electric field in target areas. TEP were analyzed to compute latency, area and slope of statistically significant peaks on the cluster of channels nearby the cortical targets. Finally, we performed a statistical analysis of neurophysiological measures with respect to the UPDRS and the presence of dyskinesia.

Results: We found that motor UPDRS subscore was correlated with the latency of occipital TEP whereas the UPDRS subscore for dyskinesia was correlated with the latency of the premotor TEP. Significant difference in excitability of premotor cortex was found in patients with dyskinesia compared to non-dyskinetic patients.

Conclusion: Our findings further support the use of TMS-EEG as a non-invasive tool to probe the role of different cortical regions in the pathophysiology of PD and disclose the functional impairment of premotor and occipital cortices with implications for rehabilitation.

Disclosure: AM and MM contributed equally.

EPR-101

Interventions to Improve Gait in Parkinson's Disease: A Systematic Review and Network Meta-Analysis

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Background and aims: Development of gait symptoms, and especially the development of Freezing of Gait (FoG), represents an important milestone in the progression of Parkinson's Disease (PD). This systematic review and network meta-analysis assessed and ranked interventions according to their effectiveness in treating gait symptoms across four dimensions and the motor component of the UPDRS.

Methods: A systematic search of the literature was carried out across PubMed, EMBASE, PubMed Central (PMC) and Cochrane Central Library. Measures of gait performance before and after intervention were extracted. From this five networks were generated, and corresponding forest plots ranking the interventions.

Results: The search returned 6,288 articles. From this 368 articles were deemed eligible. Of these 147 articles were included. Three of the gait specific networks were consistent. For dynamic gait measures, the treatment with the largest observed effect, was Aquatic Therapy with dual task exercising (SMD 1.99 [-1.00; 4.98]) and strength and balance training SMD 1.95 [-0.20; 4.11]. For measures of fitness treatment with the largest observed effects were aquatic therapy, SMD 3.41 [2.11; 4.71] and high frequency repetitive transcranial magnetic stimulation (HFrTMS) SMD 2.51 [1.48; 3.55]. For FoG measures, none of the included interventions yielded significant results.
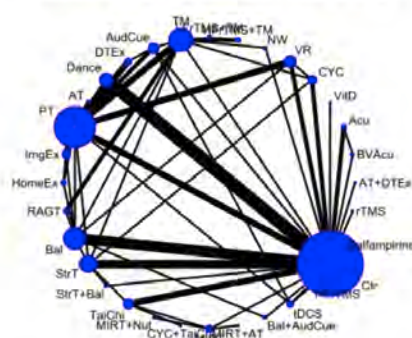
Sample Network of Measures of Dynamic Gait
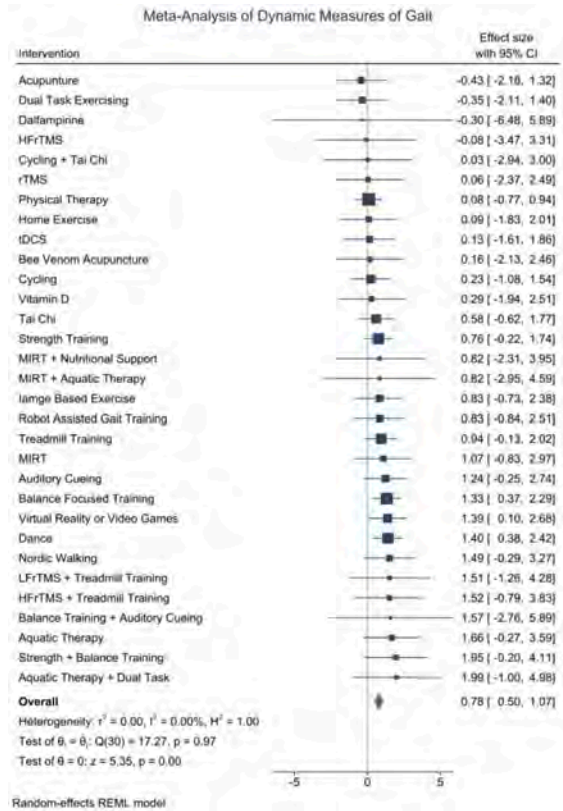
Summary sample of Meta-Analysis of interventions on measures of Dynamic Gait
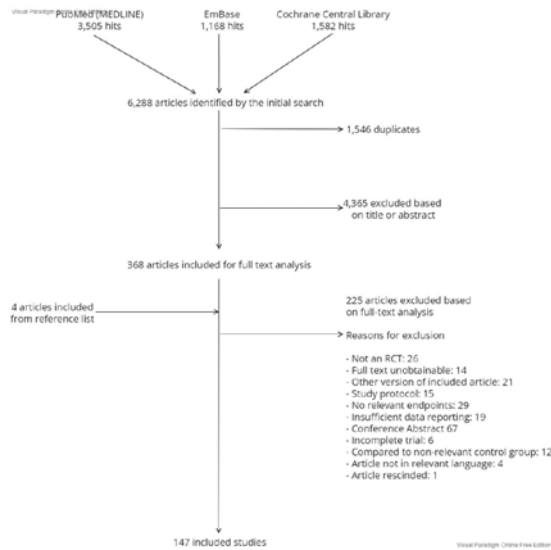
Flowchart detailing search and selection process

Conclusion: This review demonstrated that many of the included interventions ameliorate some gait symptoms in PD. No recommendation on a superior intervention can be made. None of the studied interventions proved efficacious in the treatment of FoG.

Disclosure: The authors of this review have no conflicts of interest to disclose.

EPR-102

Olfactory dysfunction and striatal dopamine transporter binding in motor subtypes of Parkinson's disease

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Background and aims: Olfactory dysfunction is seen prevalently in Parkinson's disease (PD) patients as one of the earliest non-motor symptoms (NMS). There are contradictory results regarding the association of olfactory dysfunction and dopamine uptake in striatal nuclei among PD patients. It has been shown that different motor subtypes of PD vary in the disease pathophysiology and progression. Thus, we hypothesis that there might be different associations between olfactory dysfunction and striatal dopaminergic neuronal loss among three motor subtypes of PD namely indeterminate, postural instability and gait difficulty (PIGD), and tremor-dominant (TD).

Methods: We recruited the information of 162 healthy controls (HCs) and 464 drug naïve PD patients which were underwent common PD scaling tests. Striatal binding ratios (SBRs) of DaTSCAN images in caudate and putamen nuclei were calculated. To assess the olfaction function the University of Pennsylvania Smell Identification Test (UPSIT) carried. Partial correlation models adjusted for the effect of age, years of education, and sex were used.

Results: UPSIT score was correlated with SBR score in right and left putamen nucleus in indeterminate patients (p=0.004, correlation coefficient: 0.467), (p=0.032, correlation coefficient: 0.362). There were also significant correlations between olfactory function and SBR score in right (p=0.000, correlation coefficient: 0.246) and left caudate (p=0.000, correlation coefficient: 0.233) and putamen (p=0.000, correlation coefficient: 0.323), (p= 0.000, correlation coefficient: 0.342) nucleus among TD subtype.
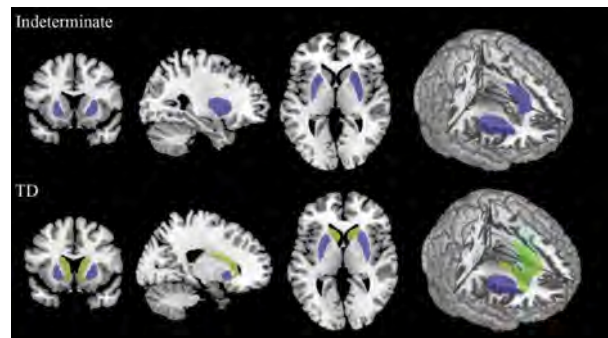
Figure. Significant results of SBR score in DATSCAN and olfactory dysfunction. Caudate nuclei (green), Putamen nuclei (purple). Tremor Dominant (TD).

Conclusion: The UPSIT score is correlated with dopamine transporter activity in striatal nuclei in indeterminate and TD subtype but not PIGD subtype. Therefore, the olfactory dysfunction PIGD subtype may not be a predictive factor for PD development in the future.

EPR-103

Electrophysiological characteristics of the tremor in patients with tick borne encephalitis

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Background and aims: Tick borne encephalitis (TBE) is endemic in focal areas of Europe, including Slovenia. Approximately 40% of TBE patients present with action tremor of the upper limbs, which is mostly transient. Tremor in TBE has not been electrophysiologically defined and the mechanism of its generation remains unknown. Theoretically, it may represent enhanced physiological tremor, caused by the activation of sympathetic response in the febrile patient or may be due to the activation of central oscillators, triggered by meningoencephalitic process. Accelerometry with concurrent surface electromyography (EMG) may differentiate between enhanced physiological and central tremors. Eye-blink conditioning (EBC) is a paradigm used to assess cerebellar function, which is known to be impaired in central tremors.

Methods: We included 22 hospitalised patients (average age 42.2 years, 17 males), with confirmed TBE and newly onset tremor. Patients underwent EMG and accelerometry recordings (without and with 500 gr mass loading) and EBC assessment.

Results: Action tremor was symmetric in 75% patients. 41% of patients manifested also tremor at rest. The average postural tremor frequency on the accelerometry, without and with weight loading, was 7.3 ($\pm$3.8) Hz and 7.6 ($\pm$2.6) Hz, respectively. All patients had corresponding frequency peak in the EMG. EBC did not differ between TBE and historical control group of essential tremor patients.

Conclusion: Our electrophysiological findings are consistent with central tremor generation in TBE. Unlike other pathologic central tremors, the TBE tremor is reversible and may be potentially used as a model of the vulnerability of the central oscillators.

Disclosure: Nothing to disclose.

EPR-104

Assessment of cognitive functions in PD and ET patients with pharmacoresistant tremor after Gamma Knife thalamotomy

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Background and aims: Tremor is one of the most common symptoms of Parkinson's Disease (PD) and essential tremor (ET). The first line of treatment is pharmacotherapy. It can sometimes be ineffective or contraindicated. In such cases, surgical treatment is an option. Deep Brain stimulation (DBS) or thalamotomy are among commonly used methods.

Methods: The purpose of our observational study was to assess the impact of unilateral Gamma Knife thalamotomy on psychological functions in ET and PD patients. We included 20 patients with PD (n=10) or ET (n=10) with pharmacoresistant tremor. The mean age was 63.5 ($\pm$9.5), 16 male and 4 female. They underwent psychological assessments before (n=20); 12 months (n=20), and 24 months (n=11) after the procedure. Mini-Mental State Examination, CLOX, Tower of London, Benton Judgment of Line Orientation test, Adverse Childhood Experience, The Wechsler Adult Intelligence Scale, Rey Auditory Verbal Learning Test, Boston Naming Test, and Beck's Depression Inventory tests were performed. Friedman's ANOVA and Wilcoxon's signed-rank test were used to compare the outcomes.

Results: There were no serious adverse events related to the procedure reported in our study. Statistical analysis revealed no significant change (p>0,05) in performed psychological tests in 2-year follow-up.

Conclusion: We conclude that Gamma Knife thalamotomy does not deteriorate the mood or cognitive functions of the patients treated due to tremor associated with PD or ET in a 2-year follow-up. It may be a safe and efficient way of treating pharmacoresistant tremors for patients who are not qualified for DBS procedure.

Disclosure: Nothing to disclose.

EPR-105

Circadian periodicity, artifacts and implications for clinical implementation of aDBS in chronic subthalamic recordings

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A. Sharott [2], A. Kühn [1]

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Background and aims: Subthalamic beta band activity has been suggested as a physiomarker for bradykinesia in Parkinson's disease (PD) in acute and chronic recordings. To date, long-term fluctuations, changes during every-day activities, especially movement, and circadian rhythmicity could not be assessed, being crucial for adaptive deep brain stimulation (aDBS). This study aims to investigate long-term characteristics in chronic recordings using the novel Percept IPG.

Methods: 6 advanced PD patients were included in chronic individual beta peak recordings for up to 59 days (mean 34 ± 12.3 days). In 2 STN, beta band power during resting state in controlled conditions (Med On/Off/Stim On/Off) and during chronic recordings were compared. In a subgroup of 4 patients, signal changes during movement were assessed during walking and head/arm movements to define artifact contamination.

Results: Beta oscillatory power fluctuates in a 24-hour-circle (time-of-day explained variance: mean 0.41, $p>0.001$). Averaged nighttime beta peaks were decreased compared to peak amplitudes during the day. However, these chronic beta peaks during daily activity were also larger as compared to resting daytime recordings. We found significant movement related changes in acticity <50Hz (e.g. when lifting arms/rest mean $p=0.0078$, shaking head/rest $p=0.031$).

Conclusion: Circadian variation shows reduced beta band activity during the night. These findings are significant for aDBS implementation, since threshold adjustments to time of day and further investigations of sleep-related changes in beta power may be necessary. Increased beta peak monitoring during the day-time could also be influenced by movement artifacts, and sources of artifact contamination need to be considered in future aDBS development.
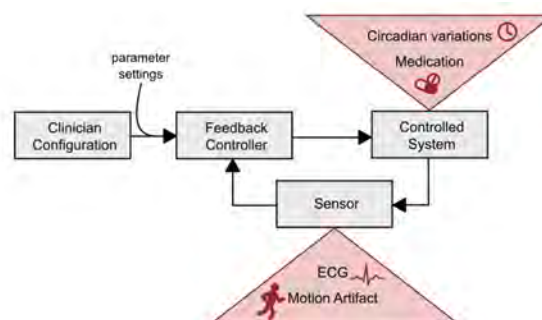
Diagram of the control system and possible influencing factors in aDBS

EPR-106

Therapeutic Potential of Histone Deacetylase Inhibitions in an In Vitro Neuroinflammation Model of Parkinson's Disease

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Background and aims: Parkinson's disease (PD) is a neurodegenerative disorder resulting from the progressive degeneration of midbrain dopamine neurons. Given the lack of disease modifying therapies, it is crucial to identify new neuroprotective agents. Neuroinflammation is a core aspect of PD pathology and a growing evidence base implicates a pathological imbalance in epigenetic regulation. To identify potential therapeutic targets, we performed gene co-expression analysis of the human SN to identify genes in these pathways that were co-expressed with mDA neuron markers. Subsequently we hypothesized that the neurotrophic factor GDF5, and the class IIa specific histone deacetylase inhibitor MC1568, would protect dopaminergic neurons from proinflammatory cytokine-induced degeneration.

Methods: To test this hypothesis we used human SH-SY5Y cells which are a widely used model of human dopaminergic neurons. These were cultured with 100ng/ml GDF5, with or without 10ng/ml of TNFα or IL-1β, for 72h. SH-SY5Y cells were additionally cultured in the presence of 0.1μM MC1568, with or without increasing concentrations of TNFα or IL-1β, for 72h. We used neurite growth as a single cell readout of neurotrophic action.

Results: GDF5 or MC1568 co-treatment prevented the detrimental effects of TNFα and IL-1β on neurite length.
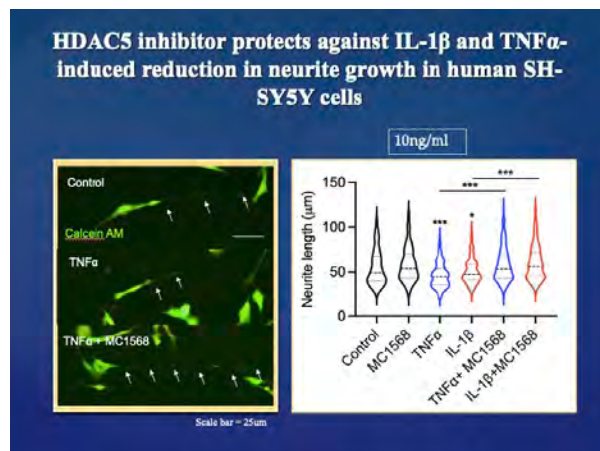
HDAC5 inhibitor protects against IL-1β and TNFα-induced reduction in neurite growth in human SH-SY5Y cells
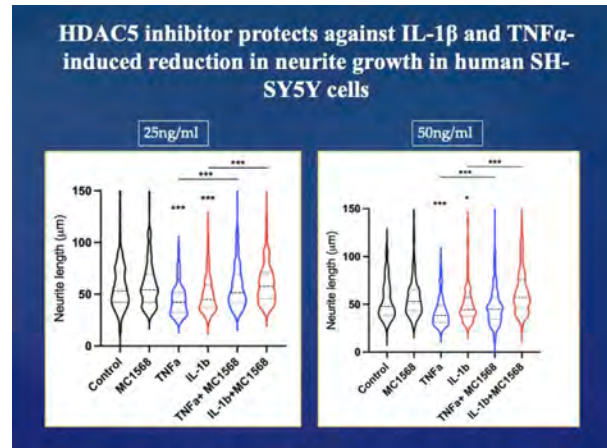
HDAC5 inhibitor protects against IL-1β and TNFα-induced reduction in neurite growth in human SH-SY5Y cells at increasing concentrations

Conclusion: In summary these data show that GDF5 and MC1568 protect against proinflammatory cytokine-induced neurite degeneration in a model of human dopaminergic neurons. Given that axonal degeneration is now recognised as a crucial neuropathological event in PD, these data are an important first step in rationalising the use of these agents as novel therapies for PD.

Disclosure: This work was partially funded by the University College Cork Summer Undergraduate Research Scholarship. The authors have nothing else to disclose.

EPR-107

Abstract withdrawn

Ageing and dementia & Sleep-wake disorders 2

EPR-108

Increasing brain gamma activity improves episodic memory and restores cholinergic dysfunction in Alzheimer's disease

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Background and aims: To assess whether non-invasive brain stimulation with transcranial alternating current stimulation at gamma-frequency (γ-tACS) applied over the precuneus can improve episodic memory and modulate cholinergic transmission by modulating cerebral rhythms in early Alzheimer's disease (AD).

Methods: In this randomized, double-blind, sham controlled, crossover study, 60 AD patients underwent a clinical and neurophysiological evaluation including assessment of episodic memory and cholinergic transmission pre- and post- 60 minutes treatment with γ-tACS targeting the precuneus or sham tACS. In a subset of 10 patients, EEG analysis and individualized modelling of electric field distribution were carried out. Predictors to γ-tACS efficacy were evaluated.

Results: We observed a significant improvement in the Rey auditory verbal learning (RAVL) test immediate recall ($p<0.001$) and delayed recall scores ($p<0.001$) after γ-tACS but not after sham tACS. Face-name associations scores improved with γ-tACS ($p<0.001$) but not after sham tACS. Short latency afferent inhibition, an indirect measure of cholinergic transmission, increased only after γ-tACS ($p<0.001$). ApoE genotype and baseline cognitive impairment were the best predictors of response to γ-tACS. Clinical improvement correlated with the increase in gamma frequencies in posterior regions and with the amount of predicted electric field distribution in the precuneus.

Conclusion: Precuneus γ-tACS, able to increase γ-power activity on the posterior brain regions, showed a significant improvement of episodic memory performances, along with restoration of intracortical connectivity measures of cholinergic transmission. Response to γ-tACS was dependent on genetic factors and disease stage.

EPR-109

Not only RBD in Parkinson's disease: the role of the video-polysomnography

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Background and aims: Parkinson's disease (PD) patients (pts) show a wide range of sleep related motor behaviors including hallucinations and arousal behavioral-related episodes. Differential diagnosis appears challenging by clinical history alone since they share anamnestic features. The video-polysomnography (VPSG) establishes an accurate diagnosis.

Methods: Three male PD pts (pt1=65, pt2=67 and pt3=72 yo) presenting sleep-related motor disorders underwent one or two nocturnal VPSG.

Results: Pt1 (disease duration – dd=4y) had a positive familial and personal history of Disorders of Arousal (DoA), Pt2 (dd=9y) and Pt3 (dd=5y) had a previous VPSG confirmed RBD diagnosis and then developed cognitive impairment with diurnal hallucinations. Pt1: VPSG showed a physiological REM sleep atonia and 10 brief episodes from NREM sleep where the pt raised his head and trunk with puzzled expression, sat up or screamed. Pt2: VPSG recorded no RBD episodes but 2 confused behaviors arising from a mixture of light sleep and wakefulness associated with coherent mental contents. Pt3: VPSG detected a prolonged episode following an early morning awakening from NREM sleep where the patient sat up, moving his arms searching for something. When questioned, the pt referred of having seen a "monster".
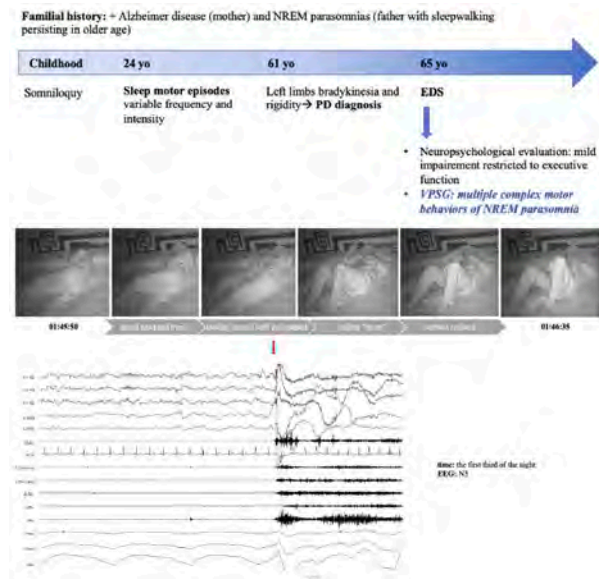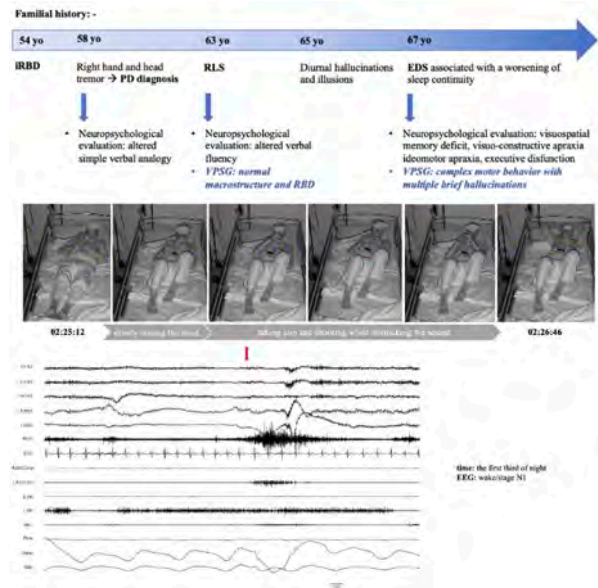
Pt2: clinical history and VPSG findings
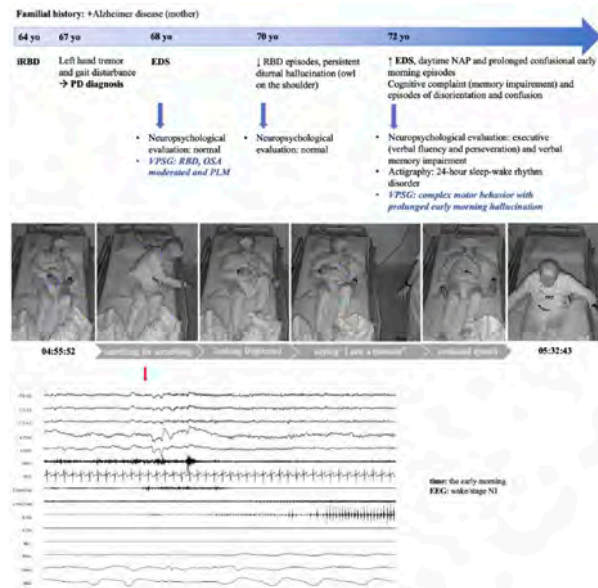
Pt3: clinical history and VPSG findings

Conclusion: In our case series, VPSG revealed sleep related behaviors distinct from RBD. In pt1 VPSG supported DoA diagnosis; while in pt2 and pt3 identified confused episodes with visual hallucinations, arising from a mixed state of light sleep and wakefulness. VPSG is crucial for detecting and characterizing episodes objectively, correlating them with polygraphic parameters.

Disclosure: The authors report no disclosures relevant to the manuscript.

Pt1: clinical history and VPSG findings

EPR-110

Imaging correlates of premorbid personality in the frontotemporal dementia–amyotrophic lateral sclerosis spectrum

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Background and aims: Frontotemporal dementia (FTD) and amyotrophic lateral sclerosis (ALS) belong to the same neurodegenerative spectrum. Factors determining phenotypic expression are unknown; however, it is common observation that personality differs between phenotypes. We therefore aimed at testing if FTD and ALS patients have different premorbid personalities, and, consequently, different organizations in the brain networks involved in social behaviour and motor function.

Methods: We recruited FTD and ALS patients presenting to Modena University Hospital Neurology Clinics. Patients' premorbid personality was assessed through the NEO-PI-3. Brain MRI scan including T1-weighted and resting state fMRI sequences was performed. Data were analysed with voxel-based morphometry and probabilistic independent component analysis.

Results: 50 patients (30 FTD, 17 ALS, 3 FTD-ALS) were recruited. A significant difference in premorbid personality emerged in Openness and Extraversion. Structural imaging analysis showed a positive correlation between premorbid Neuroticism and grey matter density of the hippocampus bilaterally (left>right) across all patients. Group comparisons showed greater functional connectivity (FC) in ALS compared to FTD patients within the Salience Network (SN) in the right insula, putamen, nucleus accumbens, and the left thalamus. FC within the SN positively correlated with premorbid Openness across all patients.
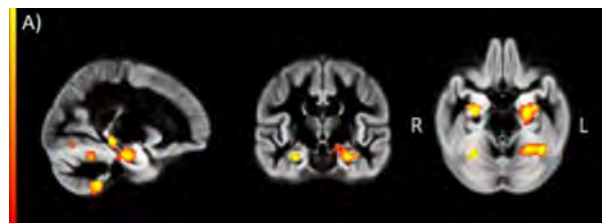
VBM correlational analysis between GM and the five NEO-PI-3 domains across all patients: A) areas of significant correlation between GM and Neuroticism (TFCE corrected, p<0.05).
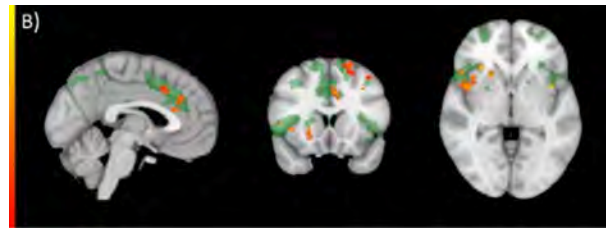
Between-group comparisons of fMRI connectivity within the Salience Network (SN), shown in transparent green in all the images: B) in red-yellow, regions of significant greater SN functional connectivity in ALS compared to FTD.

Conclusion: Premorbid personality differs between patients with ALS and FTD, and relates to different degrees of FC within the Salience Network. This suggests that premorbid personality may represent a vulnerability marker to the development of specific phenotypes along the FTD-ALS spectrum.

Disclosure: Authors declare no relevant disclosures for this study.

EPR-111

Comorbid neuropathology in a longitudinal cohort of institutionalized dementia patients: a clinico-pathological analysis

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Background and aims: Comorbid neuropathology has been described in post-mortem series of dementia patients but its significance in disease progression and relation with clinical phenotype are still not clear. In the context of a biomarker research program in moderate to advanced dementia, our purpose is to describe the prevalence of major types of co-pathology as compared with previous clinical diagnosis and trajectory.

Methods: A complete neuropathological study was performed in 147 post-mortem brains from the Vallecas Alzheimer's Center Study (VACS), with full classification and staging of Alzheimer's (AD), Lewy body, vascular (VD), TDP-43 pathologies and various age-associated tauopathies. Upon inclusion in VACS, patients received a baseline clinical diagnosis based on a thorough neurological assessment and a 3T MRI study. Patients were classified clinically either as AD, Vascular, Mixed dementia, synucleinopathy or Other.

Results: Mean age at death was 87.3±6.6, and sex ratio 78.9% female. Total survival time was 11.4±5 years and time since clinical classification (VACS) 4.4±3.2 years. High AD pathology (78% of patients), high vascular pathology (53%), Lewy body pathology (39%), TDP pathology (65%) and tau pathology (64%) were present in all clinical diagnostic groups, which differed in frequencies of co-pathologies (p<0.01), survival time and age at death (p<0.05).

Conclusion: Neurodegenerative and vascular co-morbidity is highly frequent in aged dementia patients. Different patterns and trajectories of co-pathology can be pursued between clinical and postmortem neuropathological diagnosis, that are particularly relevant for the development of biomarkers.

Disclosure: Nothing to disclose.

EPR-112

Sporadic Creutzfeldt-Jakob disease in the young: a 10 year review of United Kingdom surveillance

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Background and aims: Sporadic Creutzfeldt-Jakob Disease (sCJD) is the commonest human prion disease, with a median age of onset of 68 years. We aimed to characterise the clinical, investigation, and neuropathological features in young individuals with sCJD using data derived from national CJD surveillance in the UK.

Methods: We interrogated the NCJDRSU database for individuals diagnosed with definite (post-mortem confirmed) or probable sCJD assessed between 2011-2021. We extracted data on clinical features, MRI, EEG, RT-QuIC, 14-3-3, S-100b and PRNP sequencing. Neuropathological findings were also studied where available. We compared young individuals (≤50y age of onset) to older patients.

Results: 47 young individuals (4%) were identified (age at onset 25–50) from a total of 1,178 cases. 14 were autopsy-confirmed. Psychiatric disturbance at presentation (36.2% vs 22%, p=0.03) and longer disease duration (by 46 days, 95% CI 15–88, p<0.01) were commoner in this group. CSF RT-QuIC showed lower sensitivity (82% vs 93%, p=0.02) in younger individuals. There was no difference in the sensitivity of MR brain, CSF 14-3-3, S100b, or EEG. There were no significant neuropathological differences in autopsy confirmed cases.
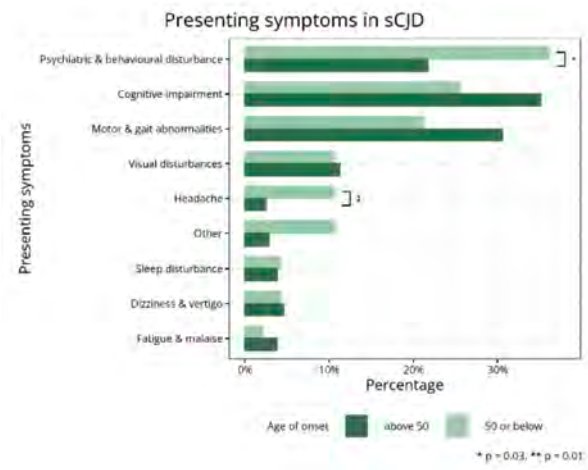
Kaplan-Meier survival curves comparing age of onset at 50 or below and above 50. Logrank test p = 0.007
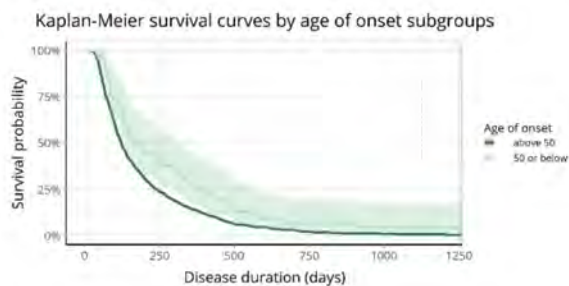
Barplot showing presenting symptoms in sCJD by age of onset at 50 or below and above 50.

Conclusion: Younger individuals with sCJD are more likely to present with neuropsychiatric symptoms, longer disease duration, and lower sensitivity of RT-QuIC.

Disclosure: The UK NCJDRSU is funded by the Department of Health and Social Care Policy Research Programme and the Government of Scotland. ("The National CJD Research and Surveillance Unit (NCJDRSU)", PR ST 0614 00008_18). The views expressed in this publication are those of the author(s) and not necessarily those of the Department of Health and Social Care or the Government of Scotland. The work conducted by the NCJDRSU depends heavily on the cooperation of neurologists and other referring clinicians as well as neuropathologists throughout the UK. We are grateful for their cooperation while delivering an altered service at this unusual time. We are particularly thankful to the families of patients for their cooperation. No competing interests to declare.

EPR-113

Disrupted sleep predicts poor memory performance in the non-demented elderly. A longitudinal follow-up study.

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Background and aims: In the wake of demographic change, identifying risk factors for dementia has become a major priority. A growing body of evidence suggest a reciprocal relationship between sleep and neurodegeneration. The aim of this study was to assess whether sleep was a significant predictor of future cognitive performance in the elderly.

Methods: We included 28 community-dwelling elderly (age >50 years), patients with Mild Cognitive Impairment (MCI, n=10) and Subjective Cognitive Decline (n=5), as well as healthy elderly (HE, n=13). Sleep was assessed using an actigraphy device wrist-worn for a minimum of 11 (median 14) consecutive days/nights. Cognitive performance was evaluated using a neuropsychological test battery and normed for age, sex, and education. Follow-up was approximately 18 months later. Linear regression models were estimated, unadjusted and adjusted for baseline cognition and the Lifestyle for Brain Health index (a risk score for cognitive decline). Analyses were corrected for multiple testing using Bonferrroni-Holm.

Results: Sleep efficiency (SE, ρ<.01), Wake after Sleep Onset (WASO, ρ<0.01) and Fragmentation Index (FI, ρ<0.01) predicted follow-up memory performance, in both unadjusted and adjusted models. There was no association with any other cognitive domain (attention, language, executive functions).

Conclusion: In community-dwelling elderly, reduced SE, longer WASO and higher FI were associated longitudinally with poorer memory performance. The results contribute to the evidence for disturbed sleep as risk factor for cognitive decline.

Disclosure: This study was supported by the Scientific Fund of the Mayor of the City of Vienna (project #15171) granted to S. Seidel.

EPR-114

Progranulin peripheral levels: a reliable screening test to identify patients with progranulin mutations

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Background and aims: Mutations in the progranulin gene (GRN) are associated with different clinical phenotypes, mainly frontotemporal dementia (FTD) and eventually Alzheimer's disease (AD). GRN mutations cause disease through haploinsufficiency, leading to low levels of progranulin, both in the central nervous system and peripherally. In 2014, we implemented in our centre the measurement of progranulin peripheral levels (progranulin-PL), as a screening method for patients with GRN mutations.

Objective: To evaluate the value of progranulin-PL as a screening test in a wider cohort of patients both in the spectrum of FTD and AD.

Methods: We included 258 patients within four groups: Mild Cognitive Impairment-due to AD (MCI-AD) (n=19) and AD-dementia (n=106), with confirmatory biomarker profile (Albert, 2011; McKhann, 2011); sporadic and genetic FTD (n=104) including GRN mutation-carriers (FTD-GRN) (n=29), according to international criteria (Rascovski, 2011). Using the previously established progranulin-PL cut-off (23.6 ng/ml), we evaluated sensitivity and specificity of this marker in the whole cohort and the following sub-groups: patients aged ≤65 (n=221), patients with FTD (n=133) and patients with genetic forms of FTD (n=45).

Results: Mean age was 60.03±7.39, with 53.5% female. The sensitivity and specificity of progranulin-PL to identify FTD-GRN were 100% both in the whole cohort and in the 3 different sub-groups evaluated.

Conclusion: Progranulin-PL are an excellent screening tool for the presence of GRN mutation, even to distinguish it from other genetic forms of FTD, supporting its importance as a disease biomarker. It also supports its possible role in the expanding field of targeted treatments already available for patients with FTD-GRN.

Disclosure: The authors report no disclosures relevant to this presentation.

EPR-115

Sleep-disordered breathing is associated with the absence of an ischemic penumbra in acute wake-up strokes

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Background and aims: In Wake-up strokes (WUS) the presence of an ischemic penumbra (critically hypoperfused but potentially salvageable brain tissue) is decisive for the indication of acute reperfusion therapy. The evolution of the penumbra mainly depends on the duration of ischemia and on the collateralisation, while the possible effects of sleep disordered breathing (SDB) are unknown. The aim of this study was to assess the impact of SDB on the penumbra in WUS in the actual night of stroke.

Methods: This is a sub-study of the observational Sleep Deficiency and Stroke Outcome cohort study. All Acute WUS (admission/perfusion-imaging <24h after stroke onset) and a control-group of acute non-WUS, matched for age, gender, stroke- and SBD-severity were selected. SDB was assessed acutely in the first days after stroke. The presence of a penumbra was determined as a dichotomous variable using acute imaging data. Multivariable logistic regression models were used to evaluate the association between SDB and the presence of a penumbra.
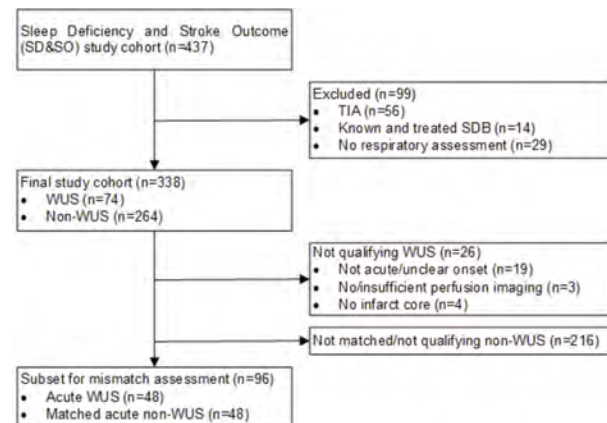
Study flow chart

Results: Among 338 stroke patients 74 (22%) had WUS. 48 WUS were acute and qualified for this analysis. WUS and non-WUS showed no difference in SDB severity (apnea-hypopnea-index (AHI) 7.4/h in WUS vs. 8.7/h in non-WUS, p=0.69). However, only in WUS a higher AHI was associated with a missing penumbra (median AHI: WUS 7.8/h vs 2.9/h, p=0.004; non-WUS: 6.7/h vs. 8.4/h, p=0.63). These results remained significant after adjustment for potential confounders (p=0.032).
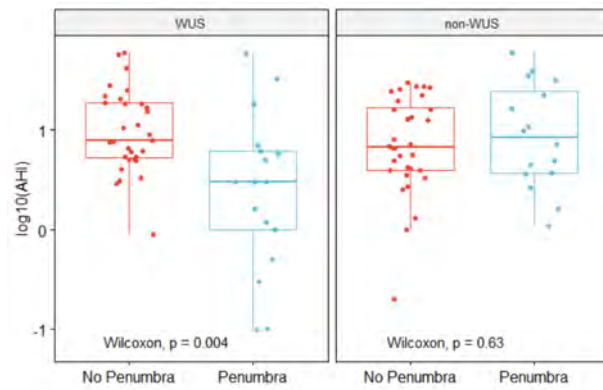
Box-plot of the Apnea-hypopnea-index (AHI) according to the presence of an ischemic penumbra in WUS and non-WUS.

Conclusion: Our results suggest a detrimental effect of SDB on the ischemic penumbra of WUS in the actual night of stroke.
Disclosure: Supported by Swiss National Science Foundation (SNF) Grant 320030_149752

Cerebrovascular diseases 1

EPR-116

Treatment of acute ischemic stroke patients outside dawn and defuse-3 criteria: a real-world retrospective analysis.

A. Ciacciarelli [1], E. Nicolini [1], I. Berto [1], M. De Michele [1], A. Falcou [1], M. Di Mascio [1], S. Lorenzano [1], L. Petraglia [1], O. Schiavo [1], N. Caracciolo [1], D. Toni [1]
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Background and aims: Mechanical thrombectomy (MT) in late time window is proved to be effective in acute ischemic strokes (AIS) fulfilling the selection criteria of DAWN and DEFUSE-3 trials. We aimed to evaluate safety and effectiveness of MT performed in patients with large vessel occlusion (LVO) not satisfying DAWN or DEFUSE-3 criteria.

Methods: We retrospectively included patients with AIS with anterior circulation LVO presenting between 6–24h from last time known well and treated with MT. We grouped cases based on the compliance with DAWN and/or DEFUSE-3 criteria and collected clinical and neuroimaging data. A comparison analysis was conducted. Primary outcome was functional independence at 90-days (mRS 0–2).

Results: Of 88 patients included (44.3% male, mean age 73+-13y), 56 (63.6%) did not fulfill DAWN, 45 (51.1%) did not fulfill DEFUSE-3, and 38 (43.2%) did not fulfill either DAWN or DEFUSE-3 (nD–nD3) criteria. Among nD-nD3 patients, 17 (44.7%) reached functional independence at 3-months compared to 19 (38.0%) fulfilling DAWN or DEFUSE-3 (p=0.524). nD-nD3 patients with good outcome were younger (63±14y vs 79±11y, p<0.001) and had lower baseline NIHSS (6+-6 vs 15±6, p<0.001) compared to those with poor outcome. However, sICH occurred more frequently in nD-nD3 patients than in those who met the criteria (18.4vs2%, p=0.008).
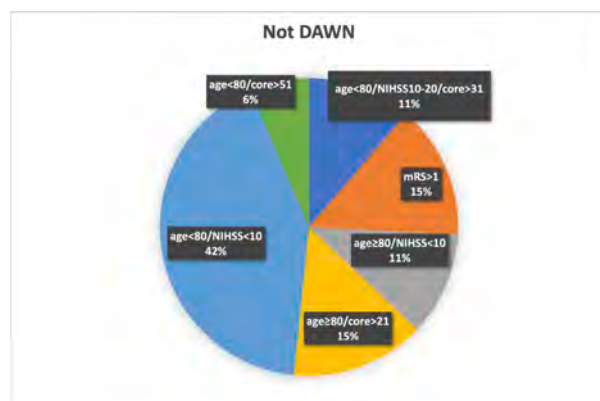
Reasons of exclusion from DAWN criteria
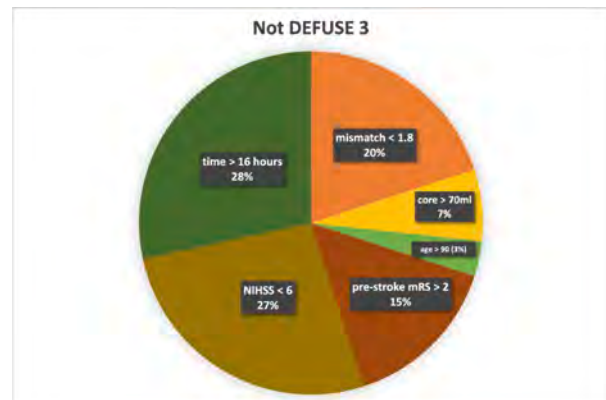
Reasons of exclusion from DEFUSE-3 criteria
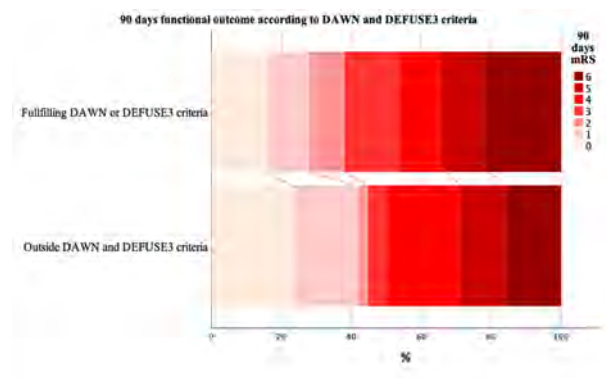
90 days mRS between patients fulfilling DAWN or DEFUSE-3 and patients outside DAWN and DEFUSE-3 criteria

Conclusion: In our cohort of patients who were outside DAWN or DEFUSE-3 inclusion criteria, MT was effective, especially in younger subjects and in those with lower NIHSS. Age and NIHSS should be considered when treating patients not fulfilling DAWN or DEFUSE-3 with MT in late time windows.

Disclosure: Nothing to disclose.

EPR-117

The importance of the magnitude of right-to-left shunt in PFO mediated stroke

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Background and aims: The RoPE score (risk of paradoxical embolism) aims to quantify the patent foramen ovale (PFO) contribution to the stroke etiology. Besides clinical information, anatomical and physiological aspects of the PFO are not accounted for in this score. We aimed to investigate if these characteristics increase the likelihood of its relevance, by evaluating the relationship between right-to-left shunt (RLS) magnitude, quantified by microembolic signals detection with transcranial doppler (MES-TCD), and the likelihood of its causality in stroke, quantified by the RoPE score.

Methods: We collected demographic and clinical data of patients admitted to a tertiary hospital between 2017 and 2020 for suspected stroke that underwent MES-DTC. Spearman's correlations were performed with SPSS®.

Results: We included 256 patients (43.8% female, median age 53.5 years). A RLS was detected in 48.4% of MES-TCD and 44.0% of transoesophageal echocardiograms and was positively concordant in 70 patients (62.5%). Its magnitude was greater after the Valsalva manoeuvre (VM) (<10 microsignals: 18.8% / 18.4%; 10-20 microsignals: 5.9% / 6.4%; shower effect: 11.3% / 14.0%; curtain effect: 2.3% / 5.2%). In younger patients (<50), a correlation between a high-grade shunt, after VM, and a greater RoPE score, was evidenced (r=0.414, p=0.028). No other correlation was noted.

Conclusion: The magnitude of RLS was associated with greater RoPE scores in younger people, after VM, suggesting its relevance to the PFO in that group. Quantification of RLS magnitude should be considered when evaluating patients for PFO closure.

Disclosure: Nothing to disclose.

EPR-118

How good are neurologists? A prospective observational study assessing the accuracy of neurologists in emergency rooms

C. Schankin [1], B. Popa-Todirenchi [1], S. Eich [1], M. Branca [2], A. Galimanis [1], M. Beyeler [1], N. Belachew [3], M. Heldner [1], J. Kaesmacher [3], T. Meinel [1], H. Mattle [1], M. El-Koussy [3], U. Fischer [4]
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Background and aims: In the emergency room (ER), swift and correct diagnosis in patients with acute neurological deficits is crucial. The aim of this study was to assess the accuracy of neurologists making the correct clinical diagnosis in the ER based solely on clinical grounds.

Methods: In this monocentric prospective observational study, neurologists at three different stages of their career (board-certified neurologists, residents and last year medical students) committed to a specific diagnosis of an acute neurological deficit including lesion location and affected blood vessel. The primary outcome was the accuracy of the first clinical diagnosis in the ER using the discharge diagnosis as reference.

Results: Of 800 patients with suspected stroke, 588 had emergency MRI, 175 CT, and 37 both. Vascular pathology was found in 567 patients (76%, 508 ischemia/TIA, 59 haemorrhagic strokes); non-vascular pathologies were epileptic seizures in 72 patients, migraine attacks in 33 patients, and others in 128 patients. Intracranial vessel occlusion was present in 227 of 410 patients with ischemic stroke. Compared to residents, neurologists were significantly better in predicting (i) vascular pathologies (accuracy 0.86 [95%CI: 0.83–0.89] vs. 0.79 [0.76–0.82]; p<0.001), (ii) presence of occlusion, (iii) the lesion territory, and (iv) the affected blood vessel. Compared to students (accuracy 0.80 [0.74–0.86]), neurologists were also better, however the difference was not significant (p=0.098), probably due to the low number of students involved.

Conclusion: Neurologists have a high accuracy in predicting vascular pathologies in patients with acute neurological deficits. Trained neurologists are therefore crucial to triage patients with acute neurological deficits in ERs.

Disclosure: Nothing to disclose.

EPR-119

Deep learning model for predicting prognosis in patients with acute stroke

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Background and aims: Prediction of functional outcome after ischemic stroke may be useful for treatment decision. We aimed to predict a 3-month functional outcome using a deep learning model that combines clinical features and neuroimaging features.

Methods: The derivation cohort included 4,445 patients, and the external validation cohort included 114 patients diagnosed with acute ischemic stroke. We applied convolutional neural network (CNN) to extract neuroimaging features (Model A), and selected the most important clinical features using a classical machine learning model (Model B). And finally, by merging the neuroimaging features and the clinical features, ensemble model was developed (Model C). Unfavorable outcome was defined as modified Rankin Scale score 3, or higher at 3 months. The performance of the model was evaluated as area under the receiving operating characteristic curve (AUC). The explainability of the model was analyzed using Gradient-weighted Class Activation Mapping (Grad-CAM)

Results: The AUC of the derivation cohort was 0.741 in Model A, 0.773 in Model B, and 0.795 in Model B. The AUCs of the external validation cohort were 0.810, 0.936, and 0.954, respectively, in models A, B, and C. Grad-CAM appeared to focus on the location of cerebral infarction lesions as well as on the eloquency area known to be associated with clinical outcome.

Conclusion: The ensemble model using neuroimaging feature and clinical feature as multimodal inputs can more accurately predict ischemic stroke outcome than models using each feature alone.

Disclosure: Nothing to disclose.

EPR-120

Blood pressure and heart rate variabilities predict future cerebro-cardiovascular events in stroke patients

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Background and aims: Blood pressure and heart rate variabilities (BPV, HRV), predict cerebro-cardiovascular risk in the general population. Considering the paucity of data in stroke patients, we assessed BPV and HRV as potential predictors cerebro-cardiovascular events (CCVE) in a series of acute stroke patients.

Methods: This project is a part of the Sleep Deficiency & Stroke Outcome Study (n=437). Assessments included demographics, stroke characteristics and medical history at admission and BPV and nocturnal HRV within the first 4 days after stroke. Recurrent stroke or transient ischemic attacks, myocardial infarction, heart failure and urgent revascularization within 3-years post-stroke were considered CCVE. Using logistic regression and survival analysis, the predictive ability of BPV (n=180) and HRV parameters (n=117) regarding cerebro-cardiovascular risk with adjustment for mean blood pressure or heart rate and cardiovascular risk factors (age, male sex, hypertension, diabetes, obesity, atrial fibrillation, sleep-disordered breathing (apnea-hypopnea index $\geq$20/h) and $\geq$1 past CCVE) were assessed. BPV and HRV parameters were presented as sample-based z-scores.

Results: A total of 21% of stroke patients developed CCVE. Both systolic blood pressure (SBP) and diastolic blood pressure (DBP) variability were associated with an increased risk of CCVE (SBP-standard deviation(SD): OR=1.70, 95% CI[1.17, 2.48], p=0.005; DBP-SD: OR=1.41, 95% CI[1.02,1.96], p=0.037) and with time to future CCVE (SBP-SD: HR=1.44, 95% CI[1.14,1.80], p=0.001; DBP-SD: HR=1.26, 95% CI[1.02,1.56], p=0.029). Among HRV metrics, only SDs from Poincaré plots predicted time to future CCVE (SD1: HR=1.26, 95% CI[1.06,1.50], p=0.008; SD2: HR=1.26, 95% CI[1.06,1.50], p=0.008).

Conclusion: In acute stroke patients BPV and, to less extent also HRV, predict future CCVE.

Disclosure: Authors have no conflict of interest to declare.

EPR-121

Cognitive functioning in the long-term period of coronary artery bypass grafting in middle-aged and older male patients

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Background and aims: Postoperative cognitive decline is associated with a decrease in surgery effectiveness and impairments in daily functioning, and is a reliable marker of unfavourable long-term prognosis. The study aimed to evaluate cognitive functioning in middle-aged and older male patients in long-term period after coronary artery bypass grafting (CABG).

Methods: A prospective, observational, cohort study was included 114 male patients with coronary artery disease (CAD). Before coronary artery bypass grafting (CABG) all the patients were divided into two groups according to the 2016 World Health Organization (WHO): 45–59 years (middle-aged) (n=76, mean age 54.0±3.99 years) and 60–74 years (older) (n=38, mean age 63.5±2.45 years). All patients underwent clinical and neuropsychological examinations before the surgery, 1 year and 5–7 years after it.

Results: It was found that older patients showed lower Frontal Assessment Battery (FAB) scores (p≤0.01) and visual-motor reaction time (p≤0.01) but not attention and short-term memory parameters, compared to middle-aged patients in the long-term CABG postoperative period. However, older patients memorized more nonsense syllables (3.2±1.03 vs. 2.7±0.96, p=0.016) in comparison to middle-aged patients, independently of time observation.

Conclusion: The results of the study do not present unambiguous evidence that older age is associated with cognitive decline in the late postoperative period in CABG patients. Middle-aged CABG patients have comparable levels of cognitive functioning in comparison to older patients. This could potentially have adverse consequences on their cognitive function in the future.

Disclosure: The authors declare that they have no conflicts of interest. This study was supported by the Russian Foundation for Basic Research, project № 19-29-01017.

EPR-122

Diagnostic work-up of acute headache and subarachnoid haemorrhage in a Norwegian population

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Background and aims: Acute headache may be the primary symptom of subarachnoid haemorrhage (SAH). Therefore, patients with hyperacute headache are usually admitted to hospital for further investigations. The standard diagnostic evaluation in Norway is history taking, non-contrast head computer tomography (CT) scan and if no findings on CT, a lumbar puncture 12 hours after onset of headache. The purpose of this study was to describe the diagnostic work-up and clinical characteristics of an unselected population with acute headache and non-traumatic SAH. Further to describe the diagnostic properties of cerebrospinal fluid (CSF) spectrophotometry and xanthochromia for detecting SAH.

Methods: A retrospective cross-sectional study conducted at Akershus University Hospital, a large primary hospital serving roughly 10% of the total Norwegian population. Diagnostic work-up and reports from all patients evaluated for acute headache between 2009–2020 were collected. All xanthochromia reports were standardized and the same spectrophotometry and CT scanner have been used during the study period.

Results: More than 3,400 patients aged 18 to 93 years were included. The median age was 45 years and 63% were women. Approximately 7% of all admitted patients had SAH. All patients without SAH on the initial CT scan underwent a lumbar puncture 12 hours after headache onset. More clinical findings, diagnosis, outcomes and the diagnostic properties of xanthochromia for detecting SAH in this representative population will be presented at the congress.

Conclusion: In this large hospital-based study, less than 1/10 who presented with acute headache had SAH. More data will be presented at the EAN 2022.

Disclosure: No conflict of interest.

EPR-123

Abstract withdrawn

EPR-124

Comparative safety and efficacy of tenecteplase versus alteplase in acute ischemic stroke before thrombectomy

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Background and aims: Intravenous thrombolysis (IVT) with alteplase is used in eligible patients with acute ischemic stroke (AIS) before mechanical thrombectomy (MT). Tenecteplase is a genetically modified variant of alteplase with greater fibrin specificity and a longer half-life. It has recently emerged as an alternative thrombolytic agent in AIS patients with large vessel occlusion (LVO) before MT.

Methods: We prospectively evaluated patients with AIS treated with IVT and mechanical thrombectomy. Patients were treated with alteplase (0.9mg/kg) or tenecteplase (0.25 mg/kg). Safety outcomes included rates of symptomatic intracranial hemorrhage (sICH) and mortality. Efficacy outcomes included rates of recanalization, early neurological improvement at 24h (NIHSS 8 points or greater) and functional status at 90 days assessed by modified Rankin Scale.

Results: 17 AIS patients with LVO received tenecteplase and 14 received alteplase. We did not observe any sICH (0% vs. 0%). The rate of 90 days mortality (14% vs. 5.8%, ns; Figure 1) was higher in the alteplase group. Early neurological improvement was more frequent with tenecteplase (21% vs. 41%, ns). Recanalization rates (87% vs. 100%, ns) and functional independence at 90 days were similar (41% vs. 52%, ns) in both groups.
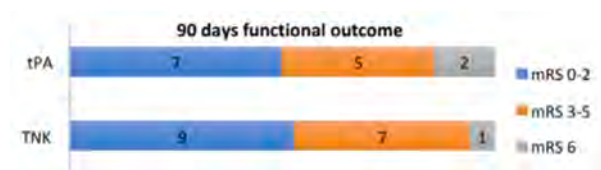
Figure 1. Functional outcomes at 90 days, showing modified Rankin Scale (mRS) of 6 (death) in 14% in the alteplase group versus 5.8% in the tenecteplase group.

Conclusion: Overall functional outcome was similar in both groups, but mortality was higher with alteplase. There were no differences in the incidence of cerebral hemorrhage. IVT with tenecteplase compared to alteplase was safe and effective before thrombectomy.

Disclosure: Nothing to disclose.

Cognitive neurology/neuropsychology & Neuropathies

EPR-125

Extending the clinical and genetic spectrum of PLEKHG5-associated neuropathies

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Background and aims: The PLEKHG5 gene, involved in the activation of the nuclear factor kappa B signaling pathway and neuronal cell differentiation, appears predominately expressed in the peripheral nervous system. Recently, mutations on this gene have been reported to be causative of autosomal recessive (AR) intermediate Charcot-Marie-Tooth (CMT) disease type C and AR distal spinal muscular atrophy type 4. We present a case of an axonal form of CMT linked to a pathogenic variant not previously reported.

Methods: Case report

Results: A 59 year-old woman born to healthy non-consanguineous parents was referred to our clinic for lower limb paraesthesia. Examination revealed left foot deformity and diminished deep tendon reflexes. Nerve conduction studies showed reduced motor and sensory potentials amplitudes, as well as chronic neurogenic changes on electromiography consistent with lower limb axonal neuropathy. During the next three years the patient developed lower limb hypoesthesia and distal weakness followed by proximal progression, and walking impairment. Lumbar MRI was normal and genetic transthyretin test was negative. Sural nerve biopsy revealed discrete axonal degeneration. A repeat nerve conduction study at age 65 showed severe axonal injury and secondary slowed motor nerve conduction velocities (>35 cm/s). Exome sequencing identified a homozygous missense variant in PLEKHG5 (c.475G>A; p.V159M) not previously reported.

Conclusion: We identified a novel homocygotic mutation in the PLEKHG5 gene in our patient, which is the first report of axonal CMT linked to this gene, broadening the genetic and phenotypic spectrum of PLEKHG5 associated neuropathies.

Disclosure: The authors declare no conflicts of interest.

EPR-126

Abstract withdrawn.

EPR-127

The involvement of social cognition in primary progressive aphasia

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Background and aims: The study investigated cognitive and affective Theory of Mind (ToM) and their neural correlates in the semantic (svPPA) and non-fluent (nfvPPA) variants of primary progressive aphasia, comparing them with the behavioural variant of frontotemporal dementia (bvFTD).

Methods: 24 PPA (12 svPPA, 12 nfvPPA) and 29 bvFTD patients at initial stages of disease matched for age, sex, education, and disease duration were recruited. Patients underwent neuropsychological assessment including the Story-based Empathy Task (SET), a non-verbal ToM test assessing intention attribution (IA) and emotion attribution (EA). Differences in SET global, IA, and EA scores, and distributions of pathological performances (based on Italian normative data) were compared across groups. Voxel-based morphometry (VBM) was used to compare differences in grey matter (GM) density between patients and 42 age-, sex-, and education-matched healthy controls. Correlations between GM density and SET scores were performed.

Results: SET scores and distribution of pathological scores did not differ across groups. VBM analyses revealed a pattern of GM reduction correlating with SET scores that overlapped across patient groups. Both in bvFTD and PPA patients, IA performance was positively associated with GM density in mid-frontal and cingulate areas, while EA performance was correlated to GM density in temporal and orbitofrontal regions.

Conclusion: ToM-related areas might be particularly vulnerable also in PPA patients, making them prone to the development of social cognition deficits even from early stages. These findings offer potential behavioral markers for diagnosis of FTLD conditions.

EPR-128

Resting state effective connectivity abnormalities of the Papez circuit and cognitive performance in multiple sclerosis

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Background and aims: The Papez circuit is central to memory and emotional processes. However, little is known about its involvement in multiple sclerosis (MS). We aim to investigate abnormalities of resting state (RS) effective connectivity (EC) between regions of the Papez circuit in MS and their relationship with cognitive performances.

Methods: 62 MS patients and 64 healthy controls (HC) underwent neuropsychological assessment, 3D T1-weighted and RS functional MRI. RS EC analysis was performed using SPM12 and dynamic causal modelling. RS EC abnormalities were investigated using parametric empirical bayes models and were correlated with cognitive scores.

Results: Compared to HC, MS patients showed (posterior probability>0.95) higher EC between the right entorhinal cortex and right subiculum, and lower EC from the anterior cingulate cortex (ACC) to the posterior cingulate cortex (PCC), from left to right subiculum, from left anterior thalamus to ACC, and within ACC and PCC. Lower RS EC from the ACC to the PCC correlated with worse global cognitive scores (rho=0.19; p=0.03), worse visuospatial memory (rho=0.19; p=0.03) and worse semantic fluency (rho=0.21; p=0.02). Lower RS EC from the left to the right subiculum correlated with worse verbal memory (rho=0.20; p=0.02), lower RS EC within the ACC correlated with worse attention (rho=-0.19; p=0.04). Higher EC from the right entorhinal cortex to right subiculum correlated with worse semantic fluency (rho=0.21, p=0.02).

Conclusion: MS patients showed altered RS EC within the Papez circuit. Reduced RS EC involving cingulate cortices and hippocampal formation contributed to explain cognitive deficits.

Disclosure: Nothing to disclose.

EPR-129

Abstract withdrawn.

EPR-130

Frontal cortico-subcortical MRI correlates of fatigue and dual-task performance in progressive multiple sclerosis

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Background and aims: Damage of frontal cortico-subcortical networks contributes to fatigue and dual-task impairment in multiple sclerosis (MS). However, the substrates underlying these clinical deficits in progressive (P) MS still need to be fully explored. We investigated the associations between structural and functional MRI abnormalities of frontal cortico-subcortical circuits and fatigue and dual-task performance in PMS.

Methods: Brain structural and functional MRI scans, modified fatigue impact scale (MFIS), single- and dual-task performances were obtained from 57 PMS patients with impaired cognitive processing speed and 10 healthy controls (HC) from 4 centers. The associations of thalamic, caudate nucleus and dorsolateral prefrontal cortex (DLPFC) atrophy, microstructural abnormalities of their connecting tracts and

their resting state effective connectivity (RS EC) with fatigue, single- and dual-task performances were investigated.

Results: Compared to HC, PMS patients had more severe fatigue (p≤0.027) and worse dual-task performance (p <0.001). Compared to those without fatigue, PMS patients with fatigue had lower RS EC from left-caudate nucleus to left-DLPFC (p=0.007). In PMS, higher MFIS-physical and MFIS-psychosocial scores were predicted by lower RS EC from left-caudate nucleus to left-DLPFC (R2=0.112, p=0.027) and higher RS EC from right-thalamus to right-DLPFC (R2=0.102, p=0.046), respectively. Dual-task motor performances were predicted by lower RS EC from left-DLPFC to left-thalamus (R2?0.137, p?0.032). Several structural MRI measures independently predicted dual-task correct response rates (R2=0.307, p=0.010) and dual-task cognitive cost (R2=0.188, p=0.002). Fatigue was not associated with single- and dual-task performances.

Conclusion: Different frontal cortico-subcortical structural and functional MRI abnormalities contribute to fatigue and single- and dual-task performance in PMS.

EPR-131
Abstract withdrawn

EPR-132
Resting state networks (RSNs) imbalance and anosognosia in Alzheimer's disease

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Background and aims: At least 60% of patients with Alzheimer's disease (AD) show anosognosia1, a symptom that can already be present in the mild cognitive impairment (MCI) phase possibly identifying a more severe phenotype of AD2-4. The neuroanatomical mechanisms underlying this symptom, are still poorly understood. We hypothesised that anosognosia in AD is associated with impaired self-related processing impinging on the Default Mode Network (DMN), one of the large-scale resting state networks (RSNs) at the basis of how the brain functions.

Methods: Patients with MCI and dementia due to AD from Oxford and Modena Dementia clinics underwent resting state functional MRI and neuropsychological assessment including the Anosognosia Questionnaire Dementia (AQ-D), which measures anosognosia as a discrepancy between the patient's and their carer's judgments. We related AQ-D scores to functional connectivity with voxel-wise correlational analyses using an independent component analysis approach.

Results: Across 78 patients, AQ-D scores negatively correlated with intrinsic functional connectivity within the DMN in the retrosplenial cortex and precuneus, over and above differences in cognitive impairment (MMSE score), age, and scan protocols (Fig.1-A). We also found that AQ-D scores positively correlated with functional connectivity within the Salience Network (SN) in the dorsal medial frontal cortex (Fig.1-B).
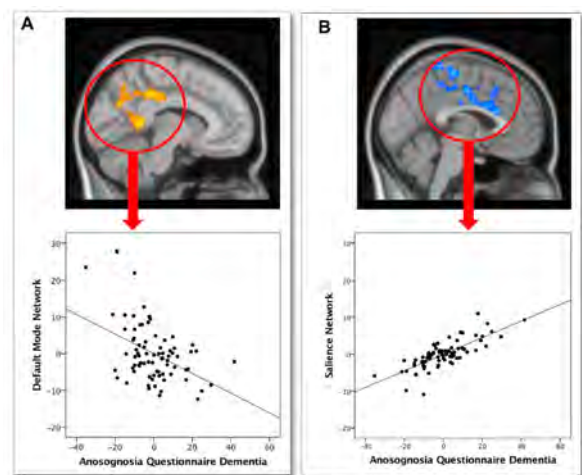
A. In orange-yellow, regions of negative correlation between Default-Mode Network functional connectivity and scores on the Anosognosia Questionnaire Dementia (AQD) | B. In blue-light blue, regions of positive correlation between Salience Network function

Conclusion: In patients with MCI and dementia due to AD lower functional connectivity within the DMN is associated with higher degrees of anosognosia irrespectively of the severity of cognitive impairment. This suggests that RSNs should be considered markers of a symptom rather than markers of a specific disease.

Disclosure: Authors declare no relevant disclosures for this study.

EPR-133

Regional brain atrophy and microstructural damage explain sex-related cognitive differences in multiple sclerosis

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Background and aims: To explore sex-related differences in gray matter (GM) volume and white matter (WM) microstructural abnormalities and their associations with cognition in people with multiple sclerosis (PwMS).

Methods: Brain 3.0 T MRI scan and Rao's battery were acquired for 287 PwMS (women=173) and 172 healthy controls (HC) (women=92). Using voxel-wise analyses, we investigated sex differences in regional GM volumes ($p<0.001$, uncorrected) and fractional anisotropy (FA) abnormalities ($p<0.05$, FWE) between PwMS and HC and their associations with cognition.

Results: In HC and PwMS, males vs females, showed a significant diffuse cortical atrophy, with larger effect of MS in males in left cingulate cortex and right precuneus. Female vs male HC and male vs female PwMS had significant higher FA in the majority of WM tracts, with a larger effect of MS in females in several WM tracts. Verbal memory was significantly worse in male vs female PwMS ($p=0.001$), whereas verbal fluency was worse in female vs male PwMS ($p=0.001$). Cognitive performance were positively associated with GM volumes and FA in most of brain regions. Female vs male PwMS showed stronger associations between cognitive performance and bilateral middle frontal gyrus and left calcarine cortex volumes and FA in several WM tracts. Male PwMS showed stronger associations between cognitive performance and right temporal pole, lingual gyrus and parahippocampal gyrus volumes, and between verbal fluency and FA in several WM tracts.

Conclusion: Sex influences the patterns of regional GM volume and WM FA abnormalities. These sex-related differences may explain heterogeneous cognitive impairment in PwMS.

Disclosure: Nothing to disclose.

Epilepsy 1

EPR-134

Efficacy of transcranial focus stimulation using the EASEE system in pharmacoresistant focal epilepsy

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Background and aims: People with pharmacoresistant focal epilepsy are in need of new neuromodulatory treatment approaches. We here report the clinical efficacy of a minimally invasive approach, focal cortex stimulation (FCS), using the EASEE System based on a meta-analysis of two prospective, first-in-man, single-arm trials.

Methods: 33 participants (18 male, 15 female, age 18–75 y, mean age 34.6 y) were implanted with a subgaleal Laplace-like electrode individually placed over the region of the epileptogenic focus connected to a pulse generator placed in the pectoral region. Unblinded stimulation consisted of intermittend 100 Hz AC stimulation and pseudo-DC stimulation for 20 min/day, 17 patients could additionally trigger ictal AC stimulation. Intraindividual effects on monthly seizure frequency were analyzed using a mixed-effects Poisson regression model.

Results: Stimulation was activated in 32 patients and performed for six months. The mean total seizure frequency declined steadily from 33.7/month at baseline to 17.3/month in month 6 (p<0.001), corresponding to a responder rate of 53.13 % (95 % CI: 34.74–70.91 %). Implantation-related adverse events mostly consisted of transient local pain at the implantation site. In the stimulation period, there were no serious adverse events considered related to the neurostimulation.

Conclusion: Data from this metaanalysis of two unblinded, prospective trials with focal cortex stimulation suggest that transcranial electrical stimulation of the epileptic focus is an effective and well tolerated new treatment approach for patients with pharmacoresistant focal epilepsy. Transcranial neurostimulation using the implanted EASEE System resulted in a statistically significant reduction in the mean seizure frequency during the final month of stimulation.

Disclosure: The presenting author has obtained research support from Precisis.

EPR-135

Insights from long-term clinical routine use of thalamic deep brain stimulation for epilepsy (MORE)

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Background and aims: Deep brain stimulation of the anterior nucleus of the thalamus (ANT-DBS) has been established as third line therapy option for refractory focal onset epilepsy. The long-term evaluation of the international multicentre Medtronic Registry for Epilepsy seeks to provide real world data to inform its routine clinical application and examine the factors that impact patient outcomes.

Methods: In the registry, 179 adult epilepsy patients with ANT-DBS therapy were followed up for safety, efficacy, and battery longevity. The follow-up ended after a maximum of five years or upon closure of the study observation phase (09/2019), with 105, 63, and 49 patients reaching their 3-year, 4-year, and 5-year follow-up (FU) visits.

Results: The median length of exposure to DBS therapy was 3.5 years. Monthly seizure frequency decreased over time, achieving a median reduction of -56% at 5-year FU (p<0.0001). At last FU, 41% were responders i.e., had a seizure frequency reduction ?50%. Better seizure outcomes were observed in those patients with unifocal epilepsy, and without previous resective epilepsy surgery. Adverse events mostly (80%) occurred within the first 2 years after implantation and included deterioration in epilepsy or seizure frequency, severity, or seizure type (31%), memory impairment (16%), depression (15%), and 5 deaths (none

ANT-DBS related). Battery depletion (Activa PC) occurred on average after 45 months.

Conclusion: The registry confirmed the improvement in seizure frequency with ANT-DBS therapy and its safe application in routine clinical practice. Although the identified outcome modifiers can help inform patient selection and management, they require further validation.

Disclosure: All authors participated in the MORE registry which was sponsored by Medtronic. (The full COI list will be provided on-site.)

EPR-136

Abstract withdrawn

EPR-137

Poststroke epilepsy after mechanical thrombectomy: clinical and imaging predictors

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Background and aims: Poststroke epilepsy (PSE) is an important long-term complication of stroke. Data regarding the frequency and predictors of PSE in patients with large-vessel occlusion stroke receiving mechanical thrombectomy (MT) are scarce. Furthermore, brain damage on post stroke MRI was not systematically considered in risk prediction of PSE. This study aims to assess PSE risk after acute stroke with MT according to clinical and MRI features.

Methods: In this bi-center study from two large tertiary stroke centers, we included consecutive acute ischemic stroke patients who had received MT for acute intracranial large vessel occlusion between 2011–2017, post-interventional brain MRI, and longterm-follow-up data. Infarct size, location, hemorrhagic complications and chronic cerebrovascular disease features were assessed on MRI.

Results: We included 1,052 stroke thrombectomy patients, 348 met the inclusion criteria (median age: 67 years, 45% women) with long-term follow of median 76 months (range 42–125). 32 patients (9.2%) developed PSE. Multivariable analysis confirmed infarct location in the area tempestas followed by larger infarct size, and presence of microbleeds as predictors, while clinical variables were not related to PSE risk.

Conclusion: In our study, patients with large vessel occlusion stroke receiving MT had a 9% risk to develop PSE after a median follow-up >6 years, which is half of the suspected risk assessed by SeLECT score. While clinical variables including the SeLECT score were not predictive, MRI is useful to identify patients at risk for PSE with infarct size, presence of microbleeds and particularly lesion location in the area tempestas as the strongest predictors.

Disclosure: None related to this study.

EPR-138

Naming fMRI-guided white matter language tract volumes predict naming decline following left temporal lobe resection

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Background and aims: The objective was to combine language functional MRI (fMRI) with fMRI-guided tractography to predict postsurgical naming decline in people with temporal lobe epilepsy (TLE).
Methods: 20 patients with unilateral TLE (10 left) were studied with auditory and picture naming functional MRI tasks. Activation maxima in the left posterobasal temporal lobe were used as seed regions for whole-brain fiber tracking. Clinical naming performance was assessed preoperatively and 4 months following anterior temporal lobe resection. Volumes of white matter language tracts in the left and right hemispheres as well as tract volume laterality indices were correlated with postoperative naming decline.
Results: In left TLE patients, larger volumes of left hemisphere white matter language tracts for both auditory and picture naming related to greater language decline. Stronger left-sided lateralization of picture naming language tracts predicted naming decline in left TLE. No correlations were seen in right TLE patients.
Conclusion: Auditory and picture naming fMRI-guided visualization of white matter language tracts can be used to predict postoperative naming decline after left temporal lobe resection in people with TLE. This can assist stratification of surgical outcome and minimize risk of postoperative language deficits in TLE.
Disclosure: Nothing to disclose.

EPR-139

Abstract withdrawn

EPR-140

Clinical course of seizures associated with autoimmune encephalitis: from acute symptomatic to chronic epilepsy

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Background and aims: This study aims to analyse the epileptic phenotypes of seizures associated with autoimmune encephalitis, assessing their clinical presentation, semiology, and paraclinical findings. Treatment options, management, development of chronic epilepsy at the long-term were also provided.
Methods: An Italian nationwide observational cohort study was retrospectively performed, enrolling patients with new-onset seizures of autoimmune aetiology. This latter was defined by the detection of antineuronal antibodies or suspected on the basis of clinical presentation and paraclinical findings.
Results: Overall, 263 patients (138 females; median age 55 years, range 4-86) were enrolled and followed-up for a median time of 30 months (range 12-120). Antineuronal antibodies were detected in 63.50% of cases. Antibody-positive patients had multiple seizure types (p=0.01) and a prevalent involvement of the temporal regions (p=0.02). A higher prevalence of episodes of status epilepticus was found in the antibody-negative patients (p<0.001). Most patients (88.60%) received immunotherapy, and 61.80% were responders. Independent predictors of a favourable outcome were early immunotherapy (p<0.001) and the detection of antineuronal surface antibodies (p=0.01). Long-term outcomes were marked by enduring seizures in 43.73% associated with cognitive and psychiatric disturbances in 81.73%. Independent predictive factors of

developing epilepsy were: more difficult to treat seizures at onset (p=0.04), with higher number of antiseizure medications prescribed (p<0.001), and poor response to immunotherapy during the acute phase (p<0.001).
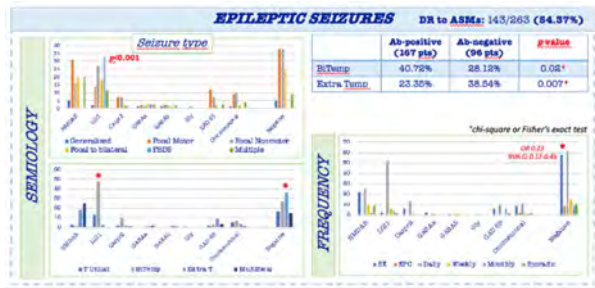
Epileptic phenotypes during acute phase
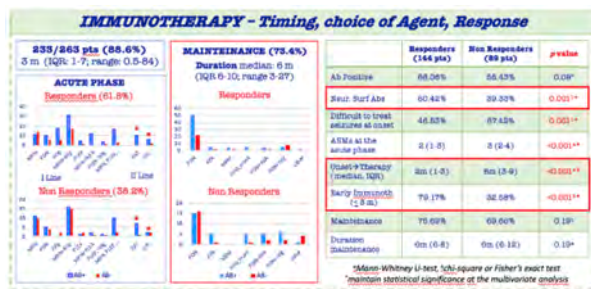
Immunotherapy: timing, agents, and response
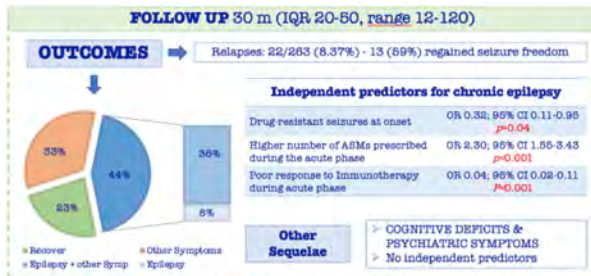
Outcomes and development of autoimmune-associated

Conclusion: An autoimmune aetiology represents a rare chance in seizures management, and an early recognition and treatment at the pathogenic level may reduce the risk of irreversible sequelae at the long-term.

Disclosure: The Authors declare that they have no conflict of interest.

EPR-141

Education increases teleneurology utilization: towards the Intersectoral Global Action Plan on epilepsy in Africa

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Background and aims: Epilepsy burden in sub-Saharan Africa (SSA) has increased dramatically in the last 20 years. People with epilepsy (PWE) are estimated to be over 20 millions, with about 1 neurologist every 3–5 millions inhabitants, meaning more than 90% of epileptic patients are managed by health workers (HW) with insufficient education in Epilepsy, and 75% of them have no access to treatments. Moreover COVID-19 pandemic is affecting epilepsy management in SSA through care disruption. Teleneurology has the potential to improve this situation, although poor education of HW is associated with its underutilization. We measured the changes of teleneurology requests from primary cares in SSA after an education program on epilepsy.

Methods: Global Health Telemedicine (GHT) offers remote advices and education to HW of the Disease Relief through Excellent and Advanced Means (DREAM) program active in 10 SSA countries. GHT-DREAM recently started an epilepsy program in Malawi and Central African Republic (CAR) with education and training courses delivered both locally and remotely.

Results: In Malawi and CAR DREAM follows 18,770 patients, 569 (3,0%) suffering from epilepsy. The total number of teleneurology requests increased from 91 in 2019 to 141 in 2020 to 802 in 2021; >90% were for PWE.
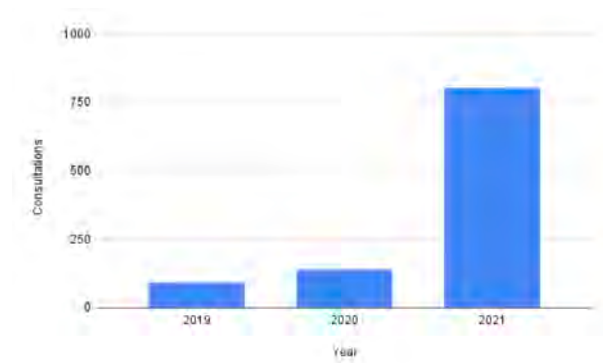
Teleconsultations through the years

Conclusion: Education and training in epilepsy increased the number of tele-requests by improving knowledge and communication between SSA HW and European neurologists. Partnerships can bring neurologists where there are none, contributing to limit COVID-19 care disruption thus reducing the treatment gap in SSA. Our results move towards the Intersectoral Global Action Plan 2022–2031 in SSA.

Disclosure: Nothing to disclose.

Headache 2

EPR-142

Natural history of nummular headache. Results in a series of 283 cases

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Background and aims: Nummular headache (NH) is a primary headache disorder, in which pain is restricted to a well-circumscribed area of the scalp, either rounded or elliptical, and sized between one and six centimeters in diameter. Since it was first described, more than 300 cases have been characterized in the literature, establishing its phenotype and giving therapeutical information. However, data regarding natural history of NH are not so far available. We aimed to describe clinical characteristics of a large series of patients with NH with a prolonged follow-up.

Methods: Prospective observational cohort and retrospective collection of the evolution of the patients. We included consecutive patients diagnosed of NH in a headache unit from January 2008 with a follow-up of at least 16 months. The sample consisted of 283 patients, of which the follow-up was completed in 212.

Results: The baseline characteristics were comparable to those previously described. Mean follow-up was 86.5 ± 37.7 months. Among the 212 patients in whom the follow-up was completed, 140 (66.0%) required preventive treatment. Regarding the evolution, 59 (27.8%) of the cases presented a spontaneous resolution, and 42 (19.8%) achieved a complete response with the treatment. Reappearance of pain was observed during follow-up in 14 (23.7%) patients with spontaneous remission and in 19 (45.2%) with complete response to treatment once it was retired.

Conclusion: Whether or not preventive treatment is required, NH usually resolves after a while. And, in that case, reappearance of pain in a long follow-up is not common.

Disclosure: Authors declare not to have any conflict of interest.

EPR-143

Vestibular signs in experimentally induced migraine attacks: a post-hoc, exploratory analysis

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Background and aims: Vestibular migraine (VM) as defined in ICHD-3 represents one of the most common vestibular syndromes, although its pathophysiology is not fully understood. The acute phase of VM is characterized by transitory oculo-vestibular signs (OVSs) that usually disappear outside of the VM attack. The difficulty to study spontaneous migraine attacks led to inconsistent results, and we believe that the adoption of human migraine models can help overcome this issue.

Methods: In this post-hoc analysis, we investigate the incidence of OVSs during experimentally induced migraine attacks in 24 episodic migraine patients without VM and 19 healthy controls exposed to sublingual nitroglycerin (NTG 0.9 mg). A comprehensive oculo-vestibular examination was performed at baseline, at migraine-like onset and before hospital discharge (180 minutes after NTG).

Results: 16 out of the 24 migraine patients developed a migraine-like attack (66.7%). Three of them (12.5%) developed OVSs during the migraine-like attack (Table 1). In line with previous results, we described a combination of central (down-beating nystagmus) and peripheral (bilateral deficit of vestibulo-ocular reflex) vestibular signs. Noteworthy, no patients with a negative induction test developed OVSs. No OVSs were detected in healthy subjects at any timepoints. Noteworthy, no subjects complained of vestibular symptoms throughout the study procedures.

Table 1 – Vestibular signs in migraine patients during the nitroglycerin induction test

Legend: Ny-Fix: nystagmus with fixation; Ny-No Fix: nystagmus without fixation; Ny-Fix-Rose: nystagmus with fixation evaluated in Rose position; Ny-No Fix-Rose: nystagmus without fixation evaluated in Rose position; SP: smooth pursuit; HST: Head Shaking Test; HIT: Head Impulse Test; TS: Test of skew and cover Test. DB: down beating nystagmus; Bil: bilateral vestibular hypofunction; ← left beating nystagmus.

Conclusion: Human migraine models may indeed be appropriate tools to evaluate the vestibular dysfunction in migraine and in VM under well-controlled experimental conditions. The present findings represent a starting point to design future ad-hoc and well-powered studies to deepen our knowledge on this topic.

Disclosure: RDI has received speaker honoraria for oral presentations from Eli-Lilly. CT has received fees for advisory boards or scientific lecturing from Allergan/AbbVie, Eli Lilly, Lundbeck, Novartis, and TEVA.

EPR-144

Is MIDAS reduction at 3 months the best indicator for erenumab treatment continuation? A real-world experience

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Background and aims: Monoclonal antibodies targeting CGRP pathway (mAbs) represent effective preventive migraine therapies, although a subset of patients fails to respond. In Italy, a 50% reduction from baseline MIDAS score (MIDASr) after three months of treatment (T3) is the gating criterion for prescribing mAbs continuation. We evaluated whether MIDASr at T3 is a reliable predictor of response to erenumab treatment at one-year in patients with chronic migraine (CM).

Methods: We enrolled 77 CM patients (78% females, age 49.8+9.5 years) who received erenumab 140 mg every 28 days for 13 treatments (T13). We prospectively collected monthly migraine days (MMD) and MIDAS scores. A logistic regression model was used to evaluate predictors to achieve a 50% reduction in MMD (MMD responder) at T13.

Results: Patients with MIDASr at T3 were 3.4 times more likely to be MMD responders at T13 (p=0.03). MMD responders at T3 were 4.5times more likely to be MMD responders at T13 (p=0.02). If we considered MIDASr at T3 alone as a predictor of response, up to 36% of future MMD responders at T13 would have been discontinued from treatment at early stages. By contrast, a lower percentage of MMD responders at T13 (16%) would be discontinued if MIDASr or MMD response at T3 were considered together (Fig.1).

Legend: MMD:monthly migraine days; MIDAS:migraine disability assessment; Responders: patients with 50% reduction of MIDAS score and/or MMD after three months of erenumab treatment (T3).
The green line depicts Responders for both MIDAS *and* MMD at T3, the blue line Responders only for MMD at T3, the yellow line Responders only for MIDAS at T3 and the red line *non* Responder at either MIDAS or MMD at T3.
Statistical analysis:
MIDAS responders vs *non* responders **p=0.342**
MMD responders vs *non* responders **p=0.001**
MIDAS *and* MMD responders vs *non* responders **p<0.001**
MIDAS responders vs MMD responders p=0.249
MIDAS responders vs MIDAS and MMD responders **p=0.039**

Figure 1 – 1-year monthly migraine days reduction according to different predictors at T3

Conclusion: MIDASr at T3 is a predictor of long-term response, but, when used as single decision-making step, it excludes nearly 40% of future 1-year erenumab responders according to migraine days. A criterion based on the combined evaluation of MIDASr and 50% reduction in MMDs at T3 may represent a more precisely predictive option.

Disclosure: RDI received speaker honoraria from Eli-Lilly. CT and GS received honoraria for advisory boards or oral presentations from: Allergan, Eli-Lilly, Novartis, TEVA & Lundbeck and from Eli-Lilly, Novartis, TEVA & Lundbeck, respectively.

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EPR-145

Primary headache disorders in Adolescents in North- and South Tyrol: Findings of the EVA-Tyrol Study

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Background and aims: Assessment of the prevalence of primary headache disorders, associated risk factors and use of acute/preventive medication in a representative large sample of adolescents.

Methods: Within the EVA-Tyrol project, a community-based non-randomized controlled cross-sectional study, data was collected from adolescents aged 14–19 years from 45 sites across North-, East- and South Tyrol. Characteristics of headaches and information about the use and the category of acute medication were collected by trained headache specialists in structured face-to-face interviews. Headaches were classified in line with the latest ICHD-3 diagnostic criteria.

Results: Of 1,923 participants 930 (48.4%) reported having headaches. Female to male ratio was 2:1. Migraine, tension-type headache and other headache were diagnosed in 10%, 30.2% and 8.2% respectively. Infrequent headaches were reported by 22.8%, episodic headaches by 65.5% and chronic headaches by 11.9% of the adolescents. Medication overuse was diagnosed in 3.4%, increasing up to 21.7% in participants with chronic headache. The use of preventative medication was not reported by any adolescent. Sleep disturbances (p=0.014), regular alcohol consumption (p=0.014), low physical activity (p=0.001) and high screen time exposure (p=0.004) were associated with an increased risk of headaches. Only 1.9% with chronic headaches reported poor health, whereas 63.0% and 11.0% of those within the highest headache frequency category still rated their health as good and excellent, respectively.

Conclusion: We report high prevalence of primary headache disorders and medication overuse in a large community-based sample of teenagers. Promoting health education in teenagers and encouraging public awareness, including that of health care providers is pivotal.

Disclosure: No potential conflict of interest to declare.

EPR-146

In-depth profiling of chronic migraine phenotype via peripheral biochemical markers

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D. Martinelli [2], A. Putortì [2], G. Sances [1], R. De Icco [2],
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Background and aims: Chronic migraine with medication overuse (CM-MO) represents one of the most disabling phenotypes across the migraine spectrum. The progression from episodic migraine (EM) to CM is still an unclear process. The aim of this study is to better define the phenotype of CM-MO by means of peripheral biochemical markers and specific clinical features.

Methods: We enrolled 13 CM-MO patients, 21 EM patients and 17 healthy controls (HC). In all subjects, we evaluated the expression of miR34a-5p and miR-382-5p in peripheral blood mononuclear cells (PBMC), and plasma levels of CGRP and PACAP. Furthermore, we considered the clinical/demographic features and the psychological profile of migraineurs. CM-MO group was also tested 2 months after an in-hospital detoxification protocol.

Results: CGRP and PACAP levels, miR34a-5p and miR-382-5p expression were higher in CM-MO group when compared to EM and HC (p<0.05 for all comparison). Headache frequency positively correlated with CGRP (Spearman's rho: 0.559, p=0.030), PACAP (Spearman's rho: 0.563, p=0.001) and miR-34a-5p (Spearman's rho: 0.496, p=0.003). Depression was prevalent in the CM-MO patients when compared to EM group (61.5% vs 33%, p=0.001). Personality disorders and anxiety were equally distributed between the two groups. In the CM-MO group tested 2 months after detoxification, we found decreased CGRP and PACAP levels (p=0.031 and p=0.008, respectively), as well as a reduction of miR34a-5p expression (p=0.004).

Conclusion: Our findings outline a specific biochemical phenotype for CM, which is, at least partially, influenced by MO. Further analyses will evaluate the association of biochemical markers with the psychological profile of these patients.

Disclosure: No conflicts of interest to declare.

EPR-147

Sustained benefit of monthly erenumab versus daily oral preventives in episodic migraine patients from APPRAISE study

R. Gil-Gouveia [1], D. Dolezil [2], K. Paemeleire [3], A. Stepien [4], P. Stude [5], C. Lopez [6], T. Stites [7], S. Ritter [7], C. Pisal [8], J. Snellman [9], M. Ferraris [9], P. Pozo-Rosich [10]
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Background and aims: APPRAISE is a global, prospective, randomised, open-label study comparing the sustained benefit of monthly subcutaneous erenumab with the standard of care daily oral preventives in episodic migraine (EM) patients.

Methods: Adults aged ≥18 years (n=621) with EM who had failed 1 or 2 previous migraine preventives due to lack of efficacy and/or tolerability were randomised (2:1) to monthly erenumab (70 mg or 140 mg) or a daily oral preventive. Switching within each arm was allowed (erenumab dose change or switch oral preventives approved locally). The primary, composite, endpoint was proportion of patients who completed the assigned treatment and achieved ≥50% reduction from baseline in monthly migraine days (MMD) at Month 12. Secondary endpoints were change in cumulative mean MMD from baseline for patients on the initially assigned treatment, proportion of patients completing the study on the initially assigned treatment and patient assessment of the change in clinical status from baseline measured by Patient Global Impression of Change (PGIC) scale at Month 12 on initially assigned treatment.

Results: A significantly higher proportion of patients stayed on the initially assigned treatment and achieved ≥50% MMD reduction from baseline with erenumab than oral preventives (56.2% vs 16.8%; p<0.0001) (Figure 1). Compared to oral preventives, erenumab treatment significantly reduced the mean MMD at each time point through Month 12 (p<0.001; Figure 2), which was also reflected in patient retention and PGIC results (Table 1).
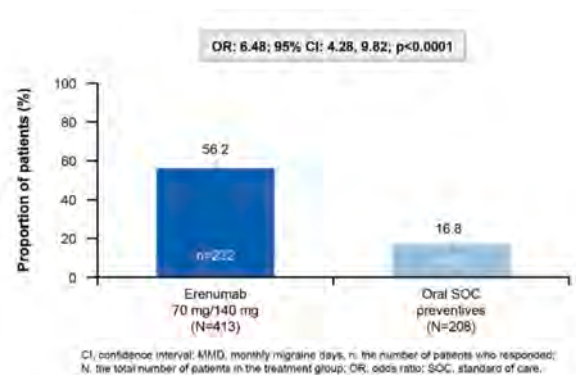
Figure 1. Proportion of patients who completed assigned treatment and achieved >=50% reduction in MMD at Month 12
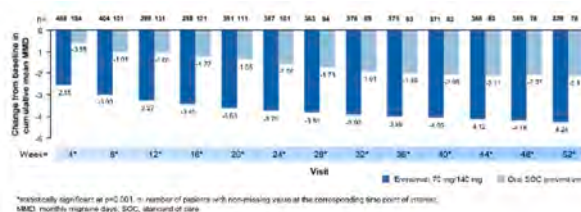
Figure 2. Change in cumulative mean MMD from baseline through Month 12 on initially assigned treatment

Treatment group	n/N (%)	Comparison (erenumab 70 mg/140 mg versus oral SOC preventives) OR (95% CI); p-value
Patient retention*		
Erenumab 70 mg or 140 mg	359/413 (86.9)	11.27 (7.53, 16.87); <0.0001
Oral SOC preventives	78/208 (37.5)	-
Proportion of patients achieving relevant clinical improvement† (PGIC)		
Erenumab 70 mg or 140 mg	314/413 (76.0)	13.75 (9.08, 20.83); <0.001
Oral SOC preventives	39/208 (18.8)	-

*Proportion of patients completing the study at Month 12 on the randomised treatment. †Patient is considered as responder if PGIC score is ≥5 at Month 12 on initially assigned treatment where score 5=moderately better, 6=better, 7=a great deal better.
CI, confidence interval; n, the number of patients who responded; N, total number of patients in the treatment group; OR, odds ratio; PGIC, Patients' Global Impression of Change; SOC, standard of care.

Table 1. Secondary endpoints: Proportion of patients completing the study and patient assessment of change in clinical status at Month 12

Conclusion: Erenumab showed sustained superior efficacy compared with oral preventives in patients with EM who had previously failed 1 or 2 migraine preventives.

Disclosure: Novartis Pharma AG, Basel, Switzerland, funded this study. Erenumab was codeveloped by Amgen and Novartis. Author disclosures will be included in oral presentation.

EPR-148

Effectiveness and safety of CGRP-mAbs in menstrual related migraine: a real-world experience

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Background and aims: Menstrual related hormonal fluctuations represent the most common migraine trigger. Menstrual migraine attacks are consistently referred as more disabling, less responsive to symptomatic treatments, longer in duration, and more prone to relapse than non-menstrual migraine attacks. Estrogen fluctuations are involved in migraine attacks worsening during the perimenstrual window through several mechanisms directly or indirectly involving the CGRP pathway. We evaluated whether mAbs blocking CGRP-ligand or receptor (CGRP-mAbs) could represent an effective and safety strategy for menstrual migraine attacks in patients with menstrual related migraine (MRM) with previous treatment failures.

Methods: 40 patients with MRM with at least three previous treatment failures received monthly CGRP-mAbs. At baseline and after six CGRP-mAbs administrations, patients underwent to extensive interviews to assess frequency, duration, intensity and responsiveness to pain-killers intake of migraine attacks occurring during the perimenstrual window.

Results: After 6 administrations of CGRP-mAbs, we observed a reduction of menstrual migraine frequency (from 5 to 2 days per month), pain intensity (from 8/10 to 6/10) and attacks duration (from 24 hours to 8 hours) ($p<0.001$). Nevertheless, a significant increase in the percentage of responding to migraine pain-killers was observed from 42.5% at baseline to 95% at T1 ($p<0.001$).

Conclusion: CGRP-mAbs could represent a safety and effective preventive therapeutic strategy able to reduce the disabling burden of menstrual migraine attacks frequency, duration, intensity and significantly improve the response to painkillers. These findings could be related to, and further indirectly prove, the greater influence of CGRP-mediated mechanisms in the pathophysiology of menstrual migraine attacks.

Disclosure: I have nothing to disclosure.

Motor neurone diseases 1

EPR-149

Brain 18Fluorodeoxyglucose-Positron-Emission Tomography changes in Amyotrophic Lateral Sclerosis with TARDBP mutations

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Background and aims: We aimed to assess the brain metabolic changes of ALS with TARDBP mutations compared to ALS patients without mutations in SOD1, TARDBP, FUS, and C9ORF72 genes (control ALS), performing 18F-FDG-PET.

Methods: We included 14 patients carrying the p.A382T TARDBP mutation (TARDBP-ALS), 40 healthy controls (HC), and 46 ALS patients without mutations in SOD1, TARDBP, FUS, and C9ORF72 (control ALS). We excluded patients with Frontotemporal Dementia. We used the full factorial design in SPM12 to evaluate whether differences among groups exist overall. In case the hypothesis was confirmed, group comparisons were performed through the two-sample t-test model of SPM12.

Results: The full factorial design resulted in a significant main effect of groups. We identified a relative hypometabolism in TARDBP-ALS in the right precentral and postcentral gyrus, superior and middle temporal gyrus and insula, compared to control ALS. We found a relative hypometabolism in TARDBP-ALS compared to HC encompassing bilateral frontal, parietal, temporal, and occipital regions. Control ALS patients showed relative hypometabolism of frontal, temporal, and occipital cortices compared to HC.
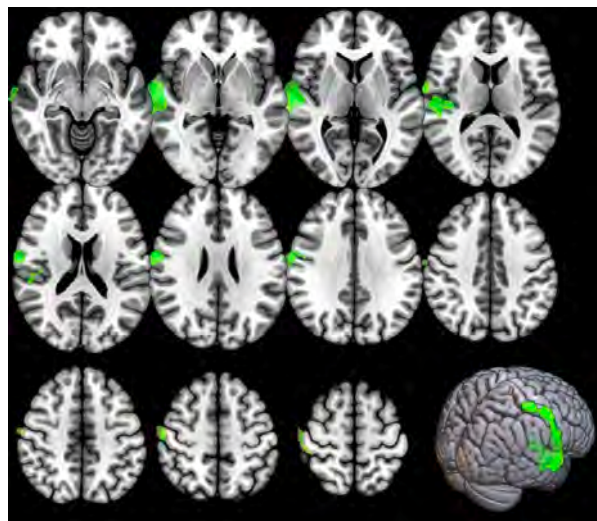
Figure 1: TARDBP group versus control ALS group. The regions showing a statistically significant relative hypometabolism in the TARDBP-ALS group as compared to the control ALS group are marked in green.

Conclusion: We found a significant relative hypometabolism in TARDBP-ALS cases compared to control ALS patients in motor and extramotor regions. Further studies including mutations other than the p.A382T might also provide a more exhaustive picture of brain metabolic changes associated with TARDBP-ALS.

Disclosure: Prof. Calvo has received a research grant from Cytokinetics. Prof. Chiò serves on scientific advisory boards for Mitsubishi Tanabe, Roche, Biogen, Cytokinetics, Denali Therapeutics, Amylyx, and AveXis. All other authors declare no competing interests.

EPR-150

Pallidal functional connectivity changes are associated with disgust recognition in pure motor ALS

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Background and aims: To investigate the resting-state functional connectivity (RS-FC) of the globus pallidus (GP) in patients with amyotrophic lateral sclerosis (ALS) compared to healthy controls, and the relationship between RS-FC changes and disgust recognition.

Methods: 26 pure-motor ALS patients and 52 controls underwent RS functional MRI and a neuropsychological assessment including the Comprehensive Affect Testing System (CATS). In all subjects, a seed-based RS-FC analysis was run between left and right GP and the rest of the brain, and was compared between groups. Correlation analyses were run between RS-FC significant changes and subjects' performance in recognizing disgust.

Results: In ALS compared to controls, the seed-based analysis showed: reduced RS-FC between bilateral GP and bilateral middle and superior frontal and middle cingulate gyri, and increased RS-FC between bilateral GP and bilateral postcentral, supramarginal and superior temporal gyri and Rolandic operculum. Decreased RS-FC was further observed between left GP and left middle and inferior temporal gyri and bilateral caudate; increased RS-FC was also shown between right GP and left lingual and fusiform gyri. In patients and controls, lower performance in recognizing disgust was related with reduced RS-FC between left GP and left middle and inferior temporal gyri.

Conclusion: In pure-motor ALS patients, we demonstrated altered RS-FC between GP and the rest of the brain. The reduced left pallidum-temporo-striatal RS-FC may have a role in the lower ability of patients in recognizing disgust. These findings offer new potential markers for monitoring extra-motor progression in ALS.

Disclosure: Supported by: Italian Ministry of Health (GR-2013-02357415); European Research Council (StG-2016_714388_NeuroTRACK).

EPR-151

Diffusion tensor imaging of facial nerve as marker of subclinical brainstem impairment in spinal onset als patients

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Background and aims: Impairment of motor neurons in the brainstem is a specific feature of Amyotrophic Lateral Sclerosis (ALS). Specifically, previous studies revealed that facial nerve (FN) atrophy characterizes ALS disease. In the present study, we evaluated the impairment of the FN using a novel probabilistic tractography method in ALS patients and in particular in a subgroup of spinal onset (sALS) without symptoms/signs of bulbar involvement.

Methods: We recruited 20 incident ALS patients, among which 11 sALS without bulbar symptoms/signs, 5 sALS with bulbar symptoms/signs, and 4 bulbar-onset patients. 11 age and sex-matched healthy subjects were recruited as controls (HCs). At the time of diagnosis, all subjects underwent diffusion tensor magnetic resonance imaging. Subsequently, a probabilistic tractography of FNs was obtained using DSI-Studio Software. FNs fractional anisotropy (FA) maps of ALS patients and sALS without bulbar symptoms/signs were compared to HCs respectively using Mann-Whitney U test.
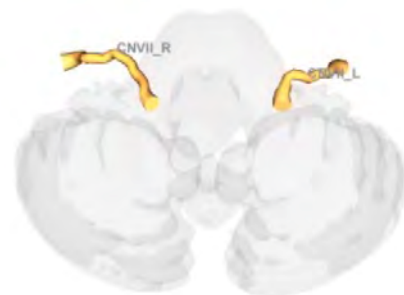
Figure: probabilistic tractography of VII cranial nerves. For visual purpose tracts were merged and represented as a single tube. CNVII_R= Facial right cranial nerve CNVII_L= Facial left cranial nerve

Results: A significant lower FA of both FNs was found in all ALS patients in comparison to HCs (p<0.001). Considering the subgroup of sALS without bulbar symptoms/signs, the significance was confirmed for both FNs versus HCs (left FN p=0.001; right FN p=0.01) S compared to HCs.

	ALS patients (n.20)	sALS patients without bulbar symptoms/signs (n.11)	Healthy controls n.11	p-value
Age (years) median (IQR range)	50 (42-60)	50 (44-60)	55 (42-65)	n.s.
Sex male/female: (Male %)	9/11 (45 %)	4/7 (31 %)	5/6 (45.5 %)	n.s.
ALSFRS-r median (IQR range)	41 (30-44)	42 (30-46)	NA	NA
Facial right cranial nerve (fractional anisotropy) median (IQR range)	0.217 (0.189-0.242)	0.218 (0.199-0.248)	0.298 (0.249-0.385)	*p< 0.001; **p= 0.01
Facial left cranial nerve (fractional anisotropy) median (IQR range)	0.203 0.189-0.239	0.203 0.191-0.243	0.291 0.249-0.385	*p< 0.001; **p=0.001

Table: Clinical and demographic characteristics of all ALS patient, spinal onset ALS patients without bulbar symptoms, healthy controls.

Conclusion: We confirmed the impairment of FNs in ALS patients, and preliminary results showed that the FA of FNs was able to detect the degeneration of this neuroanatomical structure before the appearance of clinically evaluable signs/symptoms. The data needed to be confirmed in a large population study.

Disclosure: The authors declared no disclosures.

EPR-152

Parkinsonian syndromes in motor neuron disease: a clinical and genetic study

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Background and aims: Parkinsonian syndromes may occur in motor neuron disease (MND). However, previous studies are heterogeneous and mostly case reports or small case series. Therefore, we aimed to characterize MND patients with parkinsonian syndromes extracted from a cohort of 991 consecutive cases evaluated at a tertiary MND Center.

Methods: Clinical characterization included: upper and lower motor neuron disease features, typical and atypical parkinsonian features, oculomotor disorders, cognitive testing, MRI features, and, when available, cerebrospinal fluid analysis and molecular neuroimaging. Genetic testing was carried out for four major MND-associated genes: SOD1, TARDBP, FUS, C9orf72.

Results: 16/991 patients (1.6%) showed a parkinsonian syndrome associated with MND and were categorized into ALS-parkinsonism and PLS-parkinsonism. Across the whole database, parkinsonism was significantly more common in PLS than in other MND phenotypes (13.2% vs 1.0%, p<0.001). MND patients with parkinsonian features had older age of onset, higher frequency of oculomotor disorders, cognitive impairment, and family history of parkinsonism or dementia. Two patients showed MND-associated mutations in TARDBP and C9orf72.

Conclusion: Specific patterns in MND-parkinsonism were observed, with PLS patients often showing atypical parkinsonian signs and ALS patients more frequently showing typical parkinsonism. Systematic clinical, genetic, and neuropathologic characterization may provide a better understanding of these phenotypes.

Disclosure: J. Pasquini is the recipient of a European Academy of Neurology Research Fellowship 2021 grant.

EPR-153

The value of the El Escorial Criteria

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Background and aims: In the first Edaravone trial (Abe K. et al, 2014) and later in the PRO-ACT dataset (Braun N et al. 2019) we could show that the EEC 'probable laboratory supported' category induces a bias towards slow progressors in ALS clinical trial populations. Additionally, patients in this category exhibited a significantly longer diagnostic delay. It is unclear whether this bias is only present in a clinical trial population (e.g. PROACT dataset) or in the general ALS population.

Methods: We therefore analysed prospectively entered data from ALS Progeny database from Belgium (n=411), Ireland (n=79), Italy (n=252), The Netherlands (n=623) and Switzerland (n=298). We used a linear mixed effect model with a random slope and intercept per patient and country to analyse ALSFRS-R-Score and VC changes.

Results: Diagnostic delay between EEC categories possible, probable lab supported, probable, definite (means 8.7; 9.5; 10.8; 11.5) were significantly different (p=0.005) (Fig. 1). The mean rate of decline was significantly faster with a worse EL Escorial category for the ALS FRS-R score (p<0.001) (Fig. 2) and VC (p<0.048) (Fig. 3).
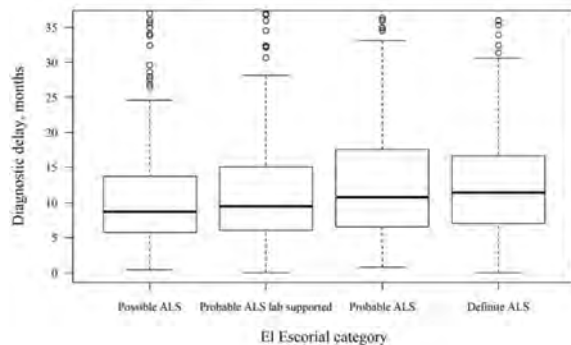
Fig. 1 –Diagnostic delay per El Escorial category; Diagnostic delay differed significantly among El Escorial categories (p=0.005).
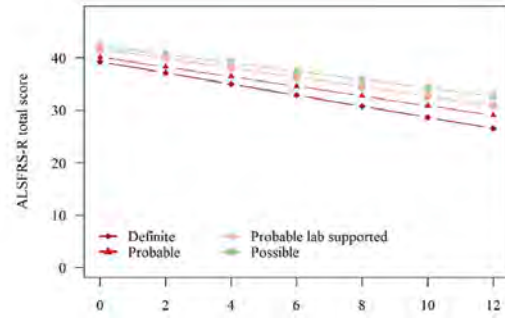
Number of patients	0	2	4	6	8	10	12
Definite	340	321	278	252	221	190	159
Probable	557	530	478	419	369	321	282
Probable lab sup	400	386	360	322	296	268	240
Possible	358	343	327	299	276	248	222

Fig. 2 - Mean rate of decline in ALSFRS-R total score per El Escorial category
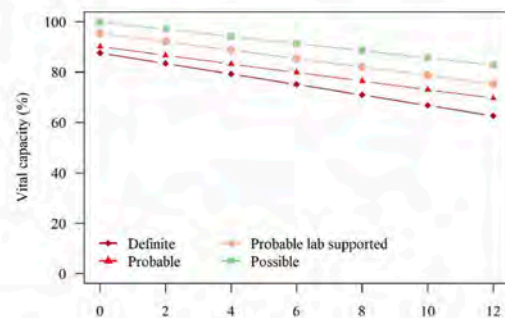
Number of patients	0	2	4	6	8	10	12
Definite	76	63	52	44	38	30	26
Probable	176	146	129	110	98	87	82
Probable lab sup	146	136	125	111	97	93	84
Possible	115	102	96	88	80	71	67

Fig. 3 - Mean rate of decline in predicted vital capacity per El Escorial category

Conclusion: The conclusion that the EEC "probable lab supported" category creates a bias toward slow progressors does not hold true in an unselected, incident ALS population. Patients belonging to this EEC category come earlier to diagnosis, which was one of the goals of the EEC revision, and should not be excluded from clinical trials. Moreover, the significantly different progression rates between EEC categories suggest they should be considered as a stratification tool for ALS clinical trials.

Disclosure: Nothing to disclose.

EPR-154

SUNFISH: 3-year efficacy and safety of risdiplam in Types 2 and 3 spinal muscular atrophy

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Background and aims: Risdiplam (EVRYSDI®) is a
centrally and peripherally distributed, oral survival of motor
neuron 2 (SMN2) pre mRNA splicing modifier approved by
the European Commission for the treatment of patients aged
≥2 months, with a clinical diagnosis of Type 1, 2 or 3 spinal
muscular atrophy (SMA) or 1–4 SMN2 copies. These
analyses aim to assess the longer-term efficacy and safety
of risdiplam in patients with Types 2 and 3 SMA.

Methods: SUNFISH (NCT02908685) is a multicentre,
two-part, randomised, placebo-controlled, double-blind
study in patients with Types 2 and 3 SMA (inclusion criteria
2–25 years at enrolment). Part 1 (n=51) assessed safety,
tolerability, and pharmacokinetics/pharmacodynamics of
different doses of risdiplam in patients with Types 2 and 3
SMA (ambulant and non-ambulant) to select the dose for
Part 2. Confirmatory Part 2 (n=180) assessed the efficacy
and safety of the Part 1-selected dose of risdiplam versus
placebo in a broad population of patients with Type 2 and
non-ambulant Type 3 SMA.

Results: In SUNFISH Part 2, total scores on the 32-item
Motor Function Measure (MFM32) increased from baseline
to Month 12 in patients treated with risdiplam; these
increases were maintained between Months 12 and 36. At
Month 36, no treatment-related safety findings leading to
withdrawal had been reported in any patient in SUNFISH.

Conclusion: SUNFISH is ongoing and will provide further
efficacy and safety data of risdiplam in a broad population
of children, teenagers, and adults with Types 2 and 3 SMA.

Disclosure: This study was sponsored by F. Hoffmann-La
Roche Ltd, Basel, Switzerland. Writing and editorial
assistance was provided by Nucleus Global in accordance
with GPP3 guidelines, and funded by F. Hoffmann-La
Roche Ltd.

EPR-155

FIREFISH Parts 1 and 2: 36-month safety and efficacy of risdiplam in Type 1 spinal muscular atrophy

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Background and aims: Risdiplam (EVRYSDI®) is a centrally and peripherally distributed, oral survival of motor neuron 2 (SMN2) pre-mRNA splicing modifier approved by the European Commission for the treatment of patients aged ≥2 months, with a clinical diagnosis of Type 1, 2 or 3 spinal muscular atrophy (SMA) or with 1–4 SMN2 copies. These analyses aim to assess longer-term safety and efficacy of risdiplam in patients with Type 1 SMA.

Methods: FIREFISH (NCT02913482) is a multicentre, open-label, two-part study of risdiplam in infants with Type 1 SMA and two SMN2 gene copies (inclusion criteria 1–7 months old at enrolment). Part 1 (n=21) assessed safety, tolerability and pharmacokinetics/pharmacodynamics of different risdiplam doses. Part 2 (n=41) assesses safety and efficacy of risdiplam at the dose selected from Part 1.

Results: In a pooled analysis (Part 1 [high-dose cohort, n=17] and Part 2 [n=41]) at Month 24, 84% of patients were alive and did not require permanent ventilation; patients continued to achieve motor milestones not observed in natural history. No treatment-related adverse events have led to withdrawal at Month 24. Here we present updated pooled safety and efficacy data on event-free survival, motor outcomes, hospitalisations and swallowing, from patients who received risdiplam at the pivotal dose for ≥36 months.

Conclusion: FIREFISH Parts 1 and 2 are ongoing globally and will provide further safety and efficacy data of risdiplam in Type 1 SMA.

EPR-156

Genetic and clinical overlap between Amyotrophic Lateral Sclerosis and Parkinson's disease Introduction

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Background and aims: Neurodegenerative disorders (NDs) are increasingly being considered as part of a continuum spectrum. Extrapyramidal features are occasionally reported in Amiotrophic Lateral Sclerosis (ALS) patients, although genetic overlap between ALS and Parkinson's disease (PD) has not been explored yet. The aim of this study is to collect clinical and genetic data from ALS patients in order to assess the presence of mutations in specific PD-related genes and their role in the resulting phenotype.

Methods: We performed the genetic analysis with Next Generation Sequencing on the DNA isolated from peripheral blood leukocytes of a cohort of 201 patients all diagnosed according to international diagnostic criteria, between 2012 and 2021. We selected a panel of 97 genes involved in NDs and performed a bioinformatic analysis. Only the most relevant genes related to PD or ALS were taken into account (Table 1). C9orf72 repeat expansion was assessed using the repeat-primed PCR assay.

ALS	PD
C9orf72	SNCA
SOD1	LRRK2
TARDBP	VPS35
FUS	PRKN
OPTN	PINK1
SQSTM1	PARK7

Table 1: List of the most relevant genes for PD and ALS analyzed in our panel

Results: 13 patients had pathogenic or of uncertain significance variants in the PD-genes analyzed, of whom five carried gene mutations in LRRK2, five in PRKN, two in PINK1 and one in PARK7 (Table 2). Four of them presented clinical extrapyramidal features. None of these patients carried mutations in ALS-related genes.

Patients	Gender	Age at diagnosis	Family History	Gene Mutation	Pathogenetic variant	ALS phenotype	Extrapyramidal symptoms
1	Female	62	Negative	LRRK2	c.3033G>A p.Glu1011Asp	Bulbar and Spinal Motoneuron	None
2	Male	74	Tremor	PRKN	c.757C>T, p.Arg402Cys	Bulbar and Spinal Motoneuron	Postural and kinetic tremor
3	Male	77	Parkinsonism	LRRK2	c.706+6G>A p.? (splicing/non coding variant)	Bulbar and Spinal Motoneuron	None
4	Female	66	Negative	PRKN	c.823C>T p.Arg275Trp	Bulbar and Spinal Motoneuron	None
5	Male	70	Negative	PRKN	c.167T>A p.Val56Glu c.1204C>T p.Arg402Cys	Bulbar and Spinal Motoneuron	None
6	Male	68	Negative	LRRK2	c.5427G>T p.Lys1809Asn	Spinal	None
7	Male	48	Negative	PRKN	c.823C>T p.Arg275Trp	Bulbar and Spinal Motoneuron	None
8	Female	89	Negative	LRRK2	c.1801+5G>A p.? (splicing/non coding variant)	Bulbar Motoneuron	None
9	Male	69	Negative	PINK1	c.587C>T p.Pro196Leu	Frontotemporal Dementia-Bulbar and Spinal Motoneuron	Akinetic-rigid parkinsonism
10	Male	74	Negative	LRRK2	c.5105T>C p.Met1702Thr	Frontotemporal Dementia-Bulbar and Spinal Motoneuron	Akinetic-rigid parkinsonism
11	Male	74	Tremor	PRKN	c.1204C>T p.Arg402Cys	Bulbar and Spinal Motoneuron	Postural and kinetic tremor
12	Female	71	Negative	PARK7	c.-24+2T>A p.? (splicing/non coding variant)	Bulbar and Spinal Motoneuron	None
13	Male	27	Negative	PINK1	c.802C>G p.Leu268Val c.770C>T p.Thr257Ile	Spinal Motoneuron	None

Table 2: Genetic analyses and clinical phenotypes of ALS patients

Conclusion: Mild extrapyramidal features are present in ALS patients and can be associated with PD specific gene mutations. No specific clinical phenotype could be associated with such variants. Our ongoing longitudinal assessment could provide more details on clinical and prognostic relevance of these mutations and on the genetic overlapping between ALS and PD.

Disclosure: Nothing to disclose.

MS and related disorders 3

EPR-157

Has the pandemic changed treatment strategy in multiple sclerosis? Insights from an Austrian registry

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Background and aims: Social distancing measures during the Covid-19 pandemic reduced access to health care and concerns were raised over the safety of immunosuppressive disease modifying treatments (DMT) for multiple sclerosis (MS). Here, we aimed to investigate changes in DMT prescription before and during the pandemic in a large and well-characterized real-world cohort of MS patients.

Methods: From the Vienna MS database (VMSD) we extracted MS patients who were initiated on a new DMT (both treatment-naïve and switching) between January 1st 2017 and December 31st 2021. Two time periods were defined: 1) the preCovid-19 era (January 1st 2017 to March 15th 2020, i.e. the day of the first lockdown in Austria) and the Covid-19 era (March 16th 2020 to December 31st 2021). Average annualized DMT prescription rates were descriptively compared between the two periods.

Results: The average annualized number of prescriptions in the preCovid-19 era was 90.3/year and dropped to 74.8/year (-17.2%) in the Covid-19 era, driven by a marked reduction to 41.7/year (-54%) in the first nine months of the Covid-19 era, partly offset by a rise to 101 in 2021. Use of alemtuzumab (-64%), antiCD20 (-49%), cladribine (-46%), and S1PM (-38%) was reduced, while natalizumab increased by 24%. Lower efficacy treatments remained stable.
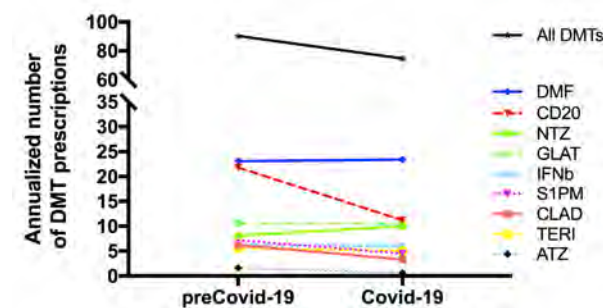
Figure 1. Change of annualized DMT prescription rate from the preCovid-19 to the Covid-19 era.

Conclusion: The pandemic coincides with a drop in DMT prescription, most markedly for immunosuppressive high-efficacy treatments, strongly suggesting the pandemic as the causal factor. If and how much this affects long-term outcome is yet to be determined.

Disclosure: Gabriel Bsteh: has participated in meetings sponsored by, received speaker and consulting honoraria or travel funding from Biogen, Celgene/BMS, Lilly, Merck, Novartis, Roche, Sanofi-Genzyme and Teva.

EPR-158

Introduction of A Connected Armband in the Neurological Examination - Beyond the Neurologist's Eye in Multiple Sclerosis

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Background and aims: Detecting early impairments in Multiple Sclerosis (MS) patients is a challenge for both care management and research. Digital biomarkers are a promising field which could bring more personalized and home-based assessments to patients. In this study, we aim to demonstrate that MYO, a connected armband can provide precise data of subtle impairments.

Methods: We conducted a prospective, open, controlled study at University Hospitals including 62 people with MS (PwMS) and 25 healthy controls who performed standard neurological tests. We studied correlation with neurological measures using Pearson's linear correlation coefficient. We also used a principal component and linear discriminant analyses in data analysis to show the potential of massive data collection in support, Support Vector Machine (SVM) classifier has allowed us to classify sEMG signals of interest to assist MS assessment.

Results: Mean values of rotation speed (rad. s-1) recorded with 3D-gyroscope captors of the MYO armband were positively correlated to EDSS scores p<0.001 for PwMS patients. sEMG correlation analysis of mean signal amplitude values and EDSS score for the anterior, lateral and posterior compartment of lower limbs respectively (p<0.001). Accelerometer analysis show a significant negative correlation of linear acceleration values between EDSS scores (p<0.001 along x, y and z axis). sEMG signal amplitudes are for the anterior, lateral and posterior muscle compartments (p<0.001).
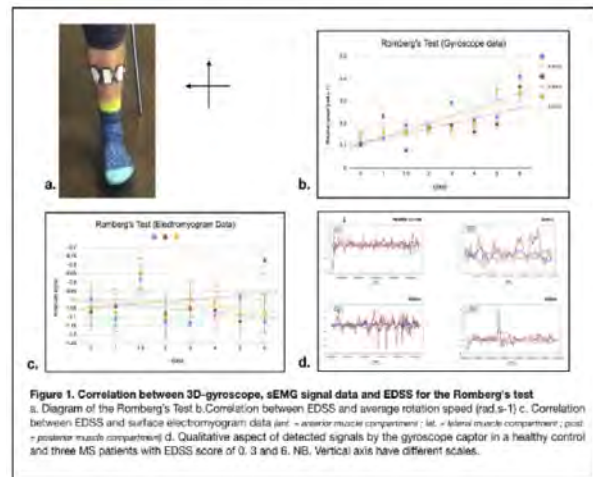
Figure 1. Correlation between 3D-gyroscope, sEMG signal data and EDSS for the Romberg's test

Conclusion: From simple linear correlations to "Big data" approach, we confirmed clinical observations and identified contraction and gait profiles in PwMS and even discriminated asymptomatic PwMS from healthy controls.
Disclosure: PA Gourraud has disclosure with AstraZeneca, Biogen, Boston Scientific, Cook, Edimark, Ellipses, Elsevier, Methodomics, Merck, Mérieux, Sanofi-Genzyme, WeData. Einar Høgestøl received honoraria from Biogen, Merck and Sanofi-Genzyme.

EPR-159

Patient reported perspectives on disease burden and early signs of progression in Germany (MSPerspectives)

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Background and aims: In clinical practice, SPMS is usually diagnosed retrospectively and the transition period is associated with a considerable period of diagnostic uncertainty. Therefore it is imperative to raise patient awareness to recognize, track and communicate subtle signs of progression early. This data collection (MSPerspectives) is aimed to comprehensively capture the personal patient perspective on the individual disease course.

Methods: From December 2020, an online survey has been collecting data from MS patients in Germany to capture their perceptions regarding MS symptoms, disability progression and impact on daily life over the past 6 months. The survey will gain insights into the patients` perspective regarding the importance of maintaining essential abilities, the burden of disease and patient expectations concerning modern MS therapy.

Results: As of Jan 5th 2022, 3519 MS patients completed the online questionnaire. At this data cut 69% had a relapsing remitting, 16% a secondary and 7% a primary progressive course. 30% of patients received the diagnosis of secondary progressive MS within the last 2 years. 68,7% of all patients received any DMT. Fatigue and gait impairment were the most bothersome symptoms. The full dataset will be available for presentation at the congress.

Conclusion: The data collection will provide personal patient perspectives on the burden of their disease, early and subtle signs of disease progression and the effects on the quality of life of patients with MS. This will help to better understand patient perspectives and disease development and possibly improve patient-physician interactions.

Disclosure: Project is funded by Novartis Pharma GmbH.

EPR-160

Long-term Outcomes With Ozanimod in the DAYBREAK Extension Trial by Number of MS Relapses During the Phase 3 Trials

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Background and aims: Early intervention with ozanimod results in control of multiple sclerosis (MS) disease activity that is maintained with long-term use. Whether long-term efficacy differs among patients with varying degrees of disease activity is unknown. We compared long-term outcomes (5–6 years) among patients who had 0, 1, or ≥2 relapses during the first 1–2 years of continuous ozanimod 0.92mg/d or intramuscular interferon β-1a 30μg/wk (IFN) followed by ozanimod 0.92mg/d.

Methods: In phase 3 "parent" trials, adults with relapsing MS were randomised to ozanimod 0.46 or 0.92mg/d or IFN for ≥12 (SUNBEAM–NCT02294058) or 24 months (RADIANCE–NCT02047734), after which they were eligible for open-label ozanimod 0.92mg/d in an extension trial (DAYBREAK–NCT02576717). Clinical and radiologic outcomes from parent-trial baseline through DAYBREAK month 48 (cutoff: Feb 2021) were compared among patients who experienced 0, 1, or ≥2 relapses during SUNBEAM/RADIANCE.

Results: There was a positive association between number of relapses during SUNBEAM/RADIANCE and annualised relapse rates (ARR) during DAYBREAK in both treatment groups. All patients with 1 or ≥2 relapses during SUNBEAM/RADIANCE had decreases in ARR during DAYBREAK (Figure 1). Regardless of number of relapses during SUNBEAM/RADIANCE, all patients who switched from IFN to ozanimod in DAYBREAK had decreases in gadolinium-enhancing and new/enlarging T2 lesion counts that were maintained through month 48 (Figures 2–3). Lesion counts in patients treated with continuous ozanimod remained low though OLE month 48 in all relapse groups.

Figure 1. Adjusted ARR by Relapse Group and Treatment During Parent Trial

Figure 1

Figure 2. Adjusted Mean Number of GdE Lesions By Relapse Group and Treatment During Parent Trial

Figure 2

Figure 3. Adjusted Mean Number of New/Enlarging T2 Lesions per Scan by Relapse Group and Treatment During Parent Trial
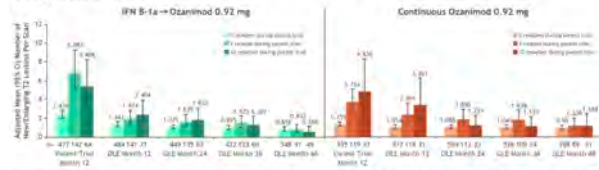
Figure 3

Conclusion: All patients, including those who relapsed during SUNBEAM/RADIANCE, experienced clinical and radiologic benefits from long-term treatment with ozanimod for up to 48 months in DAYBREAK.

Disclosure: These studies were supported by Celgene International II.

EPR-161

Longer-term Efficacy of Ofatumumab in Patients with Relapsing Multiple Sclerosis

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Background and aims: The Phase 3 ASCLEPIOS I/II trials demonstrated the superiority of ofatumumab versus teriflunomide in reducing annualised relapse rate (ARR), suppressing MRI lesion activity and delaying disability worsening while maintaining a favourable safety profile in patients with relapsing multiple sclerosis (RMS). Here, we assess the longer-term efficacy of ofatumumab treatment for up to 4 years.

Methods: Cumulative data from patients randomised to ofatumumab/teriflunomide in the ASCLEPIOS I/II trials (core study) and the ongoing, open-label, ALITHIOS extension study will be analysed (data cut-off: 25-Sep-2021). Patients randomised to ofatumumab in the core and potentially continued in the extension (continuous group) and to teriflunomide in the core with potential switch to ofatumumab in the extension (switch group) will be included. ARR, disability worsening (time-to-3-month/6-month confirmed disability worsening), disability improvement (time-to-6-month confirmed disability improvement), and brain MRI outcomes (number of Gd+T1 lesions and annualised T2 lesion rate) will be reported.

Results: Of the 1,882 patients randomised in the ASCLEPIOS I/II trials (ofatumumab/teriflunomide: 946/936), 1,367 patients enrolled into ALITHIOS (continuous/switch: 690/677; both groups, 88.8% ongoing). The Table shows baseline demographics and disease characteristics of these patients. Updated efficacy results for up to 4 years of ofatumumab treatment will be presented at the congress.

	Ofatumumab continuous (N=946)	Ofatumumab Switched from Teriflunomide (N=936)	
		Baseline from core study (N=936)	Baseline from extension study (N=677)
Age, years*	38.4±9.04	38.0±9.22	40.1±9.21
Female, n (%)	637 (67.3)	636 (67.9)	456 (67.4)
BMI, kg/m²*	25.86±6.22	25.93±6.02	25.61±5.85
Mean exposure, years*	2.9±1.31ª	1.5±0.5ᵇ	1.9±0.50ᶜ
Patient-years	2761.4ª	1397.8ᵇ	1271.1ᶜ
Treatment-naïve patients#, n (%)	386 (40.8)	363 (38.8)	NA
EDSS score at baseline*	2.93±1.35	2.90±1.36	2.81±1.45ᵈ
Number of relapses in the last 12 months prior to screening, n (%)	1.2±0.69	1.3±0.71	0.2±0.49ᵈ
Number of Gd+ T1 lesions*	1.7±4.51	1.3±3.43	0.8±2.37ᵈ
Total volume of T2 lesions, cm³*	13.72±13.8	12.55±13.8	NA

* Values are represented as mean±SD
# Treatment naïve patients are those who have not received a prior multiple sclerosis disease modifying therapy
ª Values presented are for total ofatumumab exposure in the continuous group; ᵇ Values presented are exposure to teriflunomide in core in the switch group; ᶜ Values presented are for ofatumumab in extension
ᵈ The baseline from the extension study in the ofatumumab Switch from teriflunomide group reflects the teriflunomide treatment effect during the double-blind treatment phase in the ASCLEPIOS studies.

Baseline Demographics and Disease Characteristics

Conclusion: These analyses will provide further insights on longer-term efficacy of continuous ofatumumab treatment for up to 4 years, and the effects of switching from teriflunomide to ofatumumab and add valuable information for the assessment of Ofatumumab's benefit/risk profile.

Disclosure: The study was supported by Novartis Pharma AG, Switzerland. The detailed author disclosures will be presented in the subsequent presentation.

EPR-162

Efficacy and Safety in Phase 3 EVOLVE-MS-1 After Switching from Prior MS Therapies or Continuing on Diroximel Fumarate

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Background and aims: Diroximel fumarate (DRF), a novel oral fumarate for relapsing-remitting multiple sclerosis (RRMS), is converted to the same pharmacologically active metabolite as dimethyl fumarate (DMF), with a similar safety and efficacy profile. DRF has better gastrointestinal (GI) tolerability than DMF, with fewer patients discontinuing due to GI adverse events (AEs).

Methods: EVOLVE-MS-1 (NCT02634307) is an open-label, 2-year, phase 3 study of DRF in adults with RRMS. Patients were either newly initiated on DRF, or had previously received DRF (DRF-rollover) or DMF (DMF-rollover) in the 5-week, randomised, phase 3 EVOLVE-MS-2 study (NCT03093324). This analysis evaluated safety and tolerability in patients in the DRF-rollover and DMF-rollover groups and in a subset of EVOLVE-MS-1 patients who received either glatiramer acetate (GA) or interferons (IFN) as their most recent disease-modifying treatment (GA-IFN/DRF). Efficacy was evaluated in the GA-IFN/DRF population.

Results: As of 01-Sept-2020, 1057 patients were enrolled in EVOLVE-MS-1 (DRF-rollover, n=239; DMF-rollover, n=225; GA-IFN/DRF, n=343). Baseline characteristics were generally similar across subgroups (Table 1). The DMF-rollover to DRF group had few AEs leading to treatment discontinuation (5.8%), and discontinuations due to GI AEs were low (<1%) across groups. In GA-IFN/DRF patients, annualised relapse rates (ARR) were significantly

reduced compared with the 12 months before study entry, and Gd+ lesion counts were significantly reduced at week 96 (94.3% Gd+-lesion free) versus baseline (79.4%).

Table 1. Baseline Characteristics

	Prior GA/IFN n = 343	Prior DRF n = 239	Prior DMF n = 225
Mean (SD) age, y	43.9 (10.4)	44.0 (11.0)	43.7 (9.8)
Female, *n* (%)	257 (75)	165 (69)	170 (76)
Race, *n* (%)			
White	306 (89)	220 (92)	205 (91)
Black or African American	32 (9.3)	19 (8)	16 (7)
Other	5 (1.5)	0	4 (2)
Mean (SD) BMI, kg/m^2	27.8 (6.5)	27.0 (5.9)	27.6 (6.2)
US region, *n* (%)	214 (62)	124 (52)	121 (54)
Mean (SD) time since diagnosis, y	8.9 (7.1)	7.4 (7.8)	7.8 (7.5)
Mean (SD) number of relapses in previous year	0.6 (0.7)	0.6 (0.7)	0.6 (0.7)
Mean (SD) EDSS score	2.6 (1.5)	2.6 (1.5)	2.7 (1.4)
Mean (SD) number of Gd⁺ lesions	0.8 (2.5)	0.8 (2.2)	0.9 (2.6)
Gd⁺ lesion-free, *n* (%)	266 (78)	176 (74)	159 (71)

AE adverse event, *BMI* body mass index, *DMF* dimethyl fumarate, *DMT* disease-modifying therapy, *DRF* diroximel fumarate, *EDSS* Expanded Disability Status Scale, *GA* glatiramer acetate, *Gd⁺* gadolinium-enhancing, *IFN* interferon, *IQR* interquartile range

Conclusion: Transition to DRF from GA, IFN or DMF is a reasonable treatment strategy with low discontinuation rates. GA-IFN/DRF patients experienced improvements in clinical and radiological measures of disease.

Disclosure: Supported by Biogen. Portions of this research have been submitted as a manuscript for publication in Advances in Therapy.

EPR-163

Harding disease, more than multiple sclerosis. Identification of a novel mutation m.15950G>A

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Background and aims: Harding disease is the association of multiple sclerosis (MS) with Leber hereditary optic neuropathy (LHON), a mitochondrial disease. We present a Harding disease patient harboring a novel mutation.

Methods: Whole mtDNAs were sequenced. Osteosarcoma 143B cytoplasmic hybrids (cybrids) were generated from a control and the patient to study ATP and ROS levels, oxygen consumption, respiratory complex IV and citrate synthase specific activities, respiratory complex I, II, IV and ATP synthase in gel activities, CIV p.MT-CO1 and CII SDHA subunits amount, mitochondrial protein synthesis assay.

Results: A 40-year-old woman (smoker, alcohol consumer) presented with 5 months of bilateral, subacute, sequential, painless vision loss with dyschromatopsia, and paraesthesia in lower limbs. Examination revealed mild reactive pupils without RAPD; visual acuity: hand motion (right), 0.4 (left); visual field defect: generalized (right), concentric (left); optic disc pallor; thinning of ganglion cell layer; hypopalestesia in malleoli. MRI and cerebrospinal fluid findings supported the diagnosis of MS. After methylprednisolone and plasma exchange minimal visual recovery was observed. In the presence of progressive, severe, refractory visual deficit, we though in a possible association with LHON disease (Harding disease). A genetic study revealed a novel homoplasmic variant m.15950G>A in an mtDNA-encoded tRNA gene (tRNAThr) that could be responsible for the LHON due to its low population frequency, high interspecific conservation of the affected nucleotide, results of pathogenicity prediction programs, structural and functional assays in cybrids, and previous identification of this variant in another LHON patient.

Conclusion: These results identify a novel mutation associated with Harding disease (LHON and MS).

EPR-164

Real-World Evidence on Rates of MS Relapse and Healthcare Resource Utilisation Following COVID-19 Vaccination

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Background and aims: Multiple sclerosis (MS) patients treated with certain disease-modifying therapies (DMTs) show reduced humoral response to COVID-19 vaccines. This study compared relapse, severe relapse (SR), and healthcare resource utilisation (HCRU) rates between cohorts of vaccinated MS patients treated with ocrelizumab, ofatumumab, siponimod, or fingolimod [Cohort 1 (C1)], other DMTs (C2), or untreated (C3).

Methods: Adult MS patients in the TriNetX Network with a complete COVID-19 vaccination status (CV) were included. Patients had a visit >6 months before CV (index date; ID) and were excluded when CV was undetermined or a patient switched treatment over follow-up. Definitions: C1, C2, and C3, treatment status closest to the ID; relapse and SR, steroid use in any setting and in an inpatient setting, respectively, recorded 14+ days after the ID; HCRU, MS care in any (aHCRU) and inpatient (iHCRU) settings. Person-days were accrued from ID to date of relapse/SR/aHCRU/iHCRU. Poisson models comparing cohorts were adjusted for baseline characteristics using inverse probability of treatment weights.

Results: Patients in C1 (n=518), C2 (n=1,312), and C3 (n=3,630) had a mean age (SD) of 50.8(12.0), 53.7(12.4), and 58.6 (14.1) years, were majority female (72%, 78%, and 74%). Majority DMTs: C1, ocrelizumab (62%), fingolimod (35%); C2, glatiramer acetate (30%), dimethyl fumarate (30%). Incidence rates per 1,000 person-days of MS can be seen in Table 1, rates of relapse/SR among cohorts are shown in Figure 1.

CI, confidence interval; DMT, disease-modifying therapy; MS, multiple sclerosis
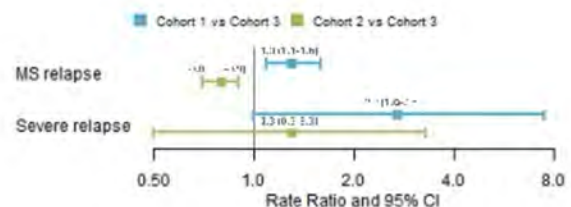
Figure 1. Rates of Relapse and Severe Relapse among Cohort 1 (ocrelizumab, ofatumumab, siponimod, or fingolimod) and 2 (other DMTs) versus Cohort 3 (untreated). CI, confidence interval; DMT, disease-modifying therapy; MS, multiple sclerosis

CI, confidence interval; HCRU, healthcare resource utilisation; MS, multiple sclerosis; PD, person days

	Cohort	Rate per 1,000 PD	95% CI		Rate ratio	95% CI	
Any MS-related HCRU	1	32.2	29.1	35.6	1.5	1.3	1.7
	2	28.1	26.3	30.0	1.3	1.2	1.5
	3	21.4	20.1	22.8	Reference		
Inpatient MS-related HCRU	1	7.6	6.4	8.9	1.7	1.4	2.0
	2	6.0	5.5	6.6	1.4	1.2	1.6
	3	4.5	4.2	4.8	Reference		

Table 1. MS-related HCRU in Cohort 1 (ocrelizumab, ofatumumab, siponimod, or fingolimod) and 2 (other DMTs) versus Cohort 3 (untreated). CI, confidence interval; HCRU, healthcare resource utilisation; MS, multiple sclerosis; PD, person-days Cohort Rate p

Conclusion: Amongst DMT-treated patients, relapses and HCRU was greatest within the patient cohort that was noted for a high proportion of ocrelizumab and fingolimod recipients.

Disclosure: This study was sponsored by Merck (CrossRef Funder ID: 10.13039/100009945).

EPR-165

Safety of Alemtuzumab in Patients with Multiple Sclerosis: Interim Results of a Post-Authorization Safety Study (PASS)

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Background and aims: In phase 3 studies, alemtuzumab demonstrated efficacy and safety in patients with RRMS. Here, we evaluated the incidence of adverse events (AEs) following alemtuzumab treatment to further characterize its long-term safety profile.

Methods: A 10-year, international, prospective, multicenter, observational, post-authorization safety study (PASS) of alemtuzumab was conducted in patients with RRMS. Eligible patients initiated alemtuzumab within 8 weeks of enrolment with bi-annual follow-up. Incidence and rate of AEs were calculated. Interim analyses were performed 5 years after study initiation.

Results: 3,024 patients were enrolled – mean age, 38.0 (9.8) years; females, 71.1%; white, 90.6%; 86.2% of patients had received prior MS treatment. Based on the data cut-off (Dec-2019), the mean follow-up was 27.1 months (range, 0.1–59.6); 97.4% of patients had any AE and treatment discontinuation due to AEs occurred in 2.2% of patients. At least one SAE occurred in 26.1% of patients; most common SAEs included infections, nervous system, and blood/lymphatic disorders and the majority were reported as recovered (79.8%). AEs of special interest (AESIs) occurred in 32.5% of participants, autoimmune-mediated thyroid disorders were most common, observed in 22.0% (10.9/100 patient-years [PYs]), followed by serious infections in 7.6% ([3.5/100 PYs]). ITP and nephropathies were observed in 0.9% and 0.1% of participants respectively. Malignancies were observed in 1.5% of participants [0.7/100 PYs]), including thyroid malignancies in 0.1% ([0.1/100 PYs]). Death due to AEs occurred in 13 patients (1 attributed to alemtuzumab).

Conclusion: This first interim analysis supports acceptable safety profile for alemtuzumab consistent with results from the clinical development program.

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MS and related disorders 4

EPR-166

Long-term outcome after COVID-19 infection in multiple sclerosis: a matched-controlled study

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Background and aims: Long-term outcome after COVID-19 in patients with multiple sclerosis (pwMS) is scarcely studied and controlled data are lacking.

Methods: From the AutMuSC registry, we included pwMS with PCR-confirmed diagnosis of COVID-19 and ≥ 6 months of follow-up available. As a control group, we recruited pwMS from the Vienna MS database (VMSD) matched for age, sex, disability level (EDSS) and disease-modifying-treatment type.

Results: Of 142 pwMS with COVID-19 (mean age 43.2 years [SD 11.8], 63.4% female, median EDSS 1.5 [range: 0–7.5], 54.2% immunomodulatory DMT, 20.4% immunosuppressive DMT), 90.1% initially had a mild COVID-19 course not requiring hospitalization. Three months (M3) after COVID-19, 76% had recovered completely, 84% after 6 months (M6) and 92% after 12 months (M12). Most frequent residual symptoms were new/worsened fatigue (M3: 18.4%, M6: 12.8%, M12: 7.8%), new/worsened hyposmia (M3: 8.5%, M6: 4.3%, M12: 1.4%) and new/worsened dyspnea (M3: 7.1%, M6: 6.4%, M12: 2.8%). Compared to matched controls (fatigue: 7.1%, hyposmia: 0.7%, dyspnea: 1.4%), fatigue and hyposmia were significantly more frequent only at M3, while dyspnea remained increased until M6. Occurrence of relapse (8.6% vs. 7.0%) and EDSS progression (5.6% vs. 4.2%) were not significantly increased in pwMS with COVID-19 compared to control group during the observation period.

Conclusion: Long-term outcome of COVID-19 is favorable in a large majority of pwMS with only a small proportion of patients suffering from persistent fatigue, hyposmia or dyspnea, usually resolving after 3–6 months. Against the background of a closely-matched-control-group, COVID-19 is neither associated with increased risk of relapse nor EDSS progression.

Disclosure: Gabriel Bsteh has no disclosures relevant to this study

EPR-167

Comparative Effectiveness and Persistence of Cladribine Tablets from GLIMPSE: Results from the MSBase Registry

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Background and aims: There are no real-world studies comparing effectiveness of cladribine tablets (CladT) to other oral disease-modifying therapies (DMT) for multiple sclerosis (MS). The MSBase Registry records demographics, DMT, Expanded Disability Status Scale (EDSS) scores, and relapses in over 74,000 MS patients globally. In this study, we compared treatment patterns and clinical outcomes in MS patients newly treated with CladT versus fingolimod, dimethyl fumarate (DMF), and teriflunomide in the real world.

Methods: We described baseline demographics and outcomes for all adult (>18 years) relapsing MS patients newly initiating CladT or oral comparators starting from January 2018 in the MSBase Registry. Propensity-score matching (PSM, 1:1) for three pairwise comparisons (CladT versus oral DMTs) included age, sex, EDSS, pre-baseline relapses, prior DMT initiation, and country. Outcomes included time-to-switch, annualised relapse rate (ARR), and time-to-first relapse. Time-to-event analyses used marginal Cox models with hazard ratio (HR) and 95% confidence intervals (CI). ARRs were compared with a weighted negative binomial model with a cluster term for matched patient sets.

Results: With PSM, cohorts were found to be well balanced on demographic and clinical characteristics. Median follow-up times were between 11 and 13 months. The ARRs for CladT versus fingolimod, DMF, and teriflunomide are seen in Table 1. The time-to-treatment switch for CladT versus fingolimod, DMF, and teriflunomide is shown in Figure 1.

CI, confidence interval; DMF, dimethyl fumarate; DMT, disease-modifying therapy
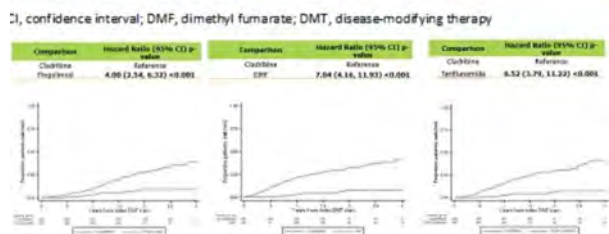
Figure 1. Time to Switch for Cladribine Tablets Versus Fingolimod, Dimethyl Fumarate, and Teriflunomide. CI, confidence interval; DMF, dimethyl fumarate; DMT, disease-modifying therapy

Table 1.

INDEX DMT	Count of on DMT relapses	On index DMT follow-up years	ARR (95% CI)	P-value*
Cladribine Tablets Versus Fingolimod				
Cladribine (n=520)	47	498.28	0.0943 (0.069, 0.1254)	0.0156
Fingolimod (n=520)	89	612.27	0.1454 (0.1167, 0.1789)	
Cladribine Tablets Versus Dimethyl Fumarate				
Cladribine (n=450)	41	426.22	0.0962 (0.069, 0.1305)	0.0307
Dimethyl fumarate (n=450)	64	433.19	0.1477 (0.1138, 0.1887)	
Cladribine Tablets Versus Teriflunomide				
Cladribine (n=458)	40	451.46	0.0886 (0.0633, 0.1207)	0.0005
Teriflunomide (n=458)	88	514.78	0.1709 (0.1371, 0.2106)	

*P-values were not corrected for multiple comparisons and are considered nominal.
ARR, annualised relapse rate; CI, confidence interval; DMT, disease modifying therapy

Table 1. Annualised Relapse Rate for Cladribine Tablets Versus Fingolimod, Dimethyl Fumarate, and Teriflunomide

Conclusion: For all three pairwise comparisons, time-to-switch and relapse outcomes were nominally significant in favour of CladT over other oral DMTs. Future analyses with longer follow-up comparing disability progression events are warranted.

Disclosure: This study was sponsored by Merck (CrossRef Funder ID: 10.13039/100009945).

EPR-168

Evobrutinib reduces relapses and MRI outcomes in MS: association with baseline serum neurofilament light chain levels

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Background and aims: Serum neurofilament light chain (sNfL) is a biomarker of neuro-axonal damage in multiple sclerosis (MS). In a post-hoc analysis of a Phase II trial (NCT02975349), evobrutinib, a Bruton's tyrosine kinase inhibitor, 75mg twice-daily, significantly lowered blood sNfL levels at Weeks (W)12 and W24. Objective: evaluate the prognostic value of baseline sNfL levels on clinical relapse and MRI lesion activities, and the treatment effect of evobrutinib.

Methods: The analysis included patients in the modified intent-to-treat population with baseline sNfL values (excluding the dimethyl fumarate arm), measured blinded to treatment (SimoaNF-light™). Patients were grouped by high-dose (evobrutinib 75mg once-daily/twice-daily) or placebo/low-dose (placebo/evobrutinib 25mg once-daily) and stratified by geometric mean baseline sNfL levels (high sNfL: ≥11.36pg/mL; low sNfL: <11.36pg/mL), to evaluate the effect of evobrutinib stratified by the baseline sNfL groups on qualified relapses over 24W, and on Gd+ T1 and new/enlarging T2 lesions over W12, W16, W20 and W24.

Results: In the sNfL analysis population (n=162), patients with high sNfL had higher disease burden at baseline and higher levels of clinical relapses and MRI lesion activity over 24W. High evobrutinib doses vs placebo/low dose reduced the odds of qualified relapse (odds ratio: 0.12; p=0.0028) when stratified by baseline sNfL, and both the cumulative number of Gd+ T1 lesions and new/enlarging T2 lesions (Figure).

Figure: (A) Number of Gd+ T1 lesions and (B) new or enlarging T2 lesions
Effect of evobrutinib stratified by baseline sNfL levels

(A) Gd+ T1 lesions
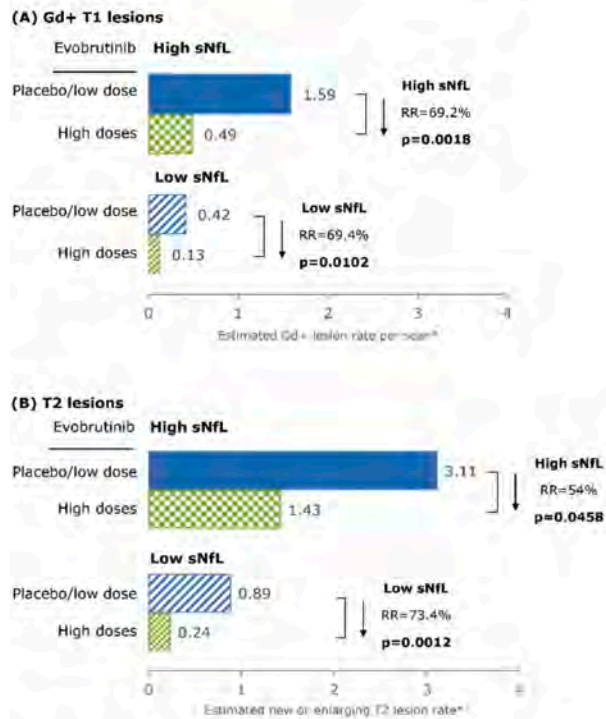
(B) T2 lesions

*Based on a negative binomial model for cumulative number of T1 Gd+ lesions count (summed over scans) or negative binomial model for total new or enlarging T2 lesions count (summed over scans). Scans over Weeks 12, 16, 20 and 24.

Gd+, gadolinium enhancing; RR, relative reduction; sNfL, serum neurofilament light chain.

(A) Number of Gd+ T1 lesions and (B) new or enlarging T2 lesions. Effect of evobrutinib stratified by baseline sNfL levels.

Conclusion: These data indicate that higher doses of evobrutinib reduced MRI activity and the number of patients with qualified relapses when stratifying for baseline sNfL levels. This further supports sNfL as a prognostic marker of MS disease activity.

Disclosure: Study was sponsored by EMD Serono Research & Development Institute, Inc., Billerica, MA, USA, an affiliate of Merck KGaA (CrossRef Funder ID: 10.13039/100004755), detailed author disclosures will be included in the presentation.

EPR-169

COVID-19 Outcomes and Vaccination in Ofatumumab-treated RMS Patients: ALITHIOS Trial and Post-marketing Setting

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Background and aims: With increasing awareness on COVID-19 and the introduction of vaccines, further evidence is required to better understand the effect of COVID-19 and vaccination in multiple sclerosis (MS) patients treated with disease-modifying therapies. Data collected since the start of the pandemic to 29-Jan-2021 on the COVID-19 outcomes in ofatumumab-treated relapsing MS (RMS) patients was previously reported. This study presents updated COVID-19 outcomes and characteristics, vaccination data, and breakthrough infections in RMS patients on ofatumumab.

Methods: Demographics, baseline characteristics, and COVID-19 incidence, seriousness, severity and outcomes were analysed from the ongoing, open-label, long-term extension Phase 3b ALITHIOS study and the post-marketing setting (Cut-off date: 25-Sep-2021). Reinfections, vaccination rates and breakthrough infections were also analysed.

Results: Overall, 245/1703 patients from the ALITHIOS study reported confirmed/suspected COVID-19. Most cases were non-serious (90.2%) and mild/moderate in severity (90.6%). Most patients recovered (98.4%) with an average duration of <20 days. Overall, 23 (9.4%) patients were hospitalised and 2 (0.8%) had fatal outcomes. No patients had COVID-19 reinfection. In total, 559 patients in the ALITHOS study were vaccinated (fully vaccinated, 476; partially vaccinated, 74; unspecified, 9). Breakthrough

infections were reported in only 1.5% (7/476) of the fully vaccinated patients of which the majority were mild to moderate and all patients recovered. Findings from the post-marketing were similar to the clinical trial results.

Characteristics	Any COVID-19 related AE			
	Overall COVID-19 N=245	Confirmed COVID-19 n=210	Suspected COVID-19 n=35	Hospitalized overall COVID-19 n=23
COVID-19 seriousness, n (%)				
Non-serious	221 (90.2)	187 (89.0)	34 (97.1)	0
Serious	24 (9.8)	23 (11.0)	1 (2.9)	23 (100)
Hospitalized	23 (9.4)	22 (10.5)	1 (2.9)	23 (100)
COVID-19 maximum severity, n (%)				
Mild	108 (44.1)	90 (42.9)	18 (51.4)	1 (4.3)
Moderate	114 (46.5)	99 (47.1)	15 (42.9)	5 (21.7)
Severe	19 (7.8)	17 (8.1)	2 (5.7)	14 (60.9)
Life-threatening	3 (1.2)	3 (1.4)	0	3 (13.0)
Missing CTCAE grading	1 (0.4)	1 (0.5)	0	0
COVID-19 outcome, n (%)				
Recovered/recovered with sequalae/recovering	241 (98.4)	206 (98.1)	35 (100)	22 (95.7)
Not recovered	2 (0.8)	2 (1.0)	0	0
Fatal	2 (0.8)	2 (1.0)	0	1ª (4.3)
COVID-19 duration in days, median (range)	15 (1–216)	15 (1–216)	14 (3–47)	14 (4–57)
COVID-19 onset time since first dose of ofatumumab in years, mean ± SD	2.32 ± 0.999	2.38 ± 1	1.91 ± 0.903	2.52 ± 0.86
AE led to ofatumumab interruption, n (%)	39 (15.9)	34 (16.2)	5 (14.3)	9 (39.1)
AE led to ofatumumab discontinuation, n (%)	2 (0.8)	2 (1.0)	0	1 (4.3)

ª One fatal case was not admitted to hospital due to personal circumstances and financial reasons. AE, adverse event; EDSS, Expanded Disability Status Scale; SD, standard deviation.

Table 1: Summary of COVID-19 cases from the ALITHIOS study (Cut-off date: 25-Sep-2021)

Characteristics	Confirmed COVID-19 N=90
COVID-19 seriousnessª, n (%)	
Non-serious	80 (88.9)
Seriousᵇ	10 (11.1)
Fatal	0
Hospitalisation	9 (0.1)
Life-threatening	0
Medically significant	1 (1.11)
COVID-19 worst outcome, n (%)	
Recovered/recovered with sequalae/recovering	30
Condition Unchanged	6
Fatal	0
Not reported	54

Severity was assessed using WHO and FDA.
ª Percentages are calculated based on available information for seriousness (N = 90).
ᵇ No information regarding co-morbidities was provided; in the post-marketing setting serious cases are likely to be reported more frequently than non-serious cases.

Table 2. Summary of confirmed COVID-19 cases from the post-marketing setting (Cut-off date: 25-Sep-2021)

Conclusion: Based on the updated results, there does not appear to be an increased risk of severe or serious COVID-19 in ofatumumab-treated RMS patients. A very small number of vaccinated patients had breakthrough infections, and all recovered.
Disclosure: The study was supported by Novartis Pharma AG, Switzerland. The detailed author disclosures will be presented in the subsequent presentation.

EPR-170

Interim Analysis of a Phase III Long Term Extension Study of Ponesimod in Relapsing Multiple Sclerosis: Safety Results

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Background and aims: Ponesimod, a selective S1P1 receptor modulator, was evaluated vs teriflunomide in a 2-year core study followed by an ongoing, open-label extension (OLE) study.
Methods: All patients received ponesimod 20mg in the OLE, following core study treatment with either ponesimod 20mg (P/P) or teriflunomide 14mg (T/P). Safety endpoints were analyzed in the combined (core and OLE, P/P) and extension (OLE only, P/P and T/P) analysis periods.
Results: In the combined analysis period, [P/P=565], mean treatment exposure was 30.03 months (a total of 1,413.77 patient-years); 92.4% of patients had at least 1 adverse event (AE). A total of 10.6% of patients experienced at least 1 serious AE (SAE). SAEs reported in >1 patient were appendicitis, abdominal pain, induced abortion, lumbar radiculopathy, and multiple sclerosis relapse. In the extension period analysis, (n=439 [P/P], n=438 [T/P]) the proportion of patients who experienced at least 1 AE was 59.9% (P/P) and 66.0% (T/P). The proportion of patients who experienced at least 1 SAE in the extension period was similar in the P/P (3.2%) and T/P (3.9%) groups. No skin malignancies were reported in the OLE. No cases of PML or death were reported with ponesimod in the core or in the OLE study.
Conclusion: The safety profile of ponesimod in the OLE study was similar to that in the core study and no unexpected safety findings were identified. Long-term exposure to ponesimod during the OLE did not lead to increased incidence of SAEs of concern.

D: day; EOS: End of study; EOT: end of treatment; FU: Follow-up; M: Month; V: visit; W: week
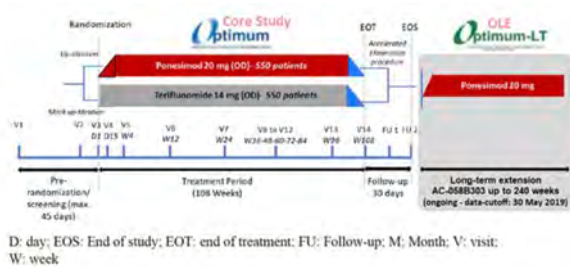
Fig 1. Study Design

Overview of treatment-emergent adverse events, by frequency and per subject-year in the combined analysis period, Safety Set

Characteristic	Ponesimod 20 mg / Ponesimod 20 mg N=565		
Cumulative observation time (subject-years)	1419.0		
Subjects with at least one	n (%)	Number of events	(rate)
AE	522 (92.4)	3519	(2.48)
Severe AE	54 (9.6)	83	(0.06)
Drug-related AE	311 (55.0)	959	(0.68)
AE leading to study drug discontinuation	57 (10.1)	69	(0.05)
Serious AE	60 (10.6)	77	(0.05)
Drug-related serious AE	19 (3.4)	24	(0.02)
Fatal AE	0	0	

Ongoing study interim analysis data cut-off: 30 May 2019

AE = adverse event

Cumulative number subject-years = cumulative observation time in the treatment-emergent period of the Analysis Period over all subjects. Total number of events = number of qualifying events in this period (multiple events per subject may be counted in each category).
Rate = events per subject-years of exposure.

Fig 2. TEAEs - combined analysis period

Extension Analysis Period

Overview of treatment-emergent adverse events in the extension analysis period, Extension Set

Characteristic	Ponesimod 20 mg / Ponesimod 20 mg N=439	Teriflunomide 14 mg / Ponesimod 20 mg N=438	Total N=877.0		
Cumulative observation time (subject-years)			697.0		
Subjects with at least one	n (%)	n (%)	n (%)	Number of events	(rate)
AE	263 (59.9)	289 (66.0)	552 (62.9)	1610	(2.31)
Severe AE	19 (4.3)	15 (3.4)	34 (3.9)	49	(0.07)
Drug-related AE	117 (26.7)	139 (31.7)	256 (29.2)	512	(0.73)
AE leading to study drug discontinuation	9 (2.1)	24 (5.5)	33 (3.8)	41	(0.06)
Serious AE	14 (3.2)	17 (3.9)	31 (3.5)	44	(0.06)
Drug-related serious AE	8 (1.8)	5 (1.1)	13 (1.5)	18	(0.03)
Fatal AE	0	0	0	0	

Ongoing study interim analysis data cut-off: 30 May 2019

AE = adverse event

Cumulative number subject-years = cumulative observation time in the treatment-emergent period of the Analysis Period over all subjects. Total number of events = number of qualifying events in this period (multiple events per subject may be counted in each category).
Rate = events per subject-years of exposure.

Fig 3. TEAEs - extension analysis period

Disclosure: MR-B, AW, AL, MA-T, AV and TS are or were employees of Janssen and may own stock or stock options in Johnson & Johnson. XM received speaker honoraria from Actelion, Alexion, Bayer, Biogen, Celgene, EMD Serono, Genzyme, Immunic, Medday.

EPR-171

Deuterium-Stabilized (R)-Pioglitazone, PXL065, for Treatment of X-Linked Adrenoleukodystrophy (ALD)

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Background and aims: X-linked Adrenoleukodystrophy (ALD) is a rare neurometabolic disorder caused by ABCD1-gene mutations, leading to Very-Long-Chain Fatty Acids (VLCFA; in particular C26:0) accumulation, inflammation, mitochondrial impairment and demyelination. PXL065, a clinical-stage deuterium-stabilized(R)-stereoisomer of pioglitazone, retains pioglitazone non-genomic actions but lacks PPARγ activity. As pioglitazone exhibits beneficial effects in ALD models and PXL065 may avoid PPARγ-related side effects, we investigated PXL065 effects of in preclinical models.

Methods: Patient-derived fibroblasts and lymphocytes and Abcd1-KO mouse glial cells were exposed to PXL065 (5-10µM) and pioglitazone (10µM) for 7 days. VLCFA content was measured by mass spectrometry, selected gene expression by RT-qPCR, and mitochondrial function using a Seahorse Analyzer (after 72hr). PXL065 or pioglitazone (15mg/kg QD) were administered to 6-8-week or 13-month old Abcd1-KO mice for 8 and 12 weeks, respectively. VLCFA content (mass spectrometry), sciatic nerve axonal morphology (electronic microscopy), and locomotor function (open field test) were measured.

Results: In patient and mouse glial cells, PXL065 and pioglitazone corrected C26:0, improved mitochondrial function, increased compensatory Abcd2-3 transporter gene expression, and decreased inflammatory gene expression.
In Abcd1-KO mice, C26:0 levels were normalized in plasma and decreased in spinal cord (-55%, p<0.01) and brain (-49%, p<0.0001). Pioglitazone had no effect in spinal cord. Following PXL065 and pioglitazone treatment, abnormal axonal morphology (stellate-shaped cells) was improved but only PXL065 showed significantly improved locomotor test results.

Conclusion: Despite reduced PPARγ activity, PXL065 showed substantial signs of efficacy and superior therapeutic potential vs. pioglitazone (in vivo) supporting clinical development for ALD. A Phase 2a study is planned in 2022.
Disclosure: Studies funded by Poxel SA.

EPR-172

Spinal cord lesions and brain grey matter atrophy predict 5-year multiple sclerosis disease worsening

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Background and aims: In MS, the combined role of brain and spinal cord damage in predicting medium-term evolution needs to be elucidated. Here, we evaluated the ability of brain and cervical cord MRI damage to predict 5-year disease worsening in a multicentre MS cohort.

Methods: Baseline 3.0 T brain/cervical cord T2- and 3D T1-weighted MRI was acquired in 367 MS patients (326 relapse-onset, 41 progressive-onset) and 179 healthy controls. Expanded Disability Status Scale (EDSS) score was obtained at baseline and after a median follow-up=5.1 years (interquartile range=4.5–5.5). Generalized linear mixed models with L1-penalized variable selection identified 5-year predictors of EDSS worsening, secondary progressive (SP) MS evolution, and reaching EDSS=3.0, 4.0 and 6.0 milestones.

Results: At follow-up, 120/367 (33%) MS patients worsened clinically; 36/256 (14%) relapsing-remitting MS evolved to SPMS. Multivariate predictors of EDSS worsening were progressive- vs relapse-onset MS (standardized beta [B]=0.97), higher baseline EDSS (B=0.41) and cord lesion number (B=0.41), as well as lower normalized cortical volume (B=-0.15) and cord area (B=-0.28) (C-index=0.81). Older age (B=0.86), higher EDSS (B=1.40) and cord lesion number (B=0.87) independently predicted SPMS conversion (C-index=0.91). Predictors of reaching EDSS=3.0 at 5-years were higher baseline EDSS (B=1.49) and cord lesion number (B=1.02), and lower normalized cortical volume (B=-0.56) (C-index=0.88). Baseline age (B=0.30), higher EDSS (B=2.03) and cord lesion number (B=0.66), and lower cord area (B=-0.41) predicted EDSS=4.0 (C-index=0.92). Finally, higher baseline EDSS score (B=1.87) and cord lesion number (B=0.54) predicted EDSS=6.0 (C-index=0.91).

Conclusion: The combined assessment of brain and spinal cord damage helped predicting worse clinical outcomes in MS at 5-years.

Disclosure: Nothing to disclose.

EPR-173

Serum NfL and GFAP biomarker analysis in early high versus low efficacy DMT paradigms for MS

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Background and aims: Serum neurofilament light chain (sNfL) and serum glial fibrillary acidic protein (sGFAP) levels may inform high efficacy early treatment (HEET) versus low efficacy early treatment (LEET) approaches in MS patients.

Methods: Patients enrolled in the CLIMB study treated with HEET (fingolimod, natalizumab, ocrelizumab, rituximab) or LEET (dimethyl fumarate, glatiramer acetate, interferons, teriflunomide) within five years of symptoms onset were divided into two cohorts. Cohort A [HEET (n=99), LEET (n=89)] had sNfL and sGFAP 3–0 years before and 0.5–3 years after treatment. Cohort B [HEET (n=56), LEET (n=158)] had two samples after treatment start (0–4 and 1–5 years). A Wilcoxon test was used to compare biomarker levels in the two groups. A Cox proportional hazards model assessed predictive associations.

Results: In cohort A, sNfL and sGFAP levels were similar prior to and on treatment with HEET and LEET. In cohort B, the first on-treatment sNfL (10.13 ± 8.89 vs. 11.51 ± 13.01; p=0.024) and sGFAP measure (80.34 ± 35.32 vs. 104.88 ± 109.98; p=0.004), was lower in the HEET vs. LEET groups respectively. sGFAP log-transformed levels at follow-up sample were associated with time to sustained progression in Cohort B (1.65 [0.98, 2.78]; p=0.06). In Cohort A, an increase in sGFAP level from pre-treatment to on-treatment was associated with time to sustained progression 2.63 [1.27, 5.45]; p=0.009, and remained significant in the HEET group.

Conclusion: On-treatment levels of sNfL and sGFAP may differ in HEET vs. LEET treatment paradigms, and sGFAP is associated with disease progression.

Disclosure: Authors report no conflicts of interest related to this work.

EPR-174

Disease activity during pregnancy and postpartum in women with MS receiving ocrelizumab in a real-world cohort

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Background and aims: Women with multiple sclerosis (MS) planning a family need to balance treatment benefits against risk to the foetus, recognising that disease-modifying therapy (DMT) discontinuation may increase relapse risk. Ocrelizumab may be a suitable treatment option due to its prolonged immunomodulatory effects, but evidence on disease activity during pregnancy and postpartum periods is scarce.

Methods: Pregnancies in women with MS receiving ocrelizumab preconception recorded in MSBase up to November 2021 were included. Annualised relapse rate (ARR) per trimester was calculated between 12-months preconception and 12-months postpartum, and compared to low-efficacy (LE) DMTs.

Results: 35 pregnancies received ocrelizumab as last DMT preconception (n[%]) with 1–2 (17[48.6]) or ≥3 (18[51.4]) doses. Ocrelizumab preconception dose timing (n[%]) was ≤6 months (26[74.3]) or >6 months (9[25.7]). Pre-ocrelizumab DMT (n[%]) was none (17[48.6]), natalizumab (10[28.6]), other (8[22.9]). Postpartum DMT (n[%]) was ocrelizumab (23[65.7]), natalizumab (1[2.9]), none (11[31.4]). Outcomes were compared with 1,082 pregnancies receiving LE DMTs within 12 months of conception. Ocrelizumab had lower ARR [95% CI] vs LE DMT during pregnancy (ocrelizumab: 0 [0–0.14]; LE: 0.12 [0.10–0.15]) and post-partum (ocrelizumab: 0.10 [0.02–0.30]; LE: 0.40 [0.36–0.44]). Three postpartum relapses occurred in three pregnancies receiving ocrelizumab, of which none had relapses in the pre-pregnancy year or during pregnancy.

Conclusion: Preliminary results suggest that women with MS receiving ocrelizumab preconception are not at increased risk of postpartum disease activity compared to LE DMT, but further data for validation and to understand relapse predictors are required. Counselling remains an important approach to ensure optimal outcomes for mothers and infants.

Disclosure: Sponsored by F. Hoffmann-La Roche Ltd.

Muscle and neuromuscular junction disorder 2

EPR-175

Late-onset myopathic RRM2B – a prospective, quantitative study on clinical outcomes

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Background and aims: Pathogenic variants in the RRM2B gene are an important cause of mitochondrial DNA maintenance disorders and can lead to late-onset myopathic phenotype. This cross-sectional study phenotypes these patients using the Newcastle Mitochondrial Disease Scale (NMDAS) and other outcome measures to quantify their functional abilities.

Methods: 10 adult participants (women n=6) with bi-allelic pathogenic variants in RRM2B were assessed at the research site or in their home environment. Outcome measures used included NMDAS, respiratory muscle testing, nine-hole peg test, quantitative muscle dynamometry, six-minute and ten metre walks, and timed water swallow test.

Results: NMDAS scores demonstrated a high disease burden (mean 54) with respiratory weakness, hearing problems, chronic external ophthalmoplegia, ptosis and exercise intolerance being prominent features. Forced vital capacity was significantly lower than predicted values (range 25–55%). Muscle strength in shoulder abduction, elbow flexion, knee extension and hip flexion were substantially lower than their predicted values. Upper limb dexterity was also shown to be significantly reduced in the performance of the nine-hole peg test. The swallowing speed achieved by these participants was also significantly lower than the predicted values. None of the participants reached the age related lower limit of normal distance expected in 6-minute-walk tests (40%). Mean self-selected speed and fast-paced speed of walking were also slower than expected (p=0.001).

Conclusion: Patients with bi-allelic pathogenic variants in RRM2B performed significantly below predicted values in assessments that are affected by muscle strength. This study has provided new and detailed quantitative data on the natural history of this rare condition.

Disclosure: Nothing to disclose.

EPR-176

Clinical characteristics and outcomes of patients with asymptomatic hyperCKemia: a retrospective single-centre study

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Background and aims: Creatine kinase (CK) is a biomarker for muscular damage. Pauci- or asymptomatic hyperCKemia is a predictor of muscular disease and malignant hyperthermia.

Methods: We conducted a retrospective single-centre study of patients who underwent muscle biopsy for pauci- or asymptomatic hyperCKemia between January 2011 and August 2021. We studied demographic (sex, age, ethnicity), and clinical variables (phenotype, drugs, comorbidities, CK elevation, electromyogram, biopsy results, and final diagnosis).

Results: 41 patients were included. 16 patients were female (39.0%), aged a mean (SD) of 59.6 (14.9) years old, with a mean (SD) follow-up time of 4.9 (2.3) years. 34 had true hyperCKemia, as defined by the European Federation of Neurological Sciences. Characteristics for the true hyperCKemia patients are displayed on Table 1. There were 9 patients with a final diagnosis of myopathy (4 mitochondrial, 2 metabolic, 2 inflammatory, 1 drug-induced), 15 patients with idiopathic hyperCKemia, and 10 patients with non-myopathic hyperCKemia. There were 11 asymptomatic patients (32.3%), and the most common symptoms overall were myalgias/cramps, in 14 patients (41.2%). All patients with exercise intolerance were either in the myopathic group or the idiopathic hyperCKemia group. 7 patients with unconfirmed hyperCKemia had been misclassified due to local laboratory cut-off values, black ethnicity, and rhabdomyolysis. None of them had exercise intolerance and all of them had normal muscle biopsy. There were neither deaths nor cases of malignant hyperthermia in our cohort.

	Myopathy (n=9)	Idiopathic hyperCKemia (n=15)	Non-myopathic hyperCKemia (n=10)	p value
Gender (female)	4 (44.4%)	5 (33.3%)	4 (40%)	0.855
Age (SD)	55,4 (18.4)	61,5 (16.2)	64,9 (9.9)	0.734
Ethnicity (black)	0	0	0	
Serum CK elevation (SD)	8,1 (8.5)	7,4 (8.3)	3,3 (2.3)	0.282
Clinical phenotype				**0.026**
Asymptomatic	0	8 (53.3%)	3 (30%)	
Undue fatigue	0	2 (13.3%)	1 (10%)	
Myalgias and/or cramps	6 (66.7%)	2 (13.3%)	6 (60%)	
Exercise intolerance	3 (33.3%)	3 (20%)	0	
Electromyogram results				**0.527**
Normal	4 (44.4%)	10 (66.7%)	4 (40%)	
Myopathic	1 (11.1%)	0	1 (10%)	
Neurogenic	1 (11.1%)	3 (20%)	3 (30%)	
Non-specific	2 (22.2%)	1 (6.7%)	0	
Muscle biopsy results				**<0.001**
Normal	0	5 (33.3%)	7 (70%)	
Pathologic	9 (100%)	4 (26.7%)	2 (20%)	
Non-specific	0	6 (40%)	1 (10%)	
Diagnosis				
Diagnosis	• 4 mitochondrial • 2 metabolic (MADA deficiency) • 2 inflammatory • 1 drug induced		• 4 connective tissue disease • 3 statin intolerance • 2 myasthenia gravis • 1 cancer	

Annotation.
- Serum CK elevation: multiplier for the upper limit of normality for CK levels, adjusted by gender and ethnicity. *European Federation of Neurological Sciences* upper limits of normality: Black females: 414. Non-black females: 217. Black males: 801. Non-black males: 336.

Table 1. Demographic and clinical variables of patients with confirmed hyperCKemia.

Conclusion: Pauci- or asymptomatic hyperCKemia should be carefully assessed as per current guidelines recommendations, selecting patients who may benefit of muscle biopsy.

Disclosure: There are no conflicts of interest regarding this research.

EPR-177

Genetic confirmation of myotonic dystrophy type II after allogeneic stem cell transplant

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Background and aims: Myotonic dystrophy type II (DM2) is caused by an unstable CCTG repeat expansion in the CNBP gene. Proximal myopathy and myotonia are the prevailing symptoms, but additional cardiac, CNS and ophthalmological features may also occur. Allogeneic bone marrow or peripheral blood stem cell transplants are successfully used for various malignant and non-malignant haematological diseases. Several studies have indicated that blood stem cells have the potential to transdifferentiate into other cell types, such as neuronal, epidermal, or muscle cells.

Methods: A 66-year-old patient presented with a long history of a slowly progressive proximal myopathy and myotonia. At age 62 he had been diagnosed with acute myeloid leukaemia and received an allogeneic peripheral blood stem cell transplant (allo-PBSCT) from his HLA-identical brother. DM2 was suspected in the patient and his blood before and after allo-PBSCT, urine sediment, buccal cells and hair follicles were examined for the CCTG repeat expansion.

Results: The pre-transplant sample showed a heterozygous CCTG repeat expansion, thus confirming DM2. The post-transplant sample only revealed two normal-sized alleles, proving successful engraftment of the donor stem cells. DNA from urine sediment and hair follicles showed mixed chimerism with 3 normal sized and one expanded allele; in buccal cells only recipient DNA was detected.

Conclusion: Stem cell transdifferentiation, as proven by the existence of donor-derived cells, was demonstrated for blood, hair follicles and urothelial, but not for buccal cells. Consequently, multiple tissues must be employed for genetic testing after allo-PBSCT because of the tissue-specific and variable degree of stem cell transdifferentiation.

Disclosure: We have nothing to disclose.

EPR-178

Longitudinal, quantitative assessment of hand muscle strength decay in myotonic dystrophy type 1 (DM1)

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Background and aims: Hand muscle weakness is a core feature of DM1 and outcome measures assessing finger pinch and grip strength should be available for natural history and trial studies.

Methods: We longitudinally evaluated self-assessed hand muscle strength with a hand-held dynamometer (HDD) in 115 consecutive DM1 patients of either gender. Three-finger pinch and handgrip strength were annually recorded in both hands with an up to six-year follow up. Descriptive statistics, t-test and correlation were performed.

Results: Within-case coefficient of variance (CV) was $7\pm7\%$ (mean$\pm$SD) for pinch and $7.2\pm6.8\%$ for handgrip. Median values of pinch and handgrip were markedly reduced at baseline for both male and female patients as compared to sex-matched normal values. Patients who showed abnormal baseline values of pinch (80%) and handgrip (98%) were evaluated for annual rate of progression. At follow-up, patients' values for both measures were significantly ($p<0.01$) decreased at each assessment compared to baseline. Mean annual loss rate was of $8.1\pm2.9\%$ for pinch and $7.2\pm2.7\%$ for handgrip.

Conclusion: Our results show that three-point pinch grip and handgrip, measured by HHD, reliably detect the baseline condition and the longitudinal progression of hand muscle power loss in DM1. These measures, therefore, seem suitable for being used as clinical outcomes within the timeframe of short-term natural history studies and clinical trials in DM1.

Disclosure: The authors declare no conflict of interests.

EPR-179

Vivacity MG Phase 3 Study: Clinical Trial of Nipocalimab Administered to Adults With Generalized Myasthenia Gravis

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Background and aims: Nipocalimab is a high affinity, fully human, aglycosylated, effectorless IgG1 anti FcRn monoclonal antibody that targets the neonatal Fc receptor (FcRn) with high affinity, thereby lowering IgG pathogenic antibodies in autoimmune disease. Data from Vivacity-MG, a Phase 2 randomized placebo-controlled study of nipocalimab in adult generalized myasthenia gravis (gMG), demonstrated safety, tolerability, and efficacy of nipocalimab (clinicaltrials.gov NCT03772587). We describe Vivacity-MG3. our pivotal Phase 3, Multicenter, Randomized, Double-Blind, Placebo-Controlled Study to Evaluate the Efficacy, Safety, Pharmacokinetics (PK), and Pharmacodynamics (PD) of Nipocalimab Administered to Adults With gMG (NCT04951622).

Methods: This global study will enroll approximately 180 participants with gMG, aged 18 and older, with an insufficient clinical response to ongoing, stable standard-of-care therapy, as reflected by a Myasthenia Gravis-Activities of Daily Living (MG-ADL) score of $\geq$ to 6 at screening and baseline, and a Myasthenia Gravis Foundation of America (MGFA) Class of IIa/b – IVa/b at screening. The study will consist of a screening period of up to 4 weeks, a 24-week double-blind placebo-controlled phase where participants will be randomly assigned in a 1:1 ratio to receive either placebo or nipocalimab intravenously every two weeks, and an open label extension phase of variable duration. The primary outcome is the average change in MG-ADL score from baseline to weeks 22, 23 and 24 of the double-blind placebo-controlled phase.

Results: Study enrollment began in July 2021 and is ongoing.

Conclusion: The ongoing Vivacity MG Phase 3 study will assess the efficacy, safety, and PK/PD of Nipocalimab in adult gMG.

Disclosure: The authors are employees of Janssen Pharmaceuticals, LLC.

EPR-180

Congenital myasthenic syndrome caused by a novel mutation on COLQ gene diagnosed on the 6th decade of life

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Background and aims: Congenital Myasthenic Syndromes (CMS) result from genetic mutations in neuromuscular junction proteins, and present with muscular weakness typically since birth or early childhood. The main differential diagnosis is usually hereditary myopathies, and it can be challenging as clinical fatigability is often subtle.

Methods: Case Report.

Results: 56-year-old man, born from consanguineous parents, had delayed motor development. Multiple hospitalizations for severe respiratory failure since early adulthood. At the first neurology visit, at the age of 53, he had severe scoliosis, rigid spine, hypotonic limbs, and generalised muscle weakness with a limb-girdle preferential distribution. Initial electromyography (without repetitive nerve stimulation [RNS]) showed myopathic features. The first diagnostic hypothesis was Congenital Myopathy due to Selenoprotein-1 deficiency, but lower limb CT scan was unremarkable and gene sequencing was normal. Reassessing the phenotype, a CMS was considered. A second EMG included RNS and displayed a pathologic decrement (>15%) in all stimulated nerves. Furthermore, a repetitive compound muscle action potential was found after single stimuli in several nerves. Assuming a CMS due to acetylcholinesterase deficiency he was started on oral Salbutamol with clear improvement. A gene panel identified a novel homozygous mutation [c.600G>A p.(Lys200=)] in COLQ gene. Bioinformatics analysis suggested pathogenicity by alteration of splicing.

Conclusion: We report a CMS due to acetylcholinesterase deficiency resulting from a novel mutation in COLQ gene. This case highlights the need to always include RNS in the initial diagnostic evaluation of a suspected muscle disease, even in the absence of overt clinical fatigability, and particularly when it begins at an early age.

Disclosure: Nothing to disclose.

EPR-181

Effect of statin use on severity of late onset myasthenia gravis

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Background and aims: There are many publications of possible deterioration of myasthenia gravis (MG) in patients due to statin administration. The purpose of our work was to compare the severity of MG in patients with late onset MG in groups with and without statin administration.

Methods: We analyzed data of 41 patients with late-onset MG, age 60 ± 14.7 years, 20 women (48.8%) and 21 men (51.2%). Examined patients were divided into 2 groups: 1 - taking 20 mg of atorvastatin daily (n=15); 2 - not taking statins (n=26). There were no significant differences in age and gender in compared groups. The severity of the disease was assessed according to the generally accepted scales of MG: MGFA and QMGS.

Results: We compare patients with immunosuppression therapy with corticosteroids and azathioprine. The dosage of pyridostigmine was comparable in both groups. All patients had a stable course of the disease, no data on myasthenic crises was received. The duration of patient observation was 3 years. In 1 group MGFA was 2,8, QMGS – 11,1, in 2 group the we did not find significant differences in the severity of myasthenia gravis in terms of MGFA (p=0.7) and QMGS (p=0.3).

Conclusion: We did not receive data in favor of significant worsening of MG course assessing patient condition. However, the study was limited by the number of patients and prescribed dosage of statins. We plan to continue the study with a larger sample of patients.

Disclosure: The study was performed without any commercial or institutional support.

Neuroimmunology 2

EPR-182

Cerebrospinal fluid kappa free light chains in patients with an isolated band in isoelectric focusing

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Background and aims: Oligoclonal band (OCB) determination in cerebrospinal fluid (CSF) using isoelectric focusing (IEF) is the gold standard to detect an intrathecal immunoglobulin synthesis. The significance of an isolated band in CSF is still matter of debate. Quantitation of kappa free light chains (k-FLC) is a promising alternative method for assessing an intrathecal inflammation. We here aimed to study the diagnostic value of quantitative k-FLC in patients with an isolated band in CSF.

Methods: We quantified k-FLCs in paired CSF and serum samples using Human Kappa Freelite Mx Kit (The Binding Site Group Ltd., Birmingham, UK) on a turbidimetric Optilite® in 47 patients with a single band in IEF. Based on the medical diagnosis we subclassified into 29x inflammatory neurological disease (IND), 2x peripheral inflammatory neurological disease (PIND), 7x non-inflammatory neurological disease (NIND) and 9x symptomatic controls (SC). k-FLC CSF/serum quotients were plotted in a k-FLC quotient diagram.

Results: In all SC and PIND, k-FLC were below the lower measurement limit of the analyser, as well as in 6 out of 7 NIND and 13 IND. Only 14 INDC were above the upper discrimination line (Qlim) (Table 1 and Figure 1). This resulted in a sensitivity for INDC of 48.3% and a specificity of 94.4%. Positive and negative predictive values (PPV and NPV) were 100% and 39.4%, respectively.

Table 1. Measurement results of the k-FLC according to the medical diagnosis of the patients with one isolated band in IEF

Relationship to the LML	Relationship to Q(lim)	IND	PIND	NIND	SC
Above the lower LML	above Q(lim)	14	0	0	0
	below Q(lim)	2	0	1	0
Below the LML		13	2	6	9

IND: inflammatory neurological disease; PIND: peripheral inflammatory neurological disease; NIND: non-inflammatory neurological disease; SC: symptomatic controls; Q(lim): upper discrimination line; LML: lower measuring limit of the analyser

Figure 1. Data of the cohort in a double logarithmic k-FLC Reibergram
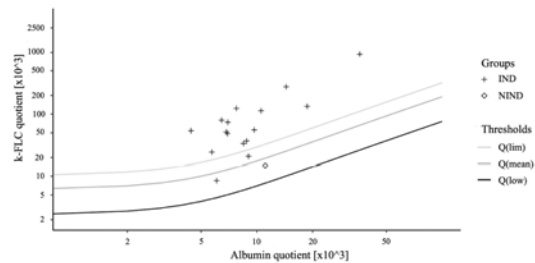
Data points of the k-FLC measurement results plotted on a double logarithmic scale, corresponding to the Reibergram. Q(lim) represents the upper discrimination line, Q(mean) the middle and Q(low) the lower. IND: inflammatory neurological disease; NIND: non-inflammatory neurological disesase

Conclusion: Positive k-FLC in patients with an isolated band in IEF suggests a neuroinflammatory nature of the diseases. Implementation of k-FLC in the clinical routine may facilitate the diagnostic process of neurological diseases.

Disclosure: Nothing to disclose.

EPR-183

Pathophysiological effects of autoantibodies against the paranodal protein neurofascin155 in vivo

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Background and aims: The paranodal protein neurofascin155 (NF155) is a target for autoantibodies in inflammatory neuropathies. Paranodal autoantibodies mostly belong to the IgG4 subclass, rarely to the IgG3 subclass. To investigate the pathomechanism of IgG3 and IgG4 autoantibodies against NF155 in vivo, passive transfer experiments were performed.

Methods: Rats were intrathecally treated with purified IgG of an anti-NF155-IgG4-positive patient, an anti-NF155/186-(pan)-IgG3-positive patient or a healthy control. Motor function was assessed by Rotarod and Catwalk and sensory function was measured by Von-Frey and Hargreaves. Nerve conduction studies (NCS) were performed before and after IgG infusion. Lumbar nerve roots were used for binding analysis.

Results: Shortly after treatment with IgG of the anti-NF155-IgG4-positive patient, animals generated symptoms such as gait ataxia. Behavioral tests showed motor and sensory deficits in animals injected with anti-NF155 IgG4 compared to controls. No conduction blocks were observed. Paranodal binding of patient IgG was detectable in lumbar nerve roots of animals injected with IgG of the anti-NF155-positive patient. Compared to the effect of anti-NF155 IgG4, we did not find any motor or sensory dysfunction in rats injected with IgG of the anti-pan-NF-IgG3-positive patient, although autoantibody binding at the nodes was detectable.

Conclusion: We suggest that NF155 IgG4 autoantibodies can reach the paranodes after long-term application and induce motor and sensory impairment that is most probably mediated by autoantibody binding. Only nodal but no paranodal binding was detectable after chronic infusion of pan-NF IgG3 autoantibodies and no corresponding symptoms were detectable indicating that nodal binding alone may not be sufficient to induce symptoms.

Disclosure: Nothing to disclose.

EPR-184

Efficacy and safety of autologous hematopoietic stem cell transplantation in multiple sclerosis in Switzerland

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Background and aims: Autologous hematopoietic stem cell transplantation (aHSCT) is used since 1995 for treating patients with highly inflammatory and aggressive relapsing-remitting or progressive multiple sclerosis (MS) and has received approval in Switzerland in June 2018 with the requirement that transplanted patients participate in a prospective registry ("aHSCT-in-MS"). We here present efficacy and safety data for aHSCT-in-MS in Switzerland.

Methods: MS patients received aHSCT following the BEAM-ATG protocol, because they had experienced inflammatory breakthrough activity and/or progression of MS despite conventional highly effective disease-modifying therapy (DMT). We prospectively monitored adverse events (AE) and efficacy outcomes such as "no evidence of disease activity (NEDA)", i.e. absence of relapses, new or contrast-enhancing MRI lesions and clinical progression.

Results: At baseline, median age was 40 years (range 25–54), median disease duration 9.1 years (range 1.6–19.7) and median EDSS 4.0 (1.5–6.5). 16 (45.7%) patients had relapsing-remitting MS, 19 (54.3%) had progressive MS. Median post-aHSCT follow-up was 23.8 months (range 6.0–62.3). Most patients developed early mucotoxic and infectious AE (82.9%). 2 patients with secondary progressive MS committed assisted suicide 19 and 23 months post-aHSCT because of subjective perception of progression, although NEDA was confirmed in both cases. NEDA status was achieved in 22/27 (81.5%) patients 1 year after aHSCT. Until last follow-up, we observed sustained EDSS improvement in 20/35 (57.1%) patients and EDSS-relevant progression in 7/35 (20%) patients.

Conclusion: Altogether, safety of aHSCT-in-MS is acceptable, and efficacy outcomes are similar to other aHSCT studies. However, aHSCT-in-MS requires vigilant monitoring especially regarding infectious and psychiatric AE and antimicrobial prophylaxis.

Disclosure: The authors have nothing to disclose in relation to this work.

EPR-185

Human organotypic retina cultures to study pathophysiology of neuromyelitis optica spectrum disorder

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Background and aims: In neuromyelitis optica spectrum disorder (NMOSD), recurrent optic neuritis leads to potentially irreversible impairment. Pathogenic antibodies against aquaporin 4 (AQP4-IgG) are present in the majority of patients. With high abundance of AQP4 water channels, the retina might be a primary target of AQP4-IgG. Human organotypic retina cultures (hORC) retain an in vivo-like tissue architecture to investigate the intraretinal pathology in response to AQP4-IgG.

Methods: Human retinas were obtained from post-mortem donors and $50mm^2$ explants cultured in porous transwell culture inserts. At 7 days in vitro, AQP4-IgG + human serum (HuS), isotype (Iso-)IgG + HuS, no treatment or detergent (Triton-X) was added for 24h prior to 4% paraformaldehyde-fixation and cryo-embedding. Supernatant was collected for longitudinal analysis of cell death (Lactate dehydrogenase (LDH) assay). Retinal cross sections were stained (hematoxylin/eosin, glutamate synthetase, glial fibrillary acidic protein, AQP4, human IgG).

Results: Cell death measured by fold increase of LDH (mean ± standard error of mean) was similar for AQP4-IgG/HuS (n=10, 0.50±0.17), Iso-IgG/HuS (n=8, 0.52±0.19) and no treatment (n=7, 0.52±0.07). Detergent exposure increased cell death (n=10, 27.45±13.25, p=0.006, Kruskal-Wallis test). Histological evaluation is ongoing.

Conclusion: hORC are viable over the observed time period without an increase of cell death upon AQP4-IgG stimulation. This may be in line with the recognized course of events in spinal cord lesions where astrocytic lysis is described in advanced demyelinating lesions. Early signs of NMOSD pathology include morphological changes rather than death. This is currently being investigated in our system.

EPR-186

Progressive post-infectious neurological syndromes: clinical profile and neurofilament light chain quantification

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Background and aims: Postinfectious neurological syndromes(PINS), among which acute disseminated encephalomyelitis(ADEM), are inflammatory and mostly monophasic CNS disorders. We previously reported that PINS patients can show relapses or even disease progression without neuroradiological/laboratory signs of overt inflammation. We aimed to describe a cohort of patients with progressive-PINS, providing laboratory evidence of axonal damage.

Methods: Among 90 patients presented to our center with PINS in 2001–2021, we identified 7 with disability progression not explained by new relapses(stable MRI lesions and negative cerebrospinal-fluid analysis). Neurofilament light chain (NFL) serum levels were determined using EllaTM in age-sex-matched patients with progressive-PINS, ADEM, secondary progressive multiple sclerosis(SPMS), amyotrophic lateral sclerosis(ALS) and healthy controls.

Results: Patients presented with encephalomyelitis (2), encephalomyeloradiculitis(4) or myeloradiculitis (1)(Table 1). Median age at presentation was 51 (IQR, 42,5–64,5). Minimum follow-up was 6,2 years. Progression occurred after a median of 11 months from onset (in 4 cases after 1/more relapses) and led to maximum disability in about a year in 1/7. In 5/7 patients clinical progression involved the previously spared upper limbs, and in 5/7 the bulbar and or respiratory function requiring tracheostomy and/or percutaneous gastrostomy. All patients received immunotherapy (high dose steroids and/or IvIG) and 6/7 additional immunosuppressive drugs (4 Rituximab, 2 cyclophosphamide), with no clinical modification (Figure 1). NFL levels (Figure 1) were significantly higher in patients with progressive-PINS compared to ADEM (p=0.023) and healthy controls (p=0.004), but not to ALS or SPMS.
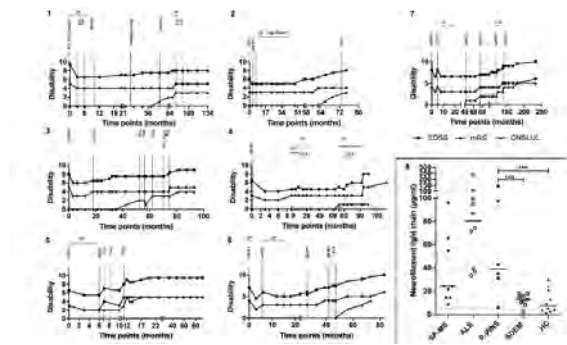
Fig 1. 1–7. P-PINS individual treatment response to therapies and disability accumulation. Red colour on X-axis indicates relapse. Green colour on X-axis shows progressive phase. Disability accumulation is depicted through EDSS, mRS, ONLSUL. 8. NFL levels

Conclusion: PINS can show a progressive course unresponsive to immunotherapy. NFL levels in these patients are comparable to those found in neurodegenerative conditions characterized by persistent axonal damage.

Disclosure: Nothing to disclose.

EPR-187

Patterned nose-to-brain transfer of therapeutic antibody in experimental autoimmune encephalomyelitis

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Background and aims: With a refined method of intranasal application targeting the olfactory mucosa, we have observed that Nogo-A-neutralizing IgG (11C7) mitigated experimental autoimmune encephalomyelitis (EAE), a mouse model of multiple sclerosis. However, the pattern of IgG distribution in the central nervous system (CNS) of EAE mice is not known. We thus sought to assess how 11C7 is distributed in the CNS of healthy and EAE mice.

Methods: Adult C57BL/6 mice intranasally received 30 ug of 11C7 or control IgG onto the olfactory mucosa of each nostril with a microcatheter. EAE was induced by injecting myelin oligodendrocyte glycoprotein peptide (MOG35–55). Motor deficits were daily assessed using a 0-3 scoring scale. 11C7 and control IgG were detected in different spinal cord and brain regions by capture ELISA and by light-sheet microscopy (LSM).

Results: High-resolution LSM revealed higher levels of 11C7 in the olfactory bulb and in the cerebellum. Preliminary data suggest that EAE potentiates the concentration of 11C7 in the cerebellum. Quantitatively, ELISA measurements corroborated higher 11C7 concentrations in the cerebellum, in addition to show accumulation in the lumbar spinal cord. We estimate that ~0.05% of 11C7 is detectable in the CNS after 5 consecutive days of application. Ongoing experiments aim at characterizing the molecular mechanisms mediating 11C7 uptake across the olfactory epithelium and its transport to CNS regions.

Conclusion: The therapeutic effects that we have previously observed on EAE after 11C7 administration on the olfactory mucosa are associated with a particular pattern of IgG distribution in the mouse CNS.

Disclosure: This study is part of the Bio-to-Brain Project (Bio2Brain), an EU-funded project of the H2020-MSCA-ITN-2020 (#956977).

EPR-188

B cell related predictive biomarkers of treatment response in myasthenia gravis

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Background and aims: Myasthenia Gravis (MG) is a B cell-mediated autoimmune disease characterized by muscle weakness and fatigability, mostly associated to antibodies against the acetylcholine receptor (AChR). MG patients are chronically treated by immunosuppressants and 10–15% are treatment refractory. The purpose of our study is to identify changes in B-cell subsets that could predict treatment response in MG subgroups with different treatment-related status, with the aim of improving MG management, leading to personalised therapy.

Methods: Peripheral blood mononuclear cells were isolated from 95 AChR-MG patients and 16 healthy-controls for the characterisation of transitional (CD19+CD20+CD24+CD38+), naïve (CD19+CD20+IgD+CD27-), double negative (CD19+CD20+IgD-CD27-), unswitched memory (CD19+CD20+IgD+IgM+CD27+), switched memory (CD19+CD20+IgD-CD27+IgG+), plasmablasts (CD19+CD27++CD38+) by multicolour flow cytometry.

Results: 47/95(49%) patients were males and median age at onset was 46 years. At sampling, 30/95(32%) patients were immunotherapy-naïve, 49/79 (52%) were immuno-therapy-responders, 18/95(19%) were refractory to standard immunotherapy and 15/95(16%) were in clinical stable remission (CSR). The frequency of total B-cells did not differ among the clinical subgroups. Naïve B-cells were significantly reduced in immunotherapy-responders and refractory patients compared to healthy-controls($p<0.001$) immunotherapy-naïve($p=0.002$), CSR patients($p=0.05$). Transitional B-cells were increased in refractory MG compared to immunotherapy-naïve($p=0.003$) and responders ($p=0.006$). Transitional B cells were also increased in patients with thymoma compared to patients with thymic hyperplasia ($p=0.037$) both before/after thymectomy.

Conclusion: The persistence of transitional B-cells, rather than antigen experienced B-cells, might predict unresponsiveness to immunotherapy in a subgroup of patients. In these cases, early B cell-directed therapies could restore the balance between regulatory and inflammatory B-cells in the pre-germinal compartment.

Disclosure: Nothing to disclose.

Movement disorders 3

EPR-189

Multimodal microstructural MRI for the identification of early Multiple System Atrophy biomarkers

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Background and aims: Multiple system atrophy (MSA) is characterized by autonomic failure with parkinsonism and/ or cerebellar dysfunction. This study aimed to investigate brain microstructural abnormalities in MSA through diffusion and neuromelanin-sensitive MRI and their relationship with clinical manifestations.

Methods: 11 MSA patients (within three years of diagnosis), 19 Parkinson's Disease (PD) and 18 healthy controls (HC) were enrolled. Neuromelanin-sensitive MRI was used to investigate integrity of substantia nigra (SN) and locus coeruleus (LC), while multi-shell diffusion MRI (dMRI) with neurite orientation dispersion and density imaging (NODDI) modelling was used to investigate microstructural abnormalities in a set of white and grey matter regions.
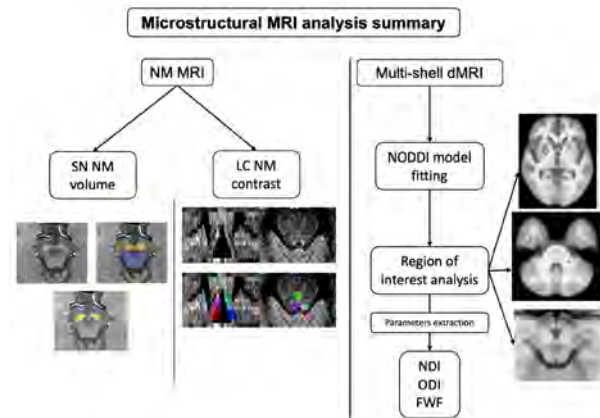
MRI analysis summary. Abbreviations: NM: neuromelanin; SN: substantia nigra; LC: locus coeruleus; dMRI: diffusion MRI; NODDI: neurite orientation dispersion and density imaging; NDI: neurite density index; FWF: free water fraction.

Results: Compared to PD, MSA patients had reduced neurite density index in the middle cerebellar peduncle and in the pons (Mann-Whitney U=44.0, p=0.019 and U=52.0, p=0.050), indicating white matter degeneration; increased free water fraction, indicating atrophy, in the putamen, caudate and cerebellar cortex (U=146.0, p=0.019; U=145.0, p=0.019; U=154.0, p=0.006 respectively). SN and LC neuromelanin content in PD and MSA were similarly reduced compared to HC. In MSA (but not in PD), rostral LC neuromelanin loss was associated with Montreal Cognitive Assessment (rho=0.770, p=0.006), Hospital Anxiety and Depression D-subscore (rho=-0.664, p=0.026), and RBD screening questionnaire scores (rho=-0.664, p=0.048). Motor impairment was not associated with neuromelanin or diffusion abnormalities.
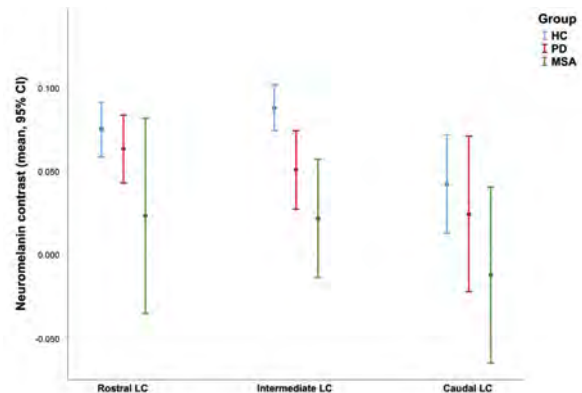
Locus coeruleus (LC) neuromelanin MRI contrast (means and 95% confidence intervals) in MSA, PD and HC, in rostral, intermediate and caudal LC.
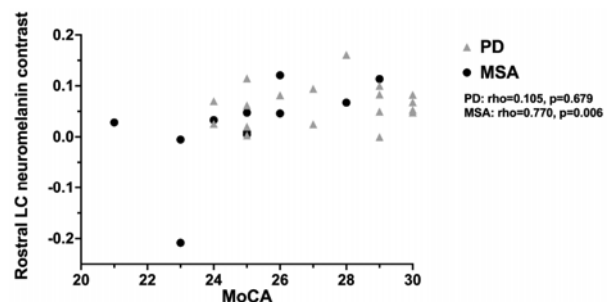
Relationship between rostral LC MRI contrast and MoCA scores in MSA and PD patients. Spearman's rho correlation coefficients and p-values for MSA and PD are displayed.

Conclusion: Neuromelanin and dMRI are suitable to investigate microstructural abnormalities in early MSA. LC degeneration is associated with severity of cognitive, depressive and RBD symptoms. Diagnostic and longitudinal assessment of microstructural abnormalities with multimodal MRI deserves further investigation as it may yield meaningful clinical biomarkers.

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EPR-190

Filling key monitoring gaps in Parkinson's Disease using AI and in-home sensor data

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Background and aims: Conventional monitoring tools for Parkinson's disease (PD) include questionnaires, diaries, and structured clinical exams focused on motor symptoms, which have known limitations such as subjectivity, adherence, and fluctuations with PD symptoms throughout the day. Spouses and partners also frequently report better performances during medical exams. All in all, clinicians can hardly trust their observations. They must rely on patient history which is often not informative enough—particularly for patients with cognitive difficulties. Combined with the fact that patients are typically examined every few months, tools powered by more continuous and objective sources of data would help fill in key monitoring gaps.

Methods: We monitored 15 patients for 6 months using in-home passive sensors including a pressure-based bed sensor measuring movement intensity as well as heart and respiration rates. Patients were asked to keep a daily diary of important events, such as medication changes, and were evaluated every 3 months using standard rating scales.

Results: We developed a cloud-based clinical decision support system (CDSS) to monitor sleep-related aspects of PD continuously and automatically through a variety of biomarkers selected and engineered with PD experts. We developed a novel deep-learning architecture to identify biomarker changes on choosable timescales, and designed a dashboard to visualise the evolution of biomarkers and quickly identify regions of interest based on changes.

Conclusion: The biomarkers and changes made available to clinicians by the developed CDSS revealed a great level of detail about patient trajectories, displaying clear correlations with clinical events such as treatment modifications.

Disclosure: Nothing to disclose.

EPR-191

Evidence of a causal relationship between Parkinson's disease and autoimmune disorders driven by HLA

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Background and aims: Epidemiological studies suggest an association between Parkinson's disease (PD) and a variety of inflammatory and autoimmune disorders. In the current study, we aim to explore the causal relationship between PD and these traits.

Methods: We selected the largest publicly availably genome-wide association studies (GWASs) for inflammatory and autoimmune disorders with participants of European ancestry. To determine potential causal associations, we used Mendelian randomization (MR). In MR, single-nucleotide polymorphisms (SNPs) are used as proxies to determine the causal association between exposure and an outcome (PD in our case). In addition, we examined genetic correlations between the different inflammatory/autoimmune traits and PD using linkage disequilibrium score regression for the same summary statistics.

Results: We selected 11 summary statistics for analysis (Table 1). The instruments in all studies had sufficient strength as demonstrated by F-statistics >10. After application of Bonferroni correction for multiple comparisons, we found a potentially protective role of type 1 diabetes (T1D) (Inverse variance weighted (IVW); beta= -0.029, se=0.010, p=0.004) and Rheumatoid arthritis (RA) for PD (IVW; beta=-0.072, se=0.021, p=4.7E-04). We repeated the analysis after the exclusion of SNPs within the major histocompatibility complex (MHC) region in RA and T1D. The causal association between RA and PD became non-significant and for T1D and PD had only nominal significance. We also found suggestive evidence for genetic correlation between T1D and PD (rg=-0.17, p=0.016).

Exposure	N, SNPs included	F-statistics	MR Egger			Inverse variance weighted		
			beta	standard error	p	beta	standard error	p
Asthma	84	100	0.002	0.037	0.951	0.005	0.015	0.728
Crohn's disease	74	20	0.072	0.034	0.037	0.014	0.013	0.259
Celiac disease	12	67	0.049	0.074	0.519	-0.003	0.019	0.859
Irritable Bowel Syndrome	3	1257	-3.259	1.934	0.341	-0.325	0.162	0.045
Multiple sclerosis	44	32	0.098	0.030	0.002	0.024	0.016	0.130
Primary biliary cirrhosis	40	35	-0.003	0.022	0.893	0.001	0.008	0.994
Primary sclerosing cholangitis	17	54	0.031	0.019	0.122	0.016	0.010	0.097
Psoriasis	61	95	-0.001	0.003	0.686	0.001	0.002	0.885
Rheumatoid arthritis	14	170	-0.119	0.031	0.002	-0.072	0.021	**4.7E-04**
Type 1 diabetes	42	93	-0.040	0.016	0.015	-0.029	0.010	**0.004**
Ulcerative colitis	56	31	0.006	0.055	0.916	0.004	0.019	0.842

Table 1: MR analysis between exposure (immune, inflammatory disorders) and outcome (PD)

Conclusion: The potentially causal relationship between T1D, RA, and PD is mainly driven by human leucocyte antigen (HLA) genes.

Disclosure: Nothing to disclose.

EPR-192

Gait Analysis in Normal Pressure Hydrocephalus: a Meta-Analysis

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Background and aims: This meta-analysis provide a synthesis of the quantitative gait data of idiopathic normal pressure hydrocephalus (iNPH) patients, to investigate gait parameters more likely to improve after tap-test (TT) and CSF shunt surgery (CSS), also differentiating responders (R) from non-responders (NR).

Methods: Studies enrolling a cohort of iNPH patients, providing at least one instrumented gait measure were selected. Three time points of gait assessment were defined: PRE, POST-TT and POST-CSS. Gait velocity, cadence, step length, stride length, and double limb support time (DLS) were the individuated outcomes. Patients were categorized on the basis of their responsiveness to CSF diversion as TT-R, CSS-R and TT-NR and CCS-NR.

Results: iNPH patients (563) improved in all gait outcomes except step length POST-TT and in each meta-analyzable parameter POST-CSS, with a significative difference between the two time points. TT-R improved significantly POST-TT and even more POST-CSS. A gait velocity of 0.55 ± 0.01 m/s with an increase to 0.70 ± 0.01 m/s POST-TT seems to be characteristic of these patients. A meta-regression analysis revealed that TT effect on gait velocity plateaus after 24h. Several parameters consistently discriminated iNPH patients from HC and, in spite of the aforementioned improvements, patients' gait never normalized.
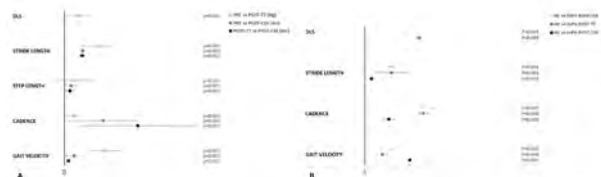
Figure 1. A) Differential values between the three time points for all the iNPH. Means difference (dm) or Hedges' g (Hg), 99 % IC. B) Comparison between all the iNPH patients and HC. Data are expressed as means difference (p-value), IC 99 %.
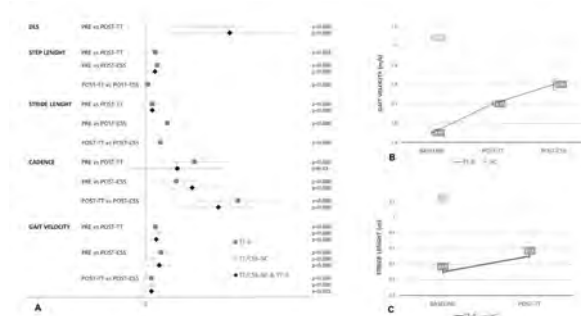
Figure 2. A Differential values at the three time points for iNPH subgroups. Means difference, IC 99 %. Comparison of gait velocity (B) and stride length (C) between TT-R at different time points and HC.
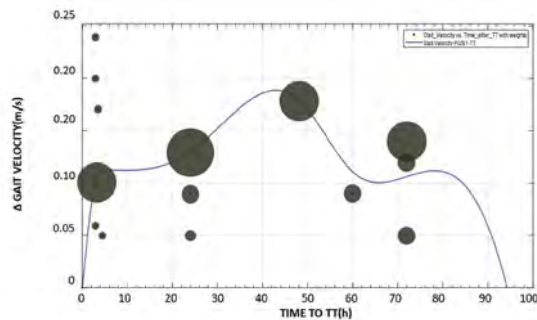
Figure 3 A. Meta-regression of the differential gait velocity POST-TT vs PRE over time. Data were obtained as difference in means at POST-TT and PRE assessment for each study subgroup (green circles, ray proportional to weigths). Abbr: TT: Tap-test

Conclusion: Gait analysis is a reliable instrument to assess gait impairment in iNPH patients, demarking a net differentiation from HC, in keeping with the notion that CSF dynamic alteration may cause an irreversible damage. In addition, specific parameters delineate the gait pattern of TT-R, providing an opportunity to select patients that will respond to CSS.

Disclosure: Nothing to disclose.

EPR-193

Sleep and Efficacy Endpoint Correlations After 6 Months of Subcutaneous Foslevodopa/Foscarbidopa in Parkinson's Disease

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Background and aims: Foslevodopa/foscarbidopa is a soluble formulation of levodopa/carbidopa prodrugs delivered via continuous subcutaneous infusion. Safety, tolerability, and exploratory efficacy of 24-hour/daily optimized doses of foslevodopa/foscarbidopa are being evaluated in a 52-week, phase 3, open-label, single-arm, multicenter study in patients with Parkinson's disease (PD) whose motor and nonmotor symptoms were inadequately controlled by their current treatment (NCT03781167).

Methods: An interim analysis was conducted when ≥ 100 patients completed 6 months of foslevodopa/foscarbidopa treatment. Here we present a post-hoc analysis of the correlations between sleep (PDSS-2), motor complications (PD Diaries), motor experiences of daily living (m-EDL [MDS-UPDRS part II]), and quality of life (QoL [PDQ-39]) based on those interim results. Spearman's rank correlation coefficients are provided.

Results: Six-month interim results showed improvements in all assessed outcomes (Table 1). At baseline, PDSS-2 scores did not correlate with "Off" time and positively correlated only with m-EDL scores ($p<0.001$) and PDQ-39 scores ($p<0.001$). Conversely, improvement in PDSS-2 scores positively correlated with improvements in "Off" time ($p<0.001$), m-EDL ($p<0.05$), and PDQ-39 scores $p<0.001$; and negatively correlated with "On" time without troublesome dyskinesia $p<0.05$ (Table 2). The correlation between improvements in PDSS-2 and "On" time without dyskinesia is not statistically significant. Most adverse events (AEs) were mild/moderate; 24.2% of patients prematurely discontinued due to an AE. Skin AEs were consistent with subcutaneous delivery. Systemic AEs were consistent with oral levodopa/carbidopa.

Characteristic	Baseline	Change From Baseline
Daily "Off" time, hours[a]	5.9 (2.3) n = 215	−2.9 (3.2)*** n = 97
Daily "On" time without dyskinesia, hours[a]	6 5 (3.3) n = 215	4.0 (4.4)*** n = 97
Daily "On" time with non-troublesome dyskinesia, hours[a]	2.7 (2.6) n = 215	−0.8 (3.4)[a] n = 97
Daily "On" time without troublesome dyskinesia, hours[a]	9.2 (2.4) n = 215	3.2 (3.2)*** n = 97
Daily "On" time with troublesome dyskinesia, hours[a]	0.9 (1.7) n = 215	−0.3 (1.5) n = 97
PDSS-2 total score	20.5 (9.7) n = 222	−5.7 (11.2)*** n = 104
MDS-UPDRS part II	15.8 (7.5) n = 223	−3.2 (6.8)*** n = 104
PDQ-39 summary index	34.3 (14.9) n = 222	−7.2 (11.4)*** n = 104

Patients Awakening In the Below Motor State	Baseline	Observed at Month 6
"Off" time	77.8% n/N = 119/153	20.8% n/N = 16/77
"On" time without dyskinesia	18.3% n/N = 28/153	68.8% n = 53/77
"On" time with non-troublesome dyskinesia	3.3% n/N = 5/153	9.1% n/N = 7/77
"On" time with troublesome dyskinesia	0.7% n/N = 1/153	1.3% n/N = 1/77

Data are mean (SD) unless otherwise specified.
*P<.05; ***P<0.001.
[a]Normalized to a 16-hour waking day.
MDS-UPDRS. Movement Disorders Society Unified Parkinson's Disease Rating Scale; PDSS-2, Parkinson's Disease Sleep Scale-2; PDQ-39, 39-item Parkinson's Disease Questionnaire.

Table 1: Clinical Characteristics at Baseline and Month 6

Variables	Spearman's Rank Correlation Coefficient	
	Baseline	Change From Baseline at Month 6
PDSS-2[a] and "Off" time[b]	0.069	0.388***
PDSS-2[a] and "On" time without troublesome dyskinesia[b]	−0.130	−0.270[c]
PDSS-2[a] and "On" time without dyskinesia[b]	−0.063	−0.193
PDSS-2[a] and MDS-UPDRS II[c]	0.281***	0.212[c]
PDSS-2[a] and PDQ-39 summary index[c]	0.436***	0.346***
Baseline PDSS-2[a] and baseline motor state at awakening	−0.096	NA
Change in PDSS-2[a] and change in motor state at awakening for patients who awoke in "Off" at baseline[d]	NA	−0.122
Change in PDSS-2[a] and change in motor state at awakening for patients who awoke in "On" with troublesome dyskinesia at baseline[e]	NA	NA[f]
Change in PDSS-2[a] and change in motor state at awakening for patients who awoke in "On" with non-troublesome dyskinesia at baseline[g]	NA	NA[h]
Change in PDSS-2[a] and change in motor state at awakening for patients who awoke in "On" without dyskinesia at baseline[i]	NA	0.207

*P<.05; ***P<0.001.
[a]Baseline n = 222; month 6 n = 104.
[b]Baseline n = 215; month 6 n = 97.
[c]Baseline n = 223; month 6 n = 104.
[d]Patients who awoke in "Off" at baseline, n/N =119/153.
[e]Patients who awoke in "On" with troublesome dyskinesia at baseline, n/N = 1/153.
[f]NA as only 2 patients with "On" with troublesome dyskinesia at baseline and "On" without dyskinesia at Month 6. [g]Patients who awoke in "On" with non-troublesome dyskinesia at baseline, n/N = 5/153.
[h]NA as 0 patients with "On" with non-troublesome dyskinesia at baseline and other motor state at awakening at Month 6.
[i]Patients who awoke in "On" without dyskinesia at baseline, n/N = 28/153.
MDS-UPDRS, Movement Disorders Society Unified Parkinson's Disease Rating Scale; NA, not assessed; PDSS-2, Parkinson's Disease Sleep Scale-2; PDQ-39, 39-item Parkinson's Disease Questionnaire.

Table 2: Spearman's Rank Correlation Between Sleep and Efficacy Endpoints

Conclusion: Improvements in sleep with 24 hour/daily foslevodopa/foscarbidopa in patients with PD significantly correlate with improvements in "Off" time, "On" time without troublesome dyskinesia, m-EDL, and QoL.

EPR-194

Abstract withdrawn

EPR-195

N-acetyl-L-leucine Improves Symptoms and Functioning in GM2 Gangliosidosis

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Background and aims: The modified amino acid N-acetyl-leucine has been associated with positive symptomatic and neuroprotective effects in animal and cellular models of GM2 Ganglisidosis (GM2) and in observational clinical case series. Therefore, the symptomatic effects of the active L-enantiomer, N-acetyl-L-leucine (IB1001/NALL) were evaluated in paediatric and adult patients.

Methods: We conducted a multi-national, open-label, rater-blinded study in subjects with a confirmed diagnosis of GM2. Subjects were assessed during a baseline period, a 6-week treatment period (orally administered NALL), and a 6-week post-treatment washout period. The primary endpoint was the Clinical Impression of Change in Severity (CI-CS) (based on a 7-point Likert scale). Secondary outcomes included cerebellar rating scales (namely Scale for the Assessment and Rating of Ataxia (SARA)), clinical global impression (CGI), and quality of life assessments.
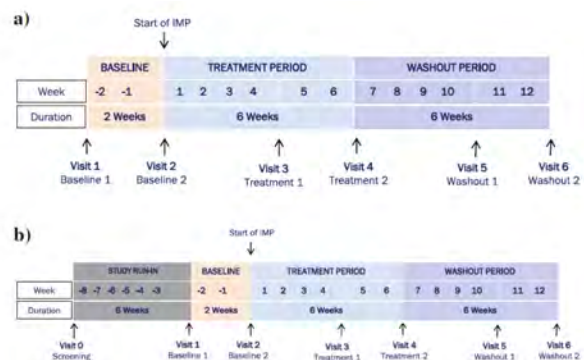
Parent study schema. A) Naïve (treated with ADLL before) patients vs. B) Non-naïve patients

Extension Phase

Results: 30 GM2 subjects aged 6 to 55 were recruited across 8 study centers. IB1001 met its CI-CS primary endpoint (NPC p=0.029; GM2 p=0.039) and secondary endpoints (SARA, physician/caregiver/patient CGI).

Result Summary

Conclusion: This study showed NALL led to a statistically significant improvement in symptoms, functioning, and quality of life in patients with GM2 gangliosidosis. It is a safe, well-tolerated, easily administered oral therapy, therefore offering a favorable risk/benefit profile for this serious, debilitating disorder. NALL is a new therapeutic option for the treatment of this rare disease that has no other approved therapies worldwide.

Disclosure: The clinical trial is sponsored and paid for by IntraBio Ltd. Dr. Bremova-Ertl received honoraria for lecturing from Actelion and Sanofi Genzyme and fees for the blinded rater services from IntraBio.

ePresentations

Monday, June 27, 2022
COVID-19 & Infectious diseases 2

EPR-196

Bacterial meningitis: five-year data from a Portuguese Hospital Centre

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Background and aims: The incidence of bacterial meningitis decreased in the last decades due to vaccination. The aim of our work was to perform a systematic retrospective analysis of bacterial meningitis during five years at a 400-bed hospital in Northern Portugal (Centro Hospitalar Entre o Douro e Vouga).
Methods: Adults with pleocytosis higher than 50 WBC/uL or bacterial growth in cerebrospinal fluid (CSF) were selected, between 2015–2020. We performed a descriptive analysis of demographic, clinical, analytical and imaging data of patients with diagnosis of bacterial meningitis.
Results: Criteria were fulfilled by 121 patients, 44.6% had diagnosis of bacterial meningitis, median age 61 years and 57.0% males. Most common risk factor was otorhinolaryngological infections in 33.3%. Fever was present in 87.0%, altered consciousness in 68.5% and headache in 55.6%. CSF analysis showed median 2751 WBC/uL, protein 2.43 g/L and glucose 0.32g/L. In 64.8% of cases an etiological agent was identified (42% CSF, 19% hemocultures): 40% Streptococcus Pneumoniae, 14% Neisseria Meningitidis, 11% Listeria Monocytogenes, 11% Staphyococcus Aureus, 9% Haemophilus Influenzae. Median time to antibiotics start was 8 hours and 48% of cases had shock criteria or required intensive care treatment. Case-fatality rate was 14.8%. Sequelae was found in 30.4% of the survivors, commonly motor or cognitive.
Conclusion: We highlight the percentage of cases without identified agent and hemocultures diagnostic rentability, reinforcing their importance in suspected cases. The delay found in antibiotics start shows the relevance of early and fast diagnosis. There is still a considerable high mortality associated with bacterial meningitis.
Disclosure: No conflicts of interest.

EPR-197

HIV-associated granular cell infection with JC virus treated with allogenic donor lymphocytes

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Background and aims: Infection of the cerebellar granular cells with JC virus in HIV-infection is rare. As with PML, apart from immune reconstitution by antiretroviral therapy (ART), there is no established anti-JCV treatment. In PML, single cases treated with infusions of BK-virus-specific allogenic donor lymphocytes (DLI) are published.
Methods: Case presentation
Results: A 43 year-old untreated HIV-infected woman developped progressive gait ataxia and dysarthria. Her CD4-count was 30/µl. Brain MRI revealed a non-contrast enhancing, T2-hyperintense lesion in the vermis cerebelli. Her CSF was non-inflammatory but JCV-PCR revealed 415 copies of JCV DNA/ml. ART was started, and the CD4-count rose to 78/µl. She further deteriorated, and alternative treatment was needed. Brain biopsy showed infection of cerebellar granule cells with JCV and perivascular lymphocytic infiltration. The frequency of lymphocytes specific for BKV (a virus antigentically closely related to JCV) were found to be low in her peripheral blood but were much higher in her haploidentical son. BK-specific lymphocytes, taken from her son, were selected by means of fluorescence associated cell sorting (FACS) and infused into the patient. Clinically the patient slowly improved. Treatment was well tolerated and the CSF remained non-inflammatory.
Conclusion: To our knowledge, this is the first case of HIV-associated granular cell infection with JC virus treated with allogenic BK virus-specific donor lymphocytes. The moderate degree of improvement can be explained by the irrevocable loss of the cerebellar granule cells.
Disclosure: Nothing to disclose.

EPR-198

Cognitive findings in patients with post-COVID-19 syndrome - results from a prospective monocentric cohort

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Background and aims: A fraction of patients who were asymptomatic or had a mild to moderate acute COVID-19 disease course report cognitive deficits as part of the post-COVID-19 syndrome. This study aimed to provide a neuropsychological profile of these patients.

Methods: Assessment at baseline (3 months or later following COVID-19) of a monocentric prospective cohort of patients with post-COVID-19 syndrome. Multidomain neuropsychological tests were performed and questionnaires on depression, anxiety, fatigue, sleep, and general health were administered.

Results: Of the 58 patients screened, six were excluded due to possible alternative causes of cognitive impairment (major depression, neurodegenerative disease). Of the remaining 52 individuals, one had a below-threshold screening test (Mini Mental State Exam cut-off ≥ 26). Multidomain neuropsychological testing revealed a neurocognitive disorder (NCD) in 31 (59.6%) cases with minor NCD in the majority (n=26). In patients with NCD, the cognitive domains learning/memory and executive functioning were impaired in 60.7%, attention in 51.6%, language in 35.5%, and perceptual-motor function in 29.0%. Cognitive performance was associated with sleep but not with depression, anxiety, general health or fatigue.

Conclusion: Neuropsychological dysfunction can occur as part of post-COVID-19 syndrome even after mild acute COVID-19. Notably, this dysfunction was not detected by screening tests and can affect all cognitive domains. Longitudinal studies are strongly needed to evaluate the course of neurocognitive deficits, and to associate the findings with blood and CSF surrogate markers of neurodegeneration and autoimmunity in post-COVID-19 syndrome.

Disclosure: CW received personal compensation for participating to a scientific discussion from Biontech. No other disclosures related to this abstracts.

EPR-199

Major neurological complications of COVID-19: Comparative features, predictors and outcome

E. Beghi [1], E. Moro [2], E. Davidescu [3], B. Popescu [3], O. Grosu [4], F. Valzania [5], M. Cotelli [6], G. Kiteva-Trenchevska [7], M. Zakharova [8], T. Kovács [9], C. Armon [10], W. Brola [11], C. Yasuda [12], L. Maia [13], A. Lovrencic-Huzjan [14], M. Laracho de Seabra [15], R. Avalos-Pavon [16], A. Aamodt [17], S. Meoni [18], V. Gryb [19], I. Krehan [20], M. Lolich [21], E. Bianchi [22], R. Helbok [23], C. Bassetti [24]

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Background and aims: SARS-Cov-2 infection is associated with the emergence of diverse neurological signs and symptoms. To study neurological manifestations and their impact on patients´ outcome the EAN Neuro-Covid Registry Consortium (ENERGY) was initiated in May 2020. In this report we compare phenotypes and outcome in COVID-19 patients with and without selected neurological manifestations.

Methods: Neurologists collected data on people with COVID-19 infection seen in in- and outpatient clinics and emergency rooms in 23 European and 7 non-European countries. Neurological manifestations documented in at least 100 patients were considered and patients with and without specific clinical conditions were compared looking for differences in patient's demographics, lifestyle habits, comorbidities, main COVID-19 complications, and outcomes (recovery, improvement, sequelae, death).

Results: By 31st July, 2021, 1523 patients (756 women, 758 men and 9 intersex/unknown, aged 16–101 years) were registered. Neurological manifestations were diagnosed in 1213 patients (79.6%). At study entry, 64.2% had one or more chronic comorbidities. Predominant signs and diseases during the acute phase were cognitive dysfunction (n=403, 26.5%), stroke (n=392, 25.7%), sleep disorders (n=250, 16.4%), dysautonomia (n=224, 14.7%), peripheral neuropathy (n=145, 9.5%), movement disorders (n=142, 9.3%), ataxia (n=134, 8.8%), and seizures (n=126, 8.3%). These disorders tended to differ with age, general and neurological comorbidities, severity and systemic manifestations of infection, extent of association with other neurological manifestations, and outcome.

Conclusion: People with COVID-19 and neurological manifestations present with distinct phenotypes. Age, general and neurological comorbidities and severity of COVID-19 have an impact on neurological manifestations and outcome of COVID-19.

Disclosure: Nothing to disclose.

EPR-200

Clinical, laboratory, neurophysiological and neuroradiological characterization of COVID-19 related encephalopathy

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Background and aims: COVID-19 related encephalopathy is the most common neurological complication of SARS-CoV-2 infection, but its definition remains incomplete. Aim of the study was the clinical, laboratory, neurophysiological and neuroradiological characterization of patients with COVID-19 related encephalopathy admitted in the Neuro-Covid Unit of the Udine University Hospital in the time interval between 30th of November 2020 and 31st of May 2021.

Methods: Study design was retrospective and monocentric. Clinical, laboratory and instrumental data of patients were collected. Statistical analysis was limited to point estimates and 95% confidence intervals. A principal component analysis was undertaken to reduce the number of variables.

Results: 13 patients (M/F=1.6) with mean age of 73.4 years-old were included. Mean Charlson comorbidity index was 3.6 and COVID-19 severity was variable. Clinically, all subjects had altered consciousness assessed with the Glasgow Coma Scale (GCS). Laboratory findings included T-CD8+ lymphopenia and hallmarks of COVID-19 related coagulopathy. Cerebrospinal fluid (CSF) analysis (11/13) showed modest pleocytosis and IgM/IgG anti SARS-CoV-2 in 67% of cases, SARS-CoV-2 was never isolated. A specific CSF cytokine pattern (i.e., IL-1, IL6, IL-10, IP-10 e TNF-alpha) was associated with altered consciousness, higher levels correlating with lower GCS scores (p=0.05). EEG alterations included diffuse background slowing (46.2%) and epileptiform abnormalities (38.5%); six patients presented epileptic seizures with evolution to status epilepticus in four cases. Brain MRI demonstrated inflammatory alterations in two cases.

Conclusion: Our study expands the characterization of COVID- 19 related encephalopathy, supporting the pathogenetic role of both an excessive intrathecal inflammatory response and of CSF anti-SARS-CoV-2 immunoglobulins.

Disclosure: None relevant to the manuscript.

EPR-201

A UHPLC-MS/MS method for the simultaneous quantification of Hypocretin 1 and 2 levels in cerebrospinal fluid

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Background and aims: Cerebrospinal fluid (CSF) levels of Hypocretin-1 (Hcrt-1) are included in the diagnostic criteria for Narcolepsy. The current standard method, a radioimmunoassay, does not allow a precise quantification of CSF-Hcrt-1 and suffers limitations (e.g. availability, cross-reactions). Measurements with liquid chromatography coupled to tandem mass spectrometry are of potential interest but three recent studies have shown conflicting results. The aim of this study is to establish a LC-MS/MS workflow to measure Hcrt-1and -2.

Methods: The analysis was done on a Shimadzu UHPLC (Shimadzu Corporation, Kyoto, Japan) coupled to a Q-TRAP 6500 plus (Sciex, Darmstadt, Germany). The established workflow bases on three recent publications on the topic (Lindström et al., 2021; Bårdsen et al., 2019; Hirtz et al., 2016). Hcrt-1 and 2 were calibrated between 10 and 1000 pg/ml. To test the workflow, we applied it to anonymized residual samples of four patients with NT1 and controls.

Distribution of Hcrt-1 measurements in NT1 and controls according to the current literature.

Results: Calibration curves for Hcrt-1 and Hcrt-2 both show a linearity of R2>0.99. In our experience, glass vials lead to more adsorption than plastic 96-well plates. Hrct-1 was quantified in the CSF of controls, and not detectable in patients with NT1. Hcrt-2 could not be detected in all samples.
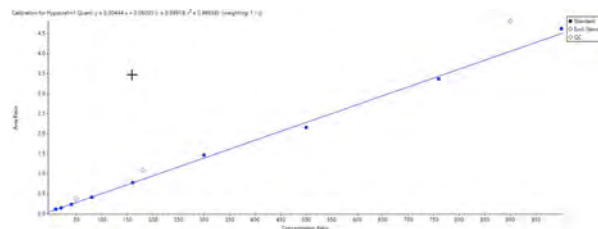
Calibration curve of Hypocretin-1.

Conclusion: Preliminary results of this study suggest that the developed LC-MS/MS workflow is able to differentiate between NT1 patients and controls. To date, LC-MS/MS is still in the technical evaluation phase for Hcrt measurements. Further technical validation and standardization is required and the method will in the next two months be applied to a clinically well-defined sample.

EPR-202

Guillain-Barré Syndrome and COVID-19 relationship after a year of pandemic: an Italian observational multicenter study

S. Cotti Piccinelli [1], S. Gazzina [2], E. Nobile-Orazio [3], A. Padovani [1], A. Uncini [4], M. Filosto [5], on behalf of the GBS-COVID-*19* North Italian Study Group [1]

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Background and aims: Single cases and small series of Guillain-Barré syndrome (GBS) associated with SARS-CoV-2 infection were reported during the COVID-19 outbreak worldwide. However, the exact relationship between COVID-19 and GBS remain unclear and the debate is still ongoing.

Methods: GBS cases diagnosed in 14 referral hospitals from Northern Italy between March 2020 and March 2021 were collected and divided into COVID-19-positive and COVID-19-negative. As a control population, GBS patients diagnosed from January 2019 to February 2020 in the same hospitals were considered. Clinical, biochemical and electrophysiological data were collected.

Results: Estimated incidence of GBS in 2020 was 1.41 cases (95% C.I. 1.18–1.68) versus 0.89 cases per 100.000 person/year (95% C.I. 0.71–1.11) in 2019. The cumulative incidence of GBS increased by 59% in the period March 2020-March 2021 and COVID-19 positive GBS patients represented more than 50% of the total GBS cases. COVID-19-negative GBS cases from March 2020 to March 2021 declined by 22% compared to February 2019-February 2020. Compared with COVID-19 negative patients, COVID-19-positive GBS had a lower MRC sum score (34.7±17.6 vs 47.8±12.1; p<0.001) and more frequent admission to ICU (49.2% vs 14.7%; p<0.001). GBS was almost exclusively associated with a moderate or severe form of COVID infection.

Conclusion: This study shows a significant increase of GBS in Northern Italy in the "COVID-19 era" compared to the previous year supporting previous studies suggesting a relationship between COVID-19 and GBS.

Disclosure: Nothing to disclose.

EPR-203

Myalgia and fatigue as "LONG COVID" Symptoms: a 1-year follow up

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Background and aims: COVID-19 main manifestation is interstitial pneumonia. Many neurological and neuromuscular manifestations were described as associated to SARS-CoV-2 infection. Multiorgan symptoms after COVID-19 are being reported by increasing numbers of patients. However, the long-term health consequences of COVID-19 remain largely unclear.

Methods: We enrolled 124 patients hospitalized between March and May 2020 for SARS-COV-2. We established a 6 and 12 months follow-up. For each patient cognitive tests, scales for depression and anxiety and Fatigue Severity Scale (FSS) were performed.

Results: 25 patients (19.8%) died during hospitalization. 87 (70%) patients were male and mean age was 67.3 years. During hospitalization 38.5% of patients complain of myalgia. Patients with reported myalgia had higher CK (534 U/L vs 93 U/l, p<0.001) and LDH levels (363 U/L vs 303 U/L) and they needed more often oxygen therapy (78% vs 42%, p<0.001) and non-invasive ventilation (20% vs 5%, p<0.001). At 12 months follow up 85 patient were evaluated and 42 % still complain about myalgia while 34% reported fatigue. Mean FSS value were significatively higher in patiets who complain about fatigue (40.2 vs 25.5 p<0.001) and muscle pain (40, 84 vs 26.80, p<0.001) compared to who did not.

Conclusion: During hospitalization for COVID-19 myalgia was associated with an higher level of CK and LDH, suggesting a possible direct muscle involvement. At 12 months myalgia and fatigue were commonly reported. These manifestation could be a main "long COVID" symptoms at one year follow-up.

Disclosure: Nothing to disclose.

Movement disorders 4

EPR-204

Impact of daily physical activity on motor performance in Parkinson's disease

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Background and aims: Physical activity (PA) is an important modulator of brain resilience and might impact on motor performances in Parkinson's disease (PD) Despite the advances in the field, the impact of daily PA on gait performance is still an open issue for PD patients. Aim of the study was to evaluate the impact of daily physical activity on gait parameters in PD patients adjusting for the effect of motor severity.

Methods: The prospective study included consecutive PD patients who underwent gait analyses using wearables in supervised conditions namely Time Up and Go (TUG), twenty meters walk (WAL) and circular walking (CIR) normal and during dual-task. The International Physical Activity Questionnaire (IPAQ) was applied to differentiate PD patients in two groups, active (AC) and no-active (NA) defined according to the recommended PA for over 65 age of Word Health Organisation (WHO). Differences were evaluated adjusting for the effect of age, sex and disease severity in multivariate analyses.

Results: 67 PD patients entered the study (mean age 65+7, mean disease duration 3+7 years). When adjusted for disease severity, age and sex, NA patients exhibited higher step time variability compared with AC patients in normal condition WAL (p=0.02) CIR normal speed (p<0.02) and dual motor task (p<0.03). In addition, during turning phase in TUG we observed a significatively greater peak velocity (p<0.02) in AC than NA.

Conclusion: Active PD patients showed better performances independently from disease severity. Our results further support the importance of daily activity as non-pharmacological intervention in patients from early to advanced stages.

Disclosure: Nothing to disclose.

EPR-205

The walking motor assessment of patients with idiopathic focal dystonia

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Background and aims: Gait difficulties in cervical dystonia (CD) patients were reported in few studies. Walking abnormalities may not be strictly related to dystonic postures and a primary neurologic dysfunction, could affect gait of CD patients. On this background we could speculate that also patients with different idiopathic focal dystonia (IFD) may have gait alterations. Aim of the present study is to investigate the walking motor pattern by computerized gait analysis (CGA) in patients with IFD not presenting postures originally impairing gait.

Methods: We enrolled 15 subjects with IFD (7 laryngeal, 6 oromandibular and 2 focal hand dystonia) and 13 healthy controls, matched at age and sex by unpaired t-test and x^2. Patients with blepharospasm were excluded because they may have walking difficulties related to vision limitations. CD patients were not included because they were assessed in the previous study. CGA was performed following the Davis protocol for each patient and spatiotemporal parameters were calculated and compared using both unpaired T-student and Mann-Whitney U tests. P-value was set at 0.05.

Results: Velocity, stride length, stride length % and step length were significantly reduced in IFD in comparison to healthy group (Details in tables 1, 2). Remaining parameters were comparable.

Unpaired T-student test HC; IFD	HC Mean	IFD Mean	P value	CI
Ln(velocity)	0.18	0.01	0.001	0.04;0.30
Ln (stride lenght)	0.19	0.01	0.001	0.10;0.28
Ln (stride length%)	4.25	4.11	0.001	0.04;0.24

Table 1. Unpaired T-student test performed after that velocity, stride length and stride length % resulted normally distributed with logarithmic transformation. Ln(velocity) mean=0.17; CI 0.04, 0.30; p<0.001; Ln (stride length) mean=0.19; CI 0.10, 0.28; p<0.001; Ln (stride length %) mean=0.14; CI 0.04, 0.24; p<0.001.

Mann-Whitney U test HC; IFD	
HC step length mean +- SD	0.48+-0.18
IFD step length mean +- SD	0.33+-0.16
Sign.	P=0.025

Table 2. Mann-Whitney U test which compared the step length of both groups. HC mean +- Standard Deviation was 0.48 ± 0.18 while in IFD was 0.33 ± 0.16. p= 0.025

Conclusion: Patients with IFD may present slight gait abnormalities consistent with a slow and short step. According with previous reports of slow gait in patients with CD our results may suggest that patients with any idiopathic focal dystonia may have a mild gait disorder possibly due to the primary neurologic dysfunction.

Disclosure: The authors have nothing to disclose.

EPR-206

Defining a Multidisciplinary Team for Rare Movement Disorders using a Delphi Consensus Approach

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Background and aims: Holistic care for patients with rare neurological diseases requires a collaborative multidisciplinary team effort. The European Reference Network for Rare Neurological Diseases (ERN-RND) has defined necessary competences required for representation in a multidisciplinary team (MDT) for rare movement disorders. The European Commission established ERN-RND in 2017, along with 23 other ERNs, with the goal of helping patients with rare neurological diseases in Europe receive faster diagnosis and access to adequate treatment and care. ERN-RND consists of healthcare professionals, representatives of patient organizations and researchers from nearly every EU country.

Methods: A stepwise Delphi process was used with clinicians for both adult and paediatric patients, as well as patient representatives, from the following disease groups: ataxia and hereditary spastic paraplegia; Huntington's disease and choreas; dystonia, paroxysmal disorders and NBIA; atypical parkinsonian syndromes and leukodystrophies.

Results: Following the collection of the required competences, a Delphi rating was conducted using the following criteria: Mandatory core members of the MDT (competence required for all patients/a majority of patients); members of the extended team (competence required for some patients/few patients); not a member of the MDT (special competence useful for a few patients, competence not necessary). The Delphi survey included 40 ERN-RND members from 18 countries.

Conclusion: The MDT was established for both adult and paediatric patients, and for three different disease stages, namely the diagnostic stage, the stage of preservation of function/active treatment stage and the final/palliative stage.

Disclosure: Nothing to disclose.

EPR-207

Orthostatic hypotension and dementia risk in Parkinson's disease and multiple system atrophy

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Background and aims: Growing evidence suggests that orthostatic hypotension (OH) increases the risk of subsequent dementia in Parkinson's disease (PD). However, the underlying pathophysiological mechanisms and impact of OH in other alpha-synucleinopathies are poorly understood.

Methods: Retrospective review of clinical records of autopsy-confirmed PD cases from the Queen Square Brain Bank archive between 2009–2018. An unselected group of pathology-proven MSA cases were used as disease control. Relevant clinical features were documented including onset and severity of OH, onset and pattern of cognitive impairment and dementia. Risk of dementia was estimated using multivariable Cox hazard regression models.

Results: 132 PD patients (61% male; 61.4±11.9 years at diagnosis) and 137 MSA patients (50% male; 60.3±8.3 years at diagnosis) were included. OH was more prevalent, developed earlier and had more severe symptoms in MSA than in PD; dementia prevalence was higher in the PD group. Early OH, but not severity of OH symptoms, was associated with subsequent dementia in PD (HR=0.86; 95% CI 0.80–0.93; p<0.001) and future cognitive impairment in MSA (HR=0.63; 95% CI 0.42–0.93; p=0.02). There was no significant association between OH onset or severity and pattern of cognitive impairment.

	PD (n = 132)	MSA (n = 137)
Age at diagnosis, years	61.4 (11.9)	60.3 (8.3)
Sex		
Male	80 (60.6)	69 (50.4)
Age at death (years)	77.8 (6.9)	65.6 (7.8)
PD motor subtype		
Tremor predominant	21 (15.9	NA
Akinetic rigid	84 (63.6)	NA
PIGD	27 (20.5)	NA
Levodopa response		
Nil to mild	6 (4.6)	NA
Moderate	9 (6.9)	NA
Good	30 (23.1)	NA
Excellent	85 (65.4)	NA
Orthostatic hypotension cumulative incidence	67 (50.8)	107 (78.1)
Orthostatic hypotension severity		
Mild	27 (20.5)	45 (32.9)
Moderate	26 (19.7)	35 (25.6)
Severe	14 (10.6)	27 (19.7)
Time from diagnosis to orthostatic hypotension (years)	8.2 (9.1)	1.1 (2.9)
Pattern of cognitive impairment		
Frontal-subcortical	25 (59.5)	12 (85.7)
Posterior-cortical	17 (40.5)	2 (14.3)
Dementia cumulative incidence	76 (57.6)	20 (14.1)
Time from diagnosis to dementia (years)	12.5 (8.3)	2.7 (4.2)

Summary of demographic and clinical characteristic of the sample, n (%) or mean (SD). PD = Parkinson's disease. MSA = multiple system atrophy. PIGD = postural instability gait disorder. NA = not applicable.

Conclusion: Despite significant differences in OH and dementia in PD and MSA, early development of OH increases the risk of subsequent cognitive impairment in both conditions. Severity of OH symptoms do not seem to have a negative association with cognition. Our results may have relevant pathophysiological implications.
Disclosure: There are no relevant financial or non-financial competing interests to report.

EPR-208
Abstract withdrawn

EPR-209
Towards the definition of patient-related outcome measurements in Hereditary Spastic Paraplegia

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Background and aims: Hereditary spastic paraplegias (HSP) are a heterogeneous group of rare neurodegenerative diseases, characterized by a progressive spastic paraparesis. Currently, the only available HSP-specific rating instrument is the clinician reported outcome measure (CROM) "Spastic Paraplegia Rating Scale" (SPRS). HSP-specific patient reported outcome measures (PROM) are lacking. As PROM have gained significant importance for clinical trials, we herein investigate progression rates of several PROM in an Austrian HSP cohort and compare them with CROM.
Methods: Genetically confirmed HSP patients were recruited at the "Centre for rare movement disorders" Innsbruck, Austria. CROM included the SPRS and Mini Mental State Examination (MMSE). PROM included the EQ-5D questionnaire, Patient-Health-Questionnaire-9 and the Barthel index. Standardized response means (SRM) were calculated for all scales, progression was estimated by the mean delta between baseline and follow-up after one year (FU).
Results: 55 HSP patients (36 males) were included in the study. FU was available for 30 subjects (21 males). Females showed higher scores in the EQ-5D domain of anxiety and depression (p=0.008) at baseline, no other gender-related differences were reported in further PROM or CROM. SPRS showed the highest responsiveness (SRM 1.11) and significantly increased at FU (p<0.001, 15.83±8.24 vs. 17.00±8.51), exhibiting a mean progression of 1.17 (SD±1.05) points. Neither MMSE nor PROM significantly increased at FU.
Conclusion: SPRS showed the highest responsiveness and significantly increased at FU. Well-established and validated but generic PROM did not show significant progression in our HSP-cohort. Our data suggest that the definition of novel, HSP-specific PROM is required to depict significant changes in HSP trials.
Disclosure: This research did not receive any funding.

EPR-210
Abstract withdrawn

EPR-211
Abstract withdrawn

Ageing and dementia & Sleep-wake disorders 3

EPR-212

Therapy adherence in narcolepsy

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Background and aims: Management of narcolepsy includes non-pharmacological approaches and symptomatic pharmacological treatment. The term "therapy adherence" is not defined uniformly. Chronic daytime sleepiness, cognitive deficits, psychiatric comorbidities and adverse events of pharmacological treatments suggest that therapy adherence may be restricted in narcolepsy. The aim if our study was to assess frequency of adherence barriers and to identify influencing factors on therapy non-adherence in narcolepsy.

Methods: For assessment an online survey was used and included demographic, disease-related data (i.e. symptoms, medication); and questionnaires. For identifying patient-specific barriers to medication-related adherence the ABQ (Adherence Barriers Questionnaire) was used. The ABQ defines the sections: medication-related/health care system-related barriers, unintentional, and intentional patient-related barriers.

Results: 253 completed questionnaires were included into analysis (n=60 male, n=192 female; n=175 narcolepsy type 1 (NT1), n=70 type 2 (NT2)). 88% of patients had an ABQ summed score above 25 points, indicating for an increased likelihood of non-adherence (NA). The highest value of NA was achieved by the subscale of unintentional NA risk (57%), followed by medication-/health care system-related NA risk (NT1: 59%, NT2: 46%), and the subscale of intentional NA risk (NT1: 47%, NT2: 41%). Single items "daily forgetfulness" (77%), and "depressive mood" (56%) were identified as the highest barriers. Only one percent of the patients had no adherence barrier at all.

Conclusion: Our results indicate for low treatment adherence in narcolepsy patients, which in partial is due to the symptoms of the disease, memory deficits and depression in particular. Future narcolepsy research addressing adherence is needed.

Disclosure: No conflicts of interest. There was no funding for the study.

EPR-213

Age-related vulnerability of the human brain connectome

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Background and aims: The study aim was to investigate whether and how brain functional connectome relates with structural changes due to aging.

Methods: The sample included 128 healthy individuals (50 young [yC] and 78 old [oC]), who underwent an MRI scan. Eight well-known hubs of the human connectome were selected as seeds: middle frontal gyrus, rostral anterior and posterior cingulate cortex, precuneus, inferior parietal, middle temporal (DMN hubs) and lingual gyri and pericalcarine cortex (occipital hubs). Per each seed, functional brain network was evaluated in yC to identify highly functionally connected regions with hubs. Then, regional cortical thickness trajectories with advancing age were modelled and changes over time were calculated. Finally, spatial similarity between functional pattern in yC and cortical atrophy in oC was estimated for each hub.

Results: Functional findings in yC revealed that DMN seeds showed distributed direct connections within DMN regions. Occipital hubs showed direct connectivity towards occipital lobe and sensorimotor areas. Structurally, greater cortical thinning was observed in the DMN hubs, while occipital hubs showed small atrophy changes across lifespan. Significant positive correlation was found between the functional pattern in yC of middle frontal hub and the cortical thinning in oC, while significant negative correlation emerged between the functional pattern of occipital hubs and the cortical thinning in oC.

Conclusion: Our findings revealed potential pattern of vulnerability to the onset of neurodegeneration in normal agers. This might hold the promise to understand the additive role of aging in modelling neurodegenerative progression trajectories in future longitudinal studies.

Disclosure: Supported by European Research Council (StG-2016_714388_NeuroTRACK).

EPR-214

eSATIS study: can treatment of sleep-disordered breathing improve cognitive recovery after stroke?

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Background and aims: Sleep-disordered-breathing (SDB) and cognitive dysfunction are common after stroke. Considering the link between SDB and cognitive dysfunction, we aimed to investigate the impact of SDB treatment on the cognitive recovery after stroke.

Methods: This project is a part of eSATIS study (Duss et al, Trials 2021). Demographics, stroke characteristics and sleep breathing (by respirography) were assessed at admission. Longitudinal assessments of cognitive functions were performed within 5 days post-stroke and at 3 months post-stroke. We investigated the association of SDB (apnea-hypopnea index≥20/h) and its treatment with cognitive parameters at subacute stroke using two multiple linear regression models (for untreated SDB versus non-SDB and for treated versus untreated SDB) adjusted for age, sex and baseline cognitive parameters.

Results: The analysis included 89 complete records (Table 1). Cognitive functioning generally improved from acute to subacute stroke (Table 2). Untreated SDB (n=27) was associated with the less improvement in verbal memory (Hopkins Verbal Learning Test, HVLT, delayed recall score: -1.13, p=0.042; HVLT recognition discrimination index: -0.93, p=0.041; Figure 1A-B) versus SDB absence. SDB treatment (n=14) was associated with larger improvement in visual memory (Brief Visuospatial memory test, total recall score: 3.38, p=0.037) and executive functioning (Trail Making Test Part B time: -25.80 msec, p=0.025; Figure 1C-D) versus no SDB treatment. No other significant effects were found.

Parameter	Overall	No SDB	Treated SDB	Untreated SDB	P-value#
N	89	48	14	27	
Age, years	64.10 [54.20, 73.80]	61.05 [48.78, 69.62]	71.05 [64.90, 75.85]	69.10 [60.65, 74.25]	0.003*
Female sex, %	30 (33.7%)	26 (54.2%)	2 (14.3%)	2 (7.4%)	<0.001*
NIHSS at admission, score	5.00 [2.00, 9.00]	5.00 [2.00, 7.00]	4.00 [3.00, 9.00]	5.00 [3.00, 12.00]	0.455
mRS at discharge, score	1.00 [1.00, 1.50]	1.00 [1.00, 1.00]	1.00 [1.00, 2.00]	1.00 [1.00, 1.75]	0.570
Intravascular treatment, %	31 (34.8%)	18 (37.5%)	6 (42.9%)	7 (25.9%)	0.491
Hypertension, %	55 (61.8%)	21 (43.8%)	13 (92.9%)	21 (77.8%)	<0.001*
Dyslipidemia, %	48 (54.5%)	21 (43.8%)	10 (76.9%)	17 (63.0%)	0.068
Diabetes, %	13 (14.6%)	1 (2.1%)	5 (35.7%)	7 (25.9%)	<0.001*
Atrial fibrillation, %	11 (12.9%)	5 (10.6%)	2 (16.7%)	4 (15.4%)	0.731
Coronary artery disease, %	13 (14.9%)	3 (6.2%)	4 (33.3%)	6 (22.2%)	0.020*
Migraine, %	18 (20.2%)	12 (25.0%)	2 (14.3%)	4 (14.8%)	0.512
Smoking, %	25 (28.4%)	14 (29.2%)	5 (38.5%)	6 (22.2%)	0.549
Past CCVE, %	26 (29.9%)	12 (25.5%)	4 (30.8%)	10 (37.0%)	0.586

Kruskall-Wallis test was used for continuous variables; Chi-Square Test was used for categorial variables.
* p<0.05
AHI – apnea-hypopnea index.
Data is presented as median and interquartile range.

Table 1: Study population. We considered the patients treated if they were randomized in the treatment group and completed the treatment from the acute phase. We considered the patients untreated if they were randomized in the control group.

Cognitive parameter		Acute stroke	Subacute stroke	P-value#
Language	Bernese Word Finding Test, total score	19.00 [17.00, 20.00]	20.00 [18.00, 20.00]	0.028*
Attention	Bells test, total number of omissions	2.00 [1.00, 4.00]	1.00 [0.00, 2.00]	0.001*
	Psychomotor Vigilance Task, mean reaction time, msec	327.00 [276.00, 422.00]	298.00 [259.00, 340.00]	0.003*
	Alertness, with warning signal, mean reaction time, msec	306.00 [268.50, 385.50]	282.00 [253.00, 334.00]	0.018*
Executive functions	Go-no Go Task, number of errors	2.00 [0.75, 4.00]	1.00 [0.00, 3.00]	0.153
	Trail Making Test, Part B, time to complete the task, sec	112.37 [67.21, 175.00]	88.84 [65.04, 112.55]	0.009*
	Victoria Stroop Test, color words time, s	37.00 [25.00, 47.00]	30.00 [23.75, 40.00]	0.024*
Visual memory	Corsi Block Test, span, units	5.00 [5.00, 6.00]	5.00 [5.00, 6.00]	0.949
	Brief Visuospatial Memory Test, total recall score	21.00 [15.00, 26.00]	26.00 [20.00, 30.25]	0.001*
	Brief Visuospatial Memory Test, delayed recall score	9.00 [6.00, 11.00]	10.00 [8.00, 12.00]	0.008*
Verbal memory	Digit span test forward, span, units	5.00 [5.00, 6.00]	6.00 [5.00, 6.00]	0.006*
	Hopkins Verbal Learning Test, total recall score	21.00 [18.00, 26.00]	24.00 [22.00, 28.00]	0.002*
	Hopkins Verbal Learning Test, delayed recall score	8.00 [6.00, 10.00]	9.00 [6.00, 11.00]	0.109

Wilcoxon paired-sample test
* p<0.05

Table 2: Cognitive functions generally improved from acute to subacute stroke.
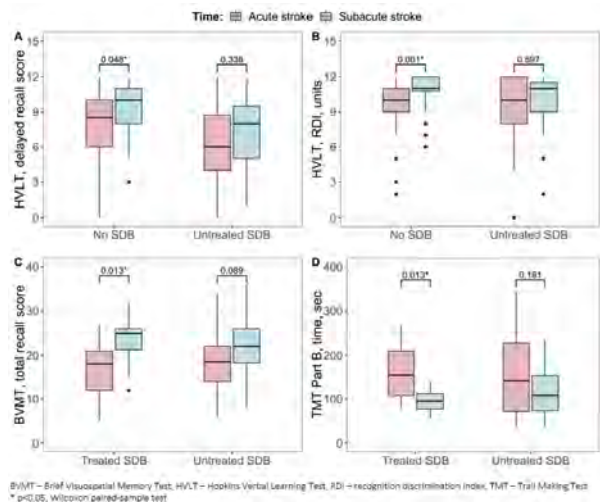
Figure 1: Verbal (A and B) memory improved over time in patients without SDB, but not in patients with untreated SDB. Visual memory (C) and attention (D) improved over time in patients with treated SDB, but not in patients with untreated SDB.

Conclusion: In our preliminary analysis, cognitive function seemed to improve from acute to subacute stroke. We will further investigate the robustness of the detected improvement in some tests for untreated SDB vs non-SDB patients and for SDB treatment versus no treatment.

Disclosure: Authors have no conflict of interest to declare.

EPR-215

Generation of novel mouse strain lacking interaction between FK506-binding protein 51 and heat shock protein 90

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Background and aims: FK506-binding protein 51 (FKBP51) recently emerged as possible therapeutic target for resolving tau aggregation in Alzheimer's disease (AD). FKBP51 can form complex with molecular chaperone heat shock protein 90 (Hsp90), which increases tau stability, facilitating its aggregation. Expression of FKBP51 increases in brains of aged mice and AD patients have higher FKBP51 expression, compared to age-matched healthy controls. We created knock-in mice with FKBP51 incapable of interacting with Hsp90 (FKBP51mut) to assess the role of FKBP51-Hsp90 interaction in ageing, AD and other diseases.

Methods: Knock-in mice harboring K352/A and R356/A point mutations in the tetratricopeptide repeat (TPR) domain of FKBP51 were generated using CRISPR/Cas9-mediated genome engineering. Genotype of mice was confirmed using PCR-based assay. Primary mouse embryonic fibroblasts (MEFs) were established and used for in vitro characterization. Interaction of FKBP51 with Hsp90 was examined using proximity ligation assay (PLA) on MEFs. Behavior of adult mice will be assessed at various ages using a battery of tests, including open field, novel object recognition, Y-maze, elevated plus maze, forced swim and fear conditioning.

Results: Mutation of FKBP51 is stable and inherited in Mendelian-like manner. Mutant homozygotes, heterozygotes and wild type mice can be clearly distinguished (Fig. 1). Mutant mice are viable and fertile. Mutation of FKBP51 leads to reduced interaction with Hsp90 (Fig. 2.).
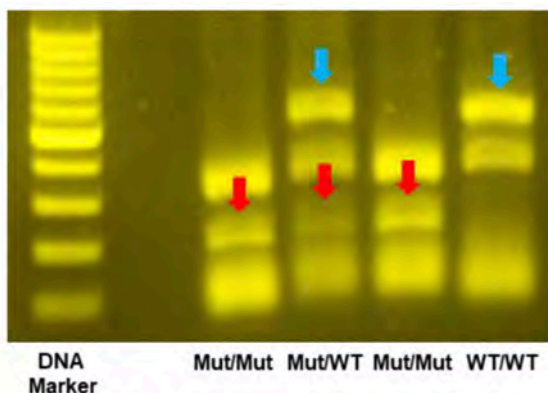
Fig. 1. Determination of mouse genotype using PCR-based assay. PCR products were incubated with BglI enzyme. Heterozygotes are characterized by the presence of both intact FKBP5 DNA (blue arrows) and cleavage product (red arrows). Homozygous mutants have only cleavage product, while in wild type only intact FKBP5 is present.

Fig. 1. Determination of mouse genotype using PCR-based assay.
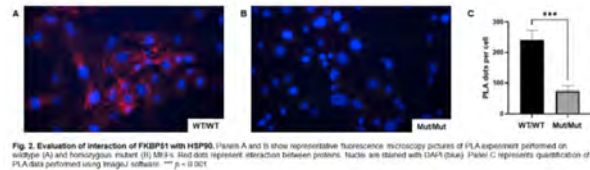
Fig. 2. Evaluation of interaction of FKBP51 with HSP90.

Conclusion: K352/A and R356/A point mutations in the TPR domain of FKBP51 render it incapable of interacting with Hsp90. Further research is granted to reveal functional significance of FKBP51-Hsp90 interactions.

Disclosure: Authors declare no conflict of interests.

EPR-216

Autosomal Dominant Cerebellar Ataxia with Deafness and Narcolepsy: follow up of 4 Italian kindred

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Background and aims: Autosomal dominant cerebellar ataxia, deafness and narcolepsy (ADCA-DN) is a multisystem degenerative disease with involvement of central and peripheral nervous system. We report the follow up of 3 Italian ADCA-DN kindreds already described adding a new ADCA-DN family.

Methods: Longitudinal follow up including peripheral nervous system, polysomnographic examinations, and cerebrospinal fluid (CSF) hypocretin-1 (hcrt-1) assay was performed in 10 patients.

Results: The first symptom (30% hypoacusia; 20% excessive daytime sleepiness/cataplexy) arose at a mean onset age (moa) of 31.33 years (y). Cerebellar ataxia, neurosensorial hypoacusia, sensorial neuropathy was documented in 70% (7/10; 38.6 y moa), in 70% (7/10; 33.6 moa y), in 50% (4/8) of our cohort, respectively. Severe psychiatric comorbidity (57.14%; 4/7) and cognitive impairment (50%; 3/6) appeared later at moa of 38.8 and of 46.7 y, respectively. Mean CSF hcrt-1 levels was 233.84±7.93 pg/mL with 2/7 patients around the cut-off of 110 pg/mL. MSLT showed pathological sleep latency and multiple SOREMPs in 3 and 4 out of 7 patients, while polysomnography at first evaluation, disclosed high rate of periodic limb movements during sleep (PLMS), REM sleep behaviour disorder (RBD), and reduced sleep efficiency in 42.9%, 28.6% and 28.7% of our cohort, respectively. Follow up at 5.42±1.14 years revealed increase in cataplexy frequency, reduction of sleep efficiency, increased PLMS and RBD.

Conclusion: Narcoleptic symptoms are the core feature of ADCA-DN. A multifaceted deterioration of sleep was evident across the disease course. CSF hcrt-1 levels were variably reduced, confirming the involvement of the hypocretin system within a widespread neurodegeneration.

Disclosure: G Plazzi participated in advisory boards for UCB Pharma, JAZZ Pharmaceuticals, Bioprojet, and Idorsia outside the submitted work. The other authors have indicated no potential conflicts of interest.

EPR-217

Subjective cognitive decline: 15 years of follow-up experience from a memory clinic

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Background and aims: Clinical research is focusing on subjective cognitive decline (SCD) to identify patients at risk of dementia. SCD has also been related to non-degenerative diseases and to a variety of poor health outcomes. In the present study we reported biomarker and follow-up data from our memory clinic.

Methods: From a sample of 445 SCD patients self-referred to our center, we considered: 119 patients followed-up for at least 10 years; 78 patients who underwent Alzheimer's disease biomarker assessment (CSF or amyloid-PET), rated according to the AT(N) system.

Results: During the follow-up, 56 patients (47.0%[38.0–56.1]) were diagnosed with MCI and 22 (18.8%[11.7–25.9]) with dementia. A patient developed Parkinson's disease and a patient had a brain tumor. Mean progression time was 7.9(5.2) years to MCI and 10.39(4.7) to dementia with annual conversion rates (ACR) of 5.9%(1.6–10.2) to MCI and 2.1% (0–6.3%) to dementia. 39 (33.3%[24.8–41.9]) patients still were SCD at the end of the follow-up (15.2[5.4] years). Among these, nine were diagnosed with depression, six had vascular leukoencephalopathy and two were diagnosed with obstructive sleep apnea syndrome (OSAS). Among 78 patients who underwent AD biomarker assessment 10 (12.8%[5.4–20.2]) were A+ (seven A+/T+/N- and five A+/T+/N+).
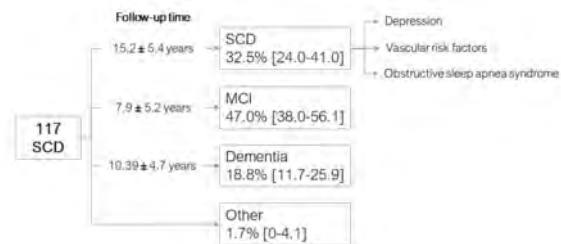
Flow-chart showing proportion of diagnosis at the end of the follow-up, reported as percentages [95% C.I.]. Follow-up times are reported as mean ± standard deviation.

Conclusion: On a very long follow-up time the proportions of conversion to MCI and dementia were significantly higher than literature data and consistent with A+ proportion. We also showed that more than half of the patients who did not progress to MCI or dementia had a medical condition possibly associated with SCD and suitable for therapeutic and preventive approaches.

Disclosure: No authors report any conflicts of interest for this study.

EPR-218

The diagnostic value of plasma ptau 181 within the AD continuum: a cross-sectional study

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Background and aims: Blood-based biomarkers have shown promising results regarding the in vivo detection of the earliest neuropathological changes in Alzheimer's disease (AD). Herein, we investigated plasma pTau 181 levels in various stages of the clinical AD continuum and examined the predictive value of pTau 181 in terms of clinical diagnosis and amyloid positivity in an outpatient memory clinic-based cohort.

Methods: We included 225 patients, 181 patients along the clinical AD continuum (i.e. subjective cognitive decline (SCD, n=20), mild cognitive impairment (MCI, n=88) and AD (n=73) and 44 age-matched healthy controls (HC) with no sign of neurodegenerative disorder or cognitive decline. Concentrations of plasma pTau 181 were quantified using ultrasensitive single molecule array (SIMOA). Furthermore, age- and sex-adjusted receiver operating characteristic (ROC) curves were calculated and the area under the curve (AUC) of each model was compared using DeLong's test for correlated AUC curves.

Results: Median (interquartile range [IQR]) concentration of plasma pTau 181 was 1.4 pg/ml (1.1–2.2) in HC, 2.0 pg/ml (1.3–2.5) in SCD, 2.4 pg/ml (1.5–3.7) in MCI and 3.4 pg/ml (2.5–4.3) in AD. Additionally, by combining plasma ptau181 with Apolipoprotein E4 (APOE4), we observed a high accuracy in differentiating between HC and patients with an objective cognitive decline (MCI and AD, AUC=0.82) as well as between amyloid positive and negative individuals (AUC=0.95).

Conclusion: We suggest that plasma pTau 181 could serve as a favourable non-invasive and feasible diagnostic tool to detect patients early in the neuropathological cascade of AD and therefore facilitating inclusion of these patients at-risk in clinical trials.

Disclosure: Nothing to disclose.

Autonomic nervous system diseases & Peripheral nerve disorders 2

EPR-219

Variation in Baroreflex Sensitivity indexes depending on the duration of Valsalva Manoeuvre.

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Background and aims: Valsalva manoeuvre (VM) is a diagnostic protocol used to assess autonomic function, evaluating baroreceptor unloading (phase II) as well as baroreceptor loading (phase IV). The duration of VM is known to alter the calculated autonomic parameter, but how baroreflex sensitivity (BRS) indexes are affected by the duration of VM remains unclear.
Methods: 16 healthy participants (8 women, mean age 22.63 ± 0.88 years old) performed VMs with an expiratory strain (ES) duration of 15 seconds and with an ES duration of 20 seconds in random order. We recorded continuously and non-invasively heart rate, systolic and diastolic blood pressure during VM phase 1, VM phase 2 early, VM phase 2 late, and VM phase 4. Upon baroreceptor unloading (phase II), we calculated vagal-BRS and adrenergic-BRS. Upon baroreceptor loading (phase IV), we calculated Valsalva ratios (VR). We performed Wilcoxon test to evaluate differences between VMs with ES duration of 15 seconds and VMs with ES duration of 20 seconds.
Results: During VMs with ES duration of 20 seconds compared to VMs with ES duration of 15 seconds, vagal-BRS (3.94 ± 2.81 vs 3.28 ± 1.73; $p>0.05$) remained unchanged, whereas adrenergic-BRS (55.47 ± 33.94 vs 77.65 ± 32.60; $p<0.05$) and VRs (2.05 ± 0.34 vs 2.20 ± 0.36) were significantly increased.
Conclusion: To conclude, our study highlights the importance of a standardized duration of VM since BRS indexes, except for vagal-BRS, are altered by the duration of VMs.
Disclosure: Nothing to disclose.

EPR-220

Cardiovascular autonomic involvement in acute SARS-CoV-2, Post-Covid and COVID-19 vaccination – a systematic review

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Background and aims: To perform a review on newly diagnosed or significant worsening of cardiovascular autonomic nervous system (ANS) dysfunction associated with SARS-CoV-2 infection or COVID-19 vaccination.
Methods: We systemically reviewed all published cases reporting new-onset or recrudescence of cardiovascular ANS dysfunction in patients with acute and long-term COVID-19 and ANS adverse effects after SARS-CoV-2 vaccination. A MEDLINE, Embase, Web of Science and preprint servers search was performed on the 30th of November 2021.
Results: Our search retrieved 131 patients with cardiovascular ANS dysfunction associated with COVID-19 and 3 with a presumable association with SARS-CoV-2 vaccination. From the 58 patients with ANS symptoms during the acute COVID-19, these were among the presenting symptoms in 36 (62%) patients, and the most common presentations were orthostatic intolerance (OI) and syncope in 30 (52%) and 24 (41%), respectively. The most common final diagnosis was reflex syncope in 21 (36%) and orthostatic hypotension in 18 (31%). Autonomic function tests (AFT) were performed in 34 (58%). Partial or complete recovery was the outcome in 42 (73%) and 14 (24%) patients died from COVID-19. From the 73 patients with ANS symptoms in the post-COVID phase, 64 (84%) presented with OI and 4 (5%) with syncope. The most common diagnosis was POTS, in 40 (55%) patients. 65 (89%) patients underwent AFT. Patients often had a partial or complete recovery 53 (72%), and no patient died.
Conclusion: Different types of cardiovascular ANS involvement may arise depending on the clinical phase of the COVID-19. The association between ANS dysfunction and the COVID-19 vaccination remains controversial.
Disclosure: The authors declare to have no disclosures relevant to this manuscript.

EPR-221

Anti-CD20 monoclonal antibody treatment in Anti Neurofascin-155 antibody-positive CIDP: a single-center experience

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Background and aims: A small number of chronic inflammatory demyelinating polyneuropathy (CIDP) patients may have autoantibodies against nodal and paranodal proteins. Anti- Neurofascin 155 antibody-positive (NF155 +) CIDP is known to be poor resistant to intravenous immunoglobulin. Rituximab, a B-cell-targeted anti-CD20 monoclonal antibody, has produced significant improvements. We present four cases with NF155 +CIDP resistant to first-line therapy and responded well to Rituximab.

Methods: The patients received rituximab at 1,000 mg/day on days 0 and 15, followed by 1,000 mg/day every 6 months. Rituximab's efficacy was evaluated by the overall neuropathy limitations scale (ONLS) score at the beginning and 6 months of treatment.

Results: Antibody testing was performed in three patients due to resistance to classical treatment and the other due to combined central and peripheral demyelination. It was revealed positivity of anti-NF-155 IgG (IgG4 -) in 1, anti-NF-155 IgM in 1, and anti-NF-155 IgG (IgG4 +) in 2 patients. One patient had serum-CSF oligoclonal band positivity, and the other had elevated CSF protein levels. The patients' before-after-rituximab ONLS scores were 6–1, 6–3, 7–3, and 8–4. Rituximab provided maximum clinical benefit when given 1,000 mg/g every six months in 3 patients and every three months in 1 patient. Patients experienced neither an attack nor drug side effects under rituximab.

Figure 1: The initial brain magnetic resonance imaging, axial fluid-attenuated inversion recovery (FLAIR) image shows a periventricular (A, arrow) lesions suggesting of multiple sclerosis. The sagittal T2- weighted (W) image discloses pericallosal (B,arrows) lesions. Coronal contrast-enhanced T1-weighted images reveals faint contrast enhancement in the centrum semiovale (C, arrow). Sagittal T2W image of the spine demonstrate focal lesions (D, arrow) located at the C4-C5 level indicating demyelinating lesion.

Conclusion: Rituximab provided effective clinical stabilization in our patients. These antibodies should be investigated in patients who are resistant to conventional immunotherapies and have central demyelination.

Disclosure: Nothing to disclose.

Table 1: Characteristics of patients

Age/gender	Antibody	Central demyelination	CSF analysis	Before-after-Rituximab ONLS scores
20/F	Neurofascin-155 IgG (IgG4 -)	+ (CCPD)	CSF protein level: normal OCBs: negative	ONLS 6-ONLS 1
33/M	Neurofascin-155 IgM	-	CSF protein level: normal OCBs: Positive (type 2)	ONLS 6-ONLS 3
41/F	Neurofascin-155 IgG (IgG4 +)	-	CSF protein level: Elevate OCBs: negative	ONLS 8-ONLS 4
59/M	Neurofascin-155 IgG (IgG4 +)	-	CSF protein level: normal OCBs: negative	ONLS 7-ONLS 3

EPR-222

Supine hypertension and cardiovascular autonomic failure in patients with alpha-synucleinopathies

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Background and aims: Orthostatic hypotension (OH) and supine hypertension (SH) are prevalent in alpha-synucleinopathies, posing a therapeutic dilemma as OH treatment may worsen SH. We aimed to characterise SH using autonomic testing and 24hr-ambulatory blood pressure monitoring (24hr-ABPM), effects of pharmacological OH treatment in pure autonomic failure (PAF), multiple system atrophy (MSA), and Lewy body disorders (LBD: Parkinson's disease and Dementia with Lewy bodies).

Methods: 166 patients (72 PAF, 59 MSA, 35 LBD) underwent cardiovascular autonomic testing and 24hr-ABPM. Demographic and clinical features, medications and cardiovascular autonomic biomarkers were compared.

Results: 51% (84/166) of patients were on anti-hypotensive medications. SH and OH commonly co-existed in patients with PAF, MSA and LBD, both with anti-hypotensive medications (75%, 63% and 60%, respectively) and without (56%, 51% and 50%, respectively). Supine pre-stand BP during 24hr-ABPM detected SH with 60% sensitivity and 86% specificity (area under the curve 0.73 (95%CI 0.66-0.81). 74% (61/82) of patients without anti-hypotensive medications had nocturnal hypertension. Mean supine and nocturnal BP was higher in patients with anti-hypotensive medications (p<0.05). Supine noradrenaline levels were significantly higher in MSA vs PAF and LBD (268 vs 183 and 210 pg/ml, p<0.01). There was a strong correlation between OH, SH and nocturnal hypertension after adjusting for age, gender, anti-hypotensive medications and supine noradrenaline levels (R2=0.48, p<0.01).

Conclusion: SH and nocturnal hypertension commonly co-exist and are independently associated with OH in alpha-synucleinopathies. 24hr-ABPM is useful in detecting SH in autonomic failure patients. The pathophysiology of SH is likely to be heterogeneous and not entirely explained by residual sympathetic tone.

Disclosure: Dr SK was supported by the Guarantors of Brain Entry Fellowship. Dr VI is supported by NIHR UCLH Biomedical Research Centre.

EPR-223

Photobiomodulation therapy for the prevention of chemotherapy-induced peripheral neuropathy (NEUROLASER trial)

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Background and aims: Taxanes are well known to cause chemotherapy-induced peripheral neuropathy (CIPN). To date, there are no evidence-based measures to prevent or minimize CIPN. Photobiomodulation (PBM) therapy is based on the application of (near)-infrared light on target tissue to stimulate cell repair processes and reduce pain and inflammation. The aim of this trial was to evaluate if PBM can prevent sensory symptoms associated with CIPN and enhance the patients' quality of life (QoL).

Methods: A RCT with 32 breast cancer patients that underwent taxane treatment was performed at the Jessa Hospital (Hasselt, Belgium). Patients were randomized to receive PBM or placebo treatments (2x/week) starting at first until the last week of their chemotherapy (CT). The patients' QoL and their neurotoxicity symptoms were assessed by the FACT/GOG-NTX questionnaire. A higher overall score indicates a better QoL. Measures were collected at four time points.

Results: Mixed ANOVA revealed a significant difference in the group by time interaction for the FACT/GOG-NTX total score (p=0.036) with a higher overall score in the PBM group. Specific questions of the FACT/GOG-NTX regarding numbness in hands and feet were analyzed separately. A significant increase in the severity of numbness in hands and feet over time was observed in the control group (ps=0.000), whereas it remained constant in the PBM group (ps≥0.173).

Conclusion: Based on these results, PBM seems to reduce the development of CIPN resulting in a better QoL. These results must be interpreted with caution because of the limited sample size. Further research in a larger patient population is necessary.

Disclosure: Nothing to disclose.

EPR-224

Implementing ESC syncope guidelines in five Dutch hospitals: higher diagnostic accuracy at lower syncope-related costs

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Background and aims: Implementing the ESC syncope guidelines in five Dutch emergency departments: higher diagnostic accuracy at lower syncope-related costs.

Methods: Patients were included prior to the implementation (control; Usual Care (UC)) and after it (Syncope Algorithm (SA)) at five Dutch EDs. The implementation consisted of several components including: education for all physicians involved in syncope care, quick referral pathways from the ED to newly established, multidisciplinary Syncope Units. We compared diagnostic yield and accuracy before and after implementation using logistic regression analysis while accounting for centre of evaluation.

Results: A total of 521 patients were included in the analysis: 275 patients in the UC group and 246 patients in the SA group. Distribution of age, sex and final diagnosis was comparable between groups. The proportion of cases with a diagnosis was higher in the SA group (n=218, 88.6%) than in the UC group (n=209, 76.0%, p<0.001). In the SA group the diagnosis of the treating physician matched the reference standard significantly more than in the Usual Care group: Odds Ratio 1.15 (95% CI 1.07–1.23). The syncope related costs were lower in the SA group.

Conclusion: Implementation of ESC syncope guidelines improved diagnostic yield and accuracy and resulted in lower syncope related health care costs. (Netherlands Trial Register NL 6129).

Disclosure: MG and WBvH reports no disclosures relevant to the manuscript. JGvD has received lecture fees from Medtronic. RDT has received fees for lectures from Medtronic, UCB, and Novartis. RDT has received consultancy fees from Theravarance and Arvelle. RDT receives research support from the Dutch National Epilepsy Fund, The Netherlands Organisation for Health Research and Development (ZonMW), NUTS Ohra Fund, Medtronic, Christelijke Vereniging voor de Verpleging van Lijders aan Epilepsie, The Netherlands.

EPR-225

Cardiovascular autonomic failure correlates with cutaneous denervation and patient symptoms in alpha-synucleinopathies

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Background and aims: Cardiovascular autonomic failure and neurogenic orthostatic hypotension (nOH) are common and disabling features in Parkinson's disease (PD) and multiple system atrophy (MSA). Compared to PD, MSA is considered a primarily central alpha-synucleinopathy. Aim: To characterise the relationship between cardiovascular autonomic failure and cutaneous somatic and autonomic innervation in early PD and MSA.

Methods: 55 patients (37 PD, 18 MSA) within 2 years of motor onset underwent: 1) cardiovascular autonomic testing including 5-minute stand, isometric exercise, deep breathing, Valsalva manoeuvre, head-up tilt 2) plasma catecholamines 3) distal leg punch skin biopsies for quantification of intraepidermal (IENF), pilomotor (PNF), and sudomotor nerve fibres (SNF), and 4) COMPASS-31 autonomic symptom questionnaires.

Results: 75% with MSA and 36% with PD had OH ($\geq$20/10mmHg). Supine noradrenaline levels were significantly higher in MSA vs PD with OH (264[241–304] vs 158[154–190] pg/ml, p=0.03, Fig.1). Compared to patients without OH, patients with OH had reduced cutaneous innervation (3.1[1.3–6.0] vs 7.4[5.3–8.7] IENF/mm, p=0.008; 2.8[0–8.2] vs 11.8[6.–23.4] PNF/mm, p=0.007; 0.9[0.1–1.4] vs 1.6[1.4–1.8] nm SNF/μm^3, p=0.002), with no significant differences between the MSA with OH vs PD with OH subgroups. Markers of cardiovascular autonomic failure, including severity of OH on stand, correlated with cutaneous denervation (IENF: rho=-0.47, p=0.007, PNF: rho=-0.51, p=0.004, SNF: rho=-0.51, p=0.006, Fig.2), and patient symptoms (COMPASS-31: rho=0.57, p=0.002, Fig. 3).
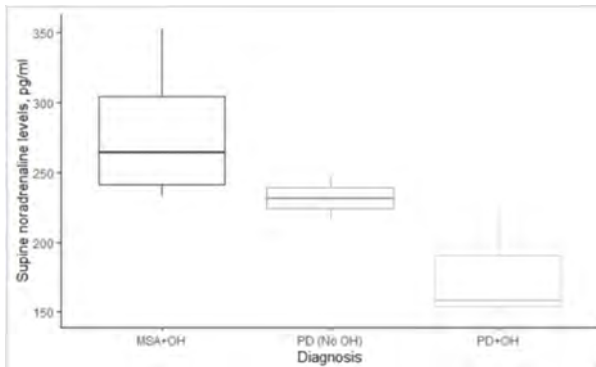
Figure 1: Supine noradrenaline levels were significantly higher in patients with multiple system atrophy (MSA), all of whom had orthostatic hypotension (OH) compared to Parkinson's disease with OH. Patients with PD without OH had intermediate levels.

Figure 2: Severity of orthostatic hypotension correlated with cutaneous somatic and somatic denervation, including intraepidermal (A), pilomotor (B) and sudomotor (C) nerve fibre density with cholinergic marker vasoactive intestinal peptide (VIP).

Figure 3: Markers of cardiovascular autonomic failure, including the severity of orthostatic hypotension on stand, correlated with patient reported autonomic symptoms on the COMPASS-31 questionnaire.

Conclusion: Cardiovascular autonomic failure correlated significantly with cutaneous denervation and patient symptoms in both MSA and PD. Postganglionic autonomic denervation may contribute to the pathophysiology of cardiovascular autonomic failure and nOH and affect responses to therapeutic agents for nOH.

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Cerebrovascular diseases 2

EPR-226
Abstract withdrawn

EPR-227

The crosstalk between Stroke and Cancer: a population-based study

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Background and aims: Cancer is a hypercoagulable state with a potential role in stroke pathogenesis. We aimed at testing whether cancer incidence would increase after the first ever cerebrovascular event.

Methods: ACIN2 is a Stroke prospective population registry with a first-ever cerebrovascular event (Stroke or Transient Ischemic Attack - TIA) diagnosed between 2009 and 2011. We used e-medical records to conduct a structured search and register cancer related variables and case fatality, for a period of 8 years following a cerebrovascular event. The incidence of cancer in Stroke and TIA patients was compared to the northern population regional cancer registry (RORENO).

Results: From 1,069 stroke and TIA patients without previous cancer history, 90 (8.4%) were diagnosed with cancer after cerebrovascular event onset. The overall annual incidence rate of a first cancer diagnosis after a stroke or TIA event was 1,951/100,000 (95% CI, 1,580–2,404) compared to 1,014/100,000 (95% CI, 1,005–1,023) in RORENO. The median time between Stroke/TIA and cancer onset was 3.2 years. Male sex (HR 1.63, 95%CI, 1.07–2.49, p<0.05), older age (HR 1.02, 95% CI, 1.01–1.04, p<0.01), tobacco use (HR 1.56, 95% CI, 1.00–2.43, p<0.05) and peripheral artery disease (HR 2.47, 95% CI, 1.14–5.34, p<0.05) were independently associated to higher cancer risk. Stroke patients without cancer had a higher 8-year survival (57% vs 33.3%, p<0.001).

Conclusion: Overall incidence of cancer in a Stroke and TIA population-based cohort was higher than in the general population. Patients with incident cancer had decreased survival, supporting comprehensive cancer screening in first-ever stroke survivors.

Disclosure: The authors declare no financial or other conflicts of interest.

EPR-228

Physiological biomarkers of silent cerebrovascular disease – direct and accessible clinical evidence

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Background and aims: Silent cerebrovascular disease and cerebral small vessels disease are considered major risk factors for developing stroke and vascular cognitive impairment. It is estimated that 90% of stroke cases and 35% of dementia are preventable or may be delayed. Yet, these conditions are not evaluated in the routine clinical care. In this study we examine clinically accessible physiological biomarkers for silent cerebrovascular disease that enable objective and early detection and promote prevention of stroke and cognitive impairment.

Methods: The study included 168 healthy patients with at least one risk factor for stroke (Table 1). Direct electrophysiological imaging (DELPHI) was used to measure magnetically induced brain network electrophysiological biomarkers. MRI scans included T1, T2, FLAIR, Diffusion Weighted Imaging (DWI) and (SWI), were analyzed according to Fazekas scale for White Matter Hyperintensities (WMH) and for Lacunar Infarctions.

Results: DELPHI physiological evaluation was able to distinguish the different severities of WMH and Lacunar Infarcts in subjects at risk for stroke. DELPHI measure of Wave Form Adherence (WFA) decreases with increase in MRI white matter hyperintensities and lacunar infarction and significantly differentiates between normal to abnormal severities (Fig.1a,b, Tables 2,3; WMH ,p<0.0001; Lacunar infarctions, p<0.0001).

Table 1- Subject's demographics and risk factors

Risk factor	N	Age
Total at risk	168	68.8 ±7.4
Gender		36% F/ 64% M
Hypertension	61	
Diabetes	20	
Dyslipidemia	82	
Smoking	4	
Obesity/ Overweight	16	
Atrial Fibrillation	8	
Cardiac conditions	24	
Family history of dementia	2	
Cognitive decline	63	
Sleep Disorders	6	

Table 2- DELPHI's WFA in subjects divided by Fazekas score

	FAZEKAS 0	FAZEKAS 1	FAZEKAS >=2	P-Value
Number of values	16	123	24	
Mean	0.7400	0.6062	0.2184	****
Std. Deviation	0.2208	0.3500	0.4653	
Std. Error of Mean	0.05519	0.03156	0.09498	

Table 3- DELPHI's WFA in subjects infarction positive versus infarction negative

	Normal (Infarctions negative)	Abnormal (Infarction positive)	P-Value
Number of values	146	22	
Mean	0.6	0.24	****
Std. Deviation	0.34	0.48	
Std. Error of Mean	0.028	0.1	

Tables 1–3
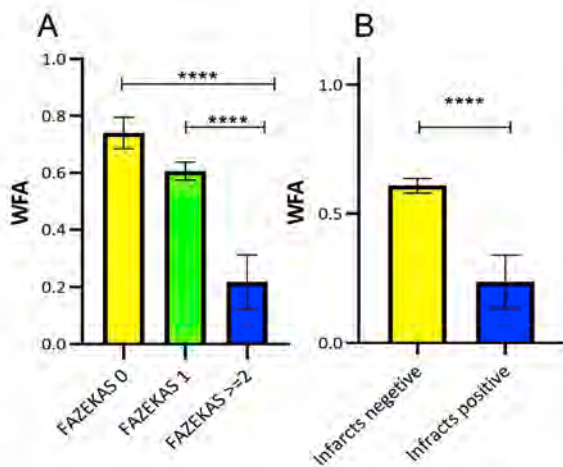
Figure 1

Conclusion: Detection of silent cerebrovascular disease is valuable for prevention of stroke and vascular cognitive impairment. Brain network physiology evaluation utilizing DELPHI technology provides means for clinically accessible and objective routine detection of silent cerebrovascular disease related findings and progression.

Disclosure: Prof. David Tanne is the Medical Director at QuantalX Neuroscience which develops DELPHI.

EPR-229

Evaluation of the fibrinolysis system in patients with cerebral small vessel disease

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Background and aims: The mechanism of development of the cerebral small vessel disease (CSVD) is undergoing examination, but a number of studies have shown the presence of a link between markers of endothelial dysfunction, hemostasis indicators and the severity of white matter lesions. The aim of this study was to investigate the relationship between CSVD and the fibrinolysis system.

Methods: The research involved examination of 117 people who were divided into a group with CSVD (n=54) and a group without CSVD (n=63), aged 57,7±11,5. Laboratory diagnostics included evaluation of the fibrinolysis system (XIIa-dependent fibrinolysis, plasminogen, alpha2-antiplasmin, PAI-1). All patients underwent MRI of the brain with an assessment of white matter on the Fazekas scale and calculate fractional anisotropy coefficient (CFA) in white matter tracts (Fig.1).

Results: The group with SVD has a higher time of XIIa dependent fibrinolysis (p=0.032), and a lower percentage of alpha2-antiplasmin (p=0.016). The analysis of tractography parameters showed that the CFA value of the anterior femur of the inner capsule depends only on XIIa dependent fibrinolysis value (p<0.05, R2=4.7%). It was found that with an increase in the time of XIIa dependent fibrinolysis, the probability of the 2nd or more stage of periventricular and subcortical leukoaraiosis increases on the Fazekas scale (OR 1.31[1.07–1.60], p=0.009), and with an increase in plasminogen, it decreases (OR 0.97 [0.95–0.98], p<0.001, R2=0.44).

Characteristics	Fazekas scale > 0, N=54	Fazekas scale = 0, N=63	P-value
XIIa-dependent fibrinolysis, min	7,6±2,9 [6,7; 8,4]	6,5±1,7 [6,1; 7,0]	0,032
Plasminogen, %	91 83 — 100	94 86 — 106	0,325
Alpha2-antiplasmin, %	111 95 — 117	105 95 — 111	0,016
PAI-1	13,4 9,3 — 42,5	12,9 8,3 — 40,1	0,898
Fractional anisotropy coefficient Anterior Limb of the Internal Capsule (right hemisphere)	595±73 [575; 615]	626±40 [616; 636]	0,006
Fractional anisotropy coefficient Anterior Limb of the Internal Capsule (left hemisphere)	594±68 [575; 612]	628±35 [619; 637]	0,001

Table 1: Laboratory and MRI characteristics
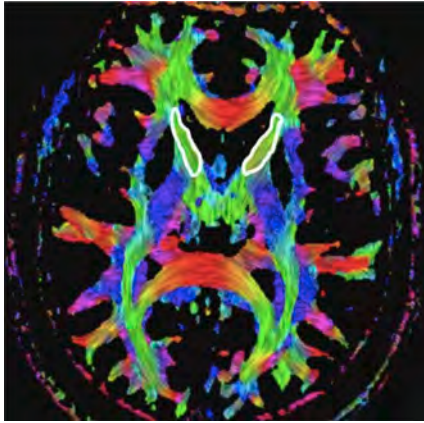
Figure 1: Diffusion tensor MRI (Fractional anisotropy). Anterior Limb of the Internal Capsule (circled)

Conclusion: Our data indicate a change in the fibrinolytic system functioning, as well as its connection with lesions of the white matter of the brain according to MRI and tractography.

Disclosure: No relationships to disclose.

EPR-230

The role of neurovascular ultrasound examination in the era of endovascular therapy

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Background and aims: Neurovascular ultrasound examination (NVUE) can demonstrate the presence and site of an arterial occlusion in patients with a suspected large artery occlusion (LAO). Early ultrasound detection of a LAO could allow direct access to the angio suite for selected patients.The objective of this study was to evaluate the yield of emergent NVUE for the evaluation of acute cerebral ischemia.

Methods: We routinely perform an urgent bedside NVUE with carotid/vertebral duplex and transcranial ColorDoppler (TCCD) in patients with acute cerebral ischemia in order to identify LAO and decide for interventional treatment. Ultrasound examination results were compared with AngioTC.

Results: Of 26 consecutive patients studied, 15 were eligible for thrombolytic therapy and 10 for endovascular treatment (1 basilar artery thrombectomy and stenting, 1 internal carotid artery thrombectomy and stenting, 9 thromboaspiration in middle cerebral artery). Neurosonology detected occlusions in 8 (53%) of thrombolysis-eligible patients and in 8 (80%) patients who underwent endovascular treatment; in 2 patients AngioTC showed a distal M2-MCA occlusions. NVUE detected 100% of the M1-ACM occlusions which were shown in the AngioTC. Of the 17 patients who were found to have no LAO, NVUE was negative in 15 (88%); in both cases thrombolysis was performed between neurosonological examination and angioTC.

Conclusion: A proximal occlusion on TCCD was found in 80% of endovascular treatment-eligible patients. NVUE detected 100% of the M1-ACM occlusions which were shown in the AngioTC. Emergent TCCD is both sensitive and specific in determining arterial occlusion in acute cerebral ischemia and demonstrated to be helpful in selecting patients for endovascular treatment.

Disclosure: Nothing to disclose.

EPR-231

Endovascular treatment in elderly patients: a single center observational study

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Background and aims: Mechanical thrombectomy represents the first-line therapy for acute ischemic stroke due to large artery occlusions (LAO). Yet, data about the efficacy of endovascular treatment (EVT) in very elderly people are needed, since this population is more likely to experience complications and bad prognosis after stroke. We sought to investigate outcome after thrombectomy in patients over 85 years of age.

Methods: An analysis was conducted on a consecutive cohort of patients with acute ischemic stroke due to LAO who underwent EVT from 2018 to 2021 in the University Hospital of Padova. Patients were divided into two subgroups according to age: 80–84 and ≥85 years old. The degree of disability before stroke and the functional outcome at 90-day follow-up were compared using the modified Rankin Scale (mRS).

Results: The analysis included 129 patients. 79 (61%) aged 80-84 years and 50 (39%) aged ≥85 years. 3-month outcome data were available for 82 of them. Functional independence pre-stroke (mRS ≤2) did not significantly differ between the two subgroups (p=0.07). At 90-day follow-up, mRS ≤2 was achieved in 28 (59.6%) and 10 (28.6%) of patients aged 80-84 and >85 years, respectively (p=0.005). Mortality rate at 3 months was 25.5% in patients aged 80–84 and 28.5% in patients aged ≥85 years, with no significant difference (p=0.758).

Conclusion: Significant differences were found in functional outcome between patients aged 80–84 and ≥85 years treated with EVT. Elderly patient had an non significantly higher risk of death during the first 90 days after stroke.

Disclosure: Nothing to disclose.

EPR-232

Atrial imaging and cardiac rhythm in cryptogenic embolic stroke: a preliminary analysis of a prospective study

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Background and aims: Cryptogenic stroke is frequently related to unknown cardioembolic sources. We aim to analyze atrial fibrillation (AF), parafibrillatory status (para-AF) and echocardiographic signs of atrial dysfunction in patients with cryptogenic stroke.

Methods: The ARIES (Atrial Imaging and cardiac Rhythm In Embolic Stroke) study includes consecutive patients with cryptogenic stroke. Cardiologic work-up consists in 30-day ECG monitoring (Nuubo) and advanced left atrial echocardiography function. Patients are classified as non-AF, AF, or para-AF defined as >3,000 atrial ectopic beats/day or >2 "micro-AF" episode (fibrillatory burst <30 seconds)/day). Signs of atrial dysfunction are defined by phasic left atrial strain (reservoir, conduit, contraction). We describe stroke etiology and recurrence at 90 days and compare echocardiographic signs of atrial dysfunction according to rhythm classification.

Results: 78 patients completed 90 days of follow-up. Stroke etiology remained cryptogenic in 44 patients (55%) and 30 (37.5%) were reclassified as cardioembolic. AF was found in 26 (32.5%) patients and para-AF in 22 (27.5%). Para-AF patients had lower left atrial strain compared to non-AF patients (reservoir 22.2±9.8 vs 32.8±12, p=0.004; conduit -9.6±4.8 vs -14.4±9, p=0.008; contraction 12.6±4.8 vs 17.9±7.8, p=0.025). We found no significant differences in strain between AF and para-AF patients. There were three stroke recurrences (3.8%), 2/3 in para-AF patients.

Conclusion: In this preliminary analysis, we found AF in 32.5% patients with cryptogenic stroke, para-AF in 27.5%. Para-AF patients showed signs of atrial dysfunction similarly to AF patients and early stroke recurrence. These results could suggest therapeutic changes in para-AF patients. However, a longer follow-up is required to confirm the findings.

Disclosure: Nothing to disclose.

EPR-233

Stroke in primary systemic vasculitis

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Background and aims: The cerebral vessels may be affected in primary systemic vasculitis (PSV), but little is known about cerebrovascular events (CVEs) in this population. This study aimed to report on the incidence of CVEs at the onset of PSV and identify associated risk factors for these events.

Methods: Data were collected from newly-diagnosed (<5 years) adults with PSV included in the multicentric prospective Diagnostic and Classification criteria for Primary systemic VASculitis(DCVAS) study. Demographic features and risk factors for vascular disease were compared between patients with PSV with and without a CVE.

Results: Data from 4,783 cases (mean age 56.2 (SD 18.6) years, 2,845 (59.5%) females) were available. History of CVE, before the diagnosis of PSV, occurred in 102 (2.1%) cases. After the onset of PSV, CVEs occurred in 161 cases (3.4%), of which 81 (1.7%) were transient ischemic attacks. CVEs were more common in Behçet's disease (8.5%), polyarteritis nodosa (6.2%), and less common in small vessel vasculitides (Table). Age, gender and time to PSV diagnosis did not differ between patients with and without CVE. The occurrence of CVEs after the onset of PSV associated with previous CVEs (OR 5.1, 95% CI 2.7–9.7, p<0.001) and history of malignancy (OR 2.4, 95% CI 1.3–4.2, p=0.002), but showed no association with diabetes mellitus, hypertension, dyslipidaemia, or smoking.

Table - Frequency of cerebrovascular events (TIA and stroke) after PSV onset

	Total N (%)	Any TIA N (%)	Any stroke N (%)	Any cerebrovascular event (TIA + stroke) N (%)
All PSV	4783	81 (1.7)	94 (2.0)	161 (3.4)*
Bechet's disease	201 (4.2)	12 (6.0)	5 (2.5)	17 (8.5)
polyarteritis nodosa	194 (4.1)	4 (2.1)	8 (4.1)	12 (6.2)
Takayasu's arteritis	630 (13.2)	19 (3.0)	20 (3.2)	36 (5.7)
giant cell arteritis	1206 (25.2)	18 (1.5)	28 (2.3)	43 (3.6)
isolated aortitis	36 (0.8)	1 (2.8)	0 (0)	1 (2.8)
other large vessel	91 (1.9)	3 (3.3)	2 (2.2)	4 (4.4)
granulomatosis with polyangiitis	1023 (21.4)	10 (1.0)	14 (1.4)	21 (2.1)
eosinophilic granulomatosis with polyangiitis	382 (8.0)	3 (0.8)	6 (1.6)	9 (2.4)
microscopic polyangiitis	507 (10.6)	6 (1.2)	8 (1.6)	11 (2.2)
other small vessel	195 (4.1)	3 (1.5)	2 (1.0)	5 (2.6)
Henoch Schönlein purpura	271 (5.7)	1 (0.4)	0 (0)	1 (0.4)
cryoglobulinaemic vasculitis	57 (1.2)	1 (1.8)	1 (1.8)	1 (1.8)

*14 patients presented with both TIA and stroke. 81 (1.7%) had TIA and 94 (2.0%) had any cerebrovascular accident

Conclusion: CVE is uncommon in PSV with prevalence of CVEs varying widely among different vasculitides. CVE in PSV is not explained by traditional risk factors for vascular disease and may require specific management. Additional analyses from the Stroke-DCVAS sub-study will provide further insight into CVEs subtypes, disability, and management in PSV.

Disclosure: No disclosures in relation to this work.

EPR-234

Effects of Sodium-Glucose Cotransporter 2 Inhibitors on Neurological Disorders: A Scoping Review

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Background and aims: Sodium-glucose cotransporter 2 inhibitors (SGLT2i) are a group of antidiabetic medications with a favourable cardiovascular, renal, and overall safety profile. The aim of this scoping review is to summarise the pre-clinical and clinical literature addressing the impact of SGLT2i on neurological disorders.

Methods: All articles published before March 20th 2021 were systematically searched in MEDLINE, EMBASE, Scopus, Web of Science, APA Psycinfo and ClinicalTrials. gov. Overall, 1,395 titles were screened, ultimately resulting in 160 studies included in qualitative analysis. Screening and data extraction were conducted by two independent authors and studies were excluded if they were not an original research study.
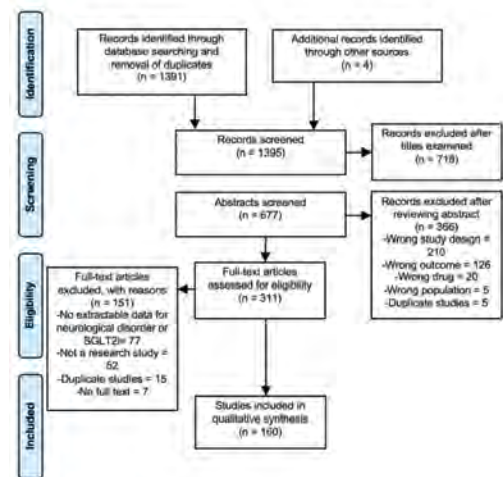
Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) flow diagram for search strategy

Results: Of 160 studies, 134 addressed stroke, 19 cognitive impairment, 4 epilepsy and 4 movement disorders, encompassing a range from systematic reviews and randomised controlled trials (RCTs) to bioinformatic and animal studies. Most animal studies demonstrated significant improvements in behavioural and neurological deficits with SGLT2i, which were reflected in beneficial changes in neurovascular units, synaptogenesis and neurotransmitter levels. SGLT2i form stable complexes with molecular targets implicated in neurological disorders, such as the acetylcholinesterase receptor. The evidence from clinical literature were conflicting and many studies did not reach statistical significance.

Table 1: Summary of the effect of SGLT2i on stroke compared to other glucose lowering drugs

	All SGLT2i	Canagliflozin	Dapagliflozin	Empagliflozin
All glucose lowering drugs	13 studies, >2.9 million patients: - 6 found a lower risk of stroke with SGLT2i - 6 found a higher risk of stroke with SGLT2i - 1 pharmacovigilance study showed higher reporting of all ischaemic stroke	-	1 study (n=28,408), no significant differences in risk of stroke.	-
Metformin	1 study (n=41020) showed higher risk of ischaemic stroke (HR 1.21).	-	-	-
Sulfonylurea	1 study (n=335542) showed lower risk of stroke (HR 0.73)	1 study (n=224,999), no significant difference in stroke outcomes	-	-
DPP4i	7 studies (n>700000): 5 found a lower risk of stroke (HR 0.46-0.86) 2 found no significant effect on stroke	1 study (n=224,999), no significant difference in stroke outcomes	3 studies (n=194422) - 1 study (n=128,066) showed reduced risk of stroke (HR 0.82, 95% CI 0.75-0.89). - 2 found no significant effect on stroke.	1 study (n=39169) showed no significant effect on ischaemic or haemorrhagic stroke.
GLP-1RA	3 studies (n>177,000) No significant effect on ischaemic or haemorrhagic stroke	1 study (n=224,999), no significant difference in stroke outcomes	-	1 study (n=17600) showed higher risk of ischaemic or haemorrhagic stroke (HR 1.45)
Insulin	1 study (n=8984), insulin was associated with higher risk of stroke (HR 7.21)			
Placebo	-	CANVAS programme (n=10142) No significant effect on fatal or non-fatal stroke (HR 0.87, 95% CI 0.69-1.09) No significant effect on ischaemic stroke Reduction in haemorrhagic stroke (HR 0.43, 95% CI 0.20-0.89) CREDANCE trial (n=4401): No significant effects on overall stroke, ischaemic stroke, haemorrhagic stroke or non-fatal stroke	DECLARE-TIMI 58 (n=17160) No significant effect on ischaemic stroke (HR 1.01, 95% CI 0.84-1.21). Reduction in risk of ischaemic stroke in a subgroup of patients with DM for >20 years (HR 0.61, 95% CI 0.38-1.00).	EMPA-REG OUTCOME (n=7020) No significant effects on overall stroke, fatal or non-fatal stroke, TIA. On 5-year follow up, higher risk of non-fatal stroke compared to liraglutide.

Abbreviations: CI – confidence interval; DM – diabetes mellitus; DPP4i - Dipeptidyl peptidadase-4 inhibitors; GLP-1RA - Glucagon-like peptide 1 receptor agonists; HR = hazard ratio; n – number of participants in the study; SGLT2i - Sodium-glucose cotransporter 2 inhibitors; TIA – transient ischaemic attack

Summary of the effect of SGLT2i on stroke compared to other glucose lowering drugs

Conclusion: SGLT2i may exert neurological benefits through three mechanisms: reduction in cardiovascular risk factors, augmentation of ketogenesis and anti-inflammatory pathways. Most clinical studies were observational, thus negating a causal relationship, whilst RCTs were heterogeneous and powered to detect cardiovascular or renal outcomes. We suggest that a longitudinal study should be conducted and specifically powered to detect neurological outcomes.
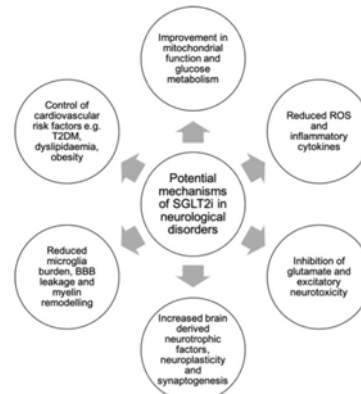
Potential mechanisms underlying the effects of SGLT2i on neurological disorders

Disclosure: Nothing to disclose.

Epilepsy 2

EPR-235

Cyclooxygenase-2 inhibition as an add-on strategy in drug resistant epilepsy – a canine translational pilot study

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Background and aims: Drug resistant epilepsy is a common complaint in dogs and affects up to 30% of dogs with idiopathic epilepsy. Experimental data suggest that targeting cyclooxygenase-2 (COX-2) mediated signalling might limit excessive excitability and prevent ictogenesis. Moreover, a role of COX-2 signalling in seizure-associated induction of P-glycoprotein has been described. Thus, targeting this pathway, may improve seizure control based on disease-modifying effects as well as enhancement of brain access and efficacy of co-administered antiseizure medication.

Methods: The study was designed as an open-label non-controlled pilot study. Client-owned dogs with phenobarbital-resistant idiopathic epilepsy served as a translational natural occuring chronic epilepsy animal model with frequent tonic-clonic seizures and cluster seizures despite adequate phenobarbital treatment. Enrolled dogs (n=17) received a firocoxib add-on therapy for 6 months. Tonic-clonic seizure and cluster seizure frequencies were analysed at baseline (6 month) and during the study (6 month). Responders were defined by a substantial reduction of tonic-clonic seizure and cluster seizure frequency (≥50%).

Results: Eleven dogs completed the study and were considered for statistical analysis. Two dogs (18%, 2/11) were classified as responders based on their change in seizure frequency. Interestingly, those two dogs had the highest baseline seizure frequency.

Conclusion: The overall tolerability was good. However, given the low percentage of responders, the present data do not support an overall considerable efficacy of COX-2 inhibitor add-on therapy to overcome natural occurring phenobarbital-resistant epilepsy in dogs. Further translational evaluation should only be considered in canine patients with a very high baseline seizure density.

EPR-236

Neuroinflammation in epilepsy – a case-control study

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Background and aims: Neuroinflammation starts to emerge as one of the processes contributing to epileptogenesis and generation of epileptic seizures. There is growing evidence of data of the activation of blood brain barrier (BBB) and induction or exacerbation of neuroinflammation in patients with epilepsy shortly after seizures. In this study we aimed to analyse serum levels of various markers of neuroinflammation and BBB activation in patients in the interictal phase of epilepsy.

Methods: Serum levels of MMP-9, MMP-2, TIMP-1, TIMP-2, S100B, CCL-2, ICAM-1, P-selectin, and TSP-2 were examined in a group of 100 patients with epilepsy who were seizure-free for a minimum of 7 days and measured by ELISA. The results were compared with an age- and sex-matched control group.

Results: Serum levels of MMP-9, MMP-2, TIMP-1, TIMP-2 and S100B were higher in patients with epilepsy in comparison to control group ($p<0.0001$; <0.0001; 0.001; <0.0001; <0.0001; respectively). Levels of CCL-2, ICAM-1, P-selectin and TSP-2 did not differ between the two groups. MMP-9/TIMP-1 ratio was comparable whereas MMP-2/TIMP-2 ratio was higher in patients with epilepsy ($p=0.0087$).

Conclusion: Serum levels of MMP-9, MMP-2, TIMP-1, TIMP-2 and S100B as well as MMP-2/TIMP-2 ratio are elevated in patients with epilepsy in the interictal phase which suggests that BBB activation and neuroinflammation are present in patients with epilepsy also in the interictal period. The pathological process initiating epilepsy, in addition to seizures, is probably the factor contributing to the elevation of matrix metalloproteinases, their inhibitors and S100B in patients with epilepsy in the interictal period.

Disclosure: Nothing to disclose.

EPR-237

Epilepsy Surgery in Morocco Procedures and long-term outcome in a series of 320 patients

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Background and aims: In Morocco, epilepsy surgery program started at 2005. We report here the presurgical and the outcome in 320 operated drug-resistant epileptic (DRE) patients.

Methods: A non invasive presurgical protocol including interictal EEG, video-EEG, MRI, PET-scan and neuropsychological tests was performed to select good candidates and appropriate surgical procedure.

Results: Among 1,582 DRE assessed patients, 320 were operated: 186 underwent temporal lobectomy and 112 had lesionectomy. The histopathology revealed hippocampal sclerosis (54%), dysembryoplastic tumor (17%), cortical dysplasia (6%), ganglioglioma (7%), astrocytoma (5%) and (4%) cavernoma. Since 2016, our experience has been extended to severe DRE in 22 (7%) patients with hemispherotomy, GAMMA knife radiosurgery, callosotomy and vagual nerve stimulation (for 10, 4, 3 and 7 patients, respectively) Follow-up in the first 5 years revealed that 244 (76.3%) patients were free of seizures (class IA - ILAE classification) with almost identical evolution for the group of patients with hippocampal sclerosis and the groups with other types of lesions. However, at 15 years, there was a more decline of the outcome in patients at class I in the first group (61%) compare to the second one (71%). Less satisfying results have been obtained in patients with cortical dysplasia and those managed by the palliative protocols but no worseness was observed in our series.

Conclusion: Our results showed the feasibility of epilepsy surgery in developing countries. Thus, we aim to collaborate and promote this experience in other African countries where epilepsy surgery is still underutilized.

Disclosure: No conflicts of interest.

EPR-238

Reproductive health challenges in women with epilepsy living in Rwanda

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Background and aims: In view of a 4.9% high epilepsy prevalence in Rwanda and a 2.5% annual population growth, understanding reproductive health challenges in women with epilepsy (WwE) is important. We explored the reciprocal influence between epilepsy, anti-seizure medication (ASM) and reproductive health in Rwandan WwE.

Methods: We conducted a cross-sectional study in WwE aged ≥18 years, presenting for a follow-up visit between December 2020 – January 2021 at the CARAES tertiary neuropsychiatric hospital, Kigali, Rwanda. Demographic data, epilepsy characteristics, ASM and reproductive health data were collected. Women with intellectual disability and/or psychiatric comorbidity were excluded.

Results: 100 WwE were enrolled (mean age 32.2± 9.70 years). Contraception was used in 27 WwE. Progesterone-only methods were used in 88.9% of whom 50% were taking enzyme-inducing ASM. One reported a contraceptive failure. Valproate was used by 49 WwE; 47 WwE in reproductive age and 10 on contraception. Pregnancy since epilepsy diagnosis was reported by 39. Folic acid was taken by only 59% and only started after conception. Seizure increase during pregnancy occurred in 23, with nine reporting poor ASM adherence. No major congenital malformations were observed. One newborn presented minor cognitive disturbances. Ten WwE reported one or more spontaneous abortions. Premature delivery occurred in four WwE; one premature newborn died after six weeks.

Conclusion: Our study underscores the need to implement contextualized clinical guidelines improving pre-, peri- and postnatal care of WwE. Availability of and access to safer ASM may decrease the risks of teratogenicity and drug interaction compared to currently available ASM.

Disclosure: Peter Dedeken has received consultancy fees from Merck, UCB Pharma and Novartis. Paul AMJ Boon received speaker and consultancy fees from UCB Pharma and various other pharmaceutical companies, and research grants through his institution. The remaining authors have no conflicts of interest to disclose.

EPR-239

Evaluation of visual acuity in patients with epilepsy: functional impairment due to retinal atrophy or pharmacotherapy?

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Background and aims: Epilepsy patients reveal impaired visual acuity under therapy with sodium channel blockers (SCB). However, it remains unknown whether similar effects occur under new generation SCB and whether impaired visual acuity is due to retinal neuroaxonal degeneration.

Methods: In a prospective single centre study, visual acuity (VA) measures (Snellen visual acuity chart) and contrast vision (Sloan letter charts, 100% high contrast, HCVA; 2.5% low contrast, LCVA) were acquired in 70 adult epilepsy patients (52 treated with SCB, 18 without SCB) and 76 healthy controls. The total number of correct letters identified on each chart was tested to determine VA (maximum 70 letters). Optical coherence tomography was used to measure the thickness of the retinal nerve fibre layer (RNFL).

Results: Epilepsy patients had a significantly reduced HCVA and LCVA 2.5% compared to healthy controls (Epilepsy: HCVA 52.28±8.56 letters, LCVA: 31.71±8.49 vs. HC: HCVA 56.57±4.47; LCVA 35.13±5.50; HCVA p< 0.001, LCVA p=0.004), while Snellen VA did not differ between groups. Effects were most pronounced in patients with SCB (LCVA: with vs. without SCB: p= 0.003; SCB vs. HC: p<0.001). Although epilepsy patients with SCB also had significantly thinner RNFL measures than healthy controls (RNFL p=0.012), no association was found between the thickness of the retinal layers and contrast vision scores.

Conclusion: Epilepsy patients had reduced contrast vision especially in case of SCB intake, though independent of retinal atrophy. These findings may impact epilepsy patient management but require further validation.

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EPR-240

Morphometric analysis of T1-weighted MR images in patients with „second look" MRI-negative focal epilepsy

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Background and aims: In the presurgical evaluation of epilepsy, identifying the epileptogenic zone is more difficult in magnetic resonance imaging (MRI) negative patients. Quantitative Analysis of MRI with a morphometric analysis program (MAP) can guide focused re-evaluation of the original MRI, to identify previously overlooked structural lesions. There is limited data on truly MRI negative patients, where this second look did not reveal any lesions. This study evaluates the diagnostic yield of MAP18 in "second look" MRI-negative patients.

Methods: T1 data of 68 patients with MRI-negative focal epilepsy and a clear localization of the epileptogenic zone by intracranial EEG or postoperative seizure freedom were acquired. Morphometric analysis was performed with MAP18, creating six feature maps, reflecting different structural properties of the brain and a patient's deviation from the control population. Ten brain regions were specified to quantify whether MAP findings were located in the correct region. ROC analyses were performed to identify the optimal thresholds for each map.

Results: MAP guided visual re-evaluation of the original MRI revealed overlooked lesions in three patients. The 65 second look negative patients were included in the analysis. At the optimal thresholds, balanced accuracy of the respective maps ranged from 51% to 60% (maximum sensitivity was 84%, with 35% specificity), creating three to six times as many false positive than true positive findings. ROC-analysis of cluster size did not significantly improve the diagnostic yield.

Conclusion: While MAP18 software is useful in detecting previously overlooked subtle structural lesions, in „second look" MRI-negative patients, the additional diagnostic yield is limited.

Disclosure: Nothing to disclose.

EPR-241

Visual Outcomes after Epilepsy Surgery – A Quantitative Comparison of Surgical Approaches

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Background and aims: Anterior temporal lobectomy (ATL) and selective amygdalohippocampectomy (SAHE) are both effective treatment strategies for intractable temporal lobe epilepsy (TLE) but may result in a contralateral superior visual field deficit (VFD). VFDs following epilepsy surgery are caused by intraoperative damage to Meyer's loop (ML), the optic radiation's (OR) most anterior portion.

Methods: We studied 62 patients undergoing ATL (n=32) and SAHE (n=30). Incidence rates of VFDs (n=44) and quantitative perimetry outcomes, (n=43) were compared between treatment groups. Whole brain connectomes were calculated from preoperative diffusion data and individual OR tractographies extracted from atlas regions. The results were warped onto postoperative T1w images. OR damage was quantified (n=55) by calculating the volume overlap with the resection zone. Furthermore, tract damage was correlated to postoperative perimetry results (n=36).
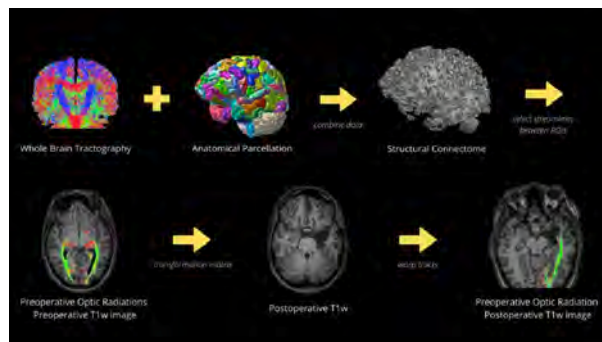
Structural connectomes of 100 million streamlines were calculated and the optic radiation extracted between standardized atlas regions. Tracts were warped onto postoperative T1w images and volumetric overlap with the resection zone quantified.

Results: Altogether, 56% of patients had postoperative VFDs (78.9% after ATL, 36.36% after SAHE, p=0.011). VFDs and OR damage tend to be more severe within the ATL group (mean defect -3.99dB vs. -1.36dB, p=0.007; OR damage 69.2mm^3 vs. 3.8mm^3, p=0.002). OR damages were able to predict postoperative VFDs with a sensitivity of 86% and a specificity of 78%. A linear regression model with OR damage as dependent variable showed a significant correlation with postoperative vision decline and could explain 47% of variance (R^2=0.47, p=0.0001).
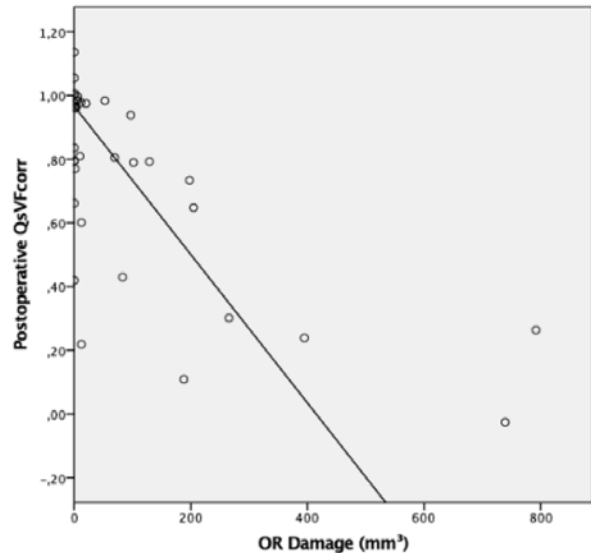
Visual outcomes of perimetry (QsVFcorr - corrected quadrant specific vision loss) and quantified optic radiation damage compared between treatment groups.
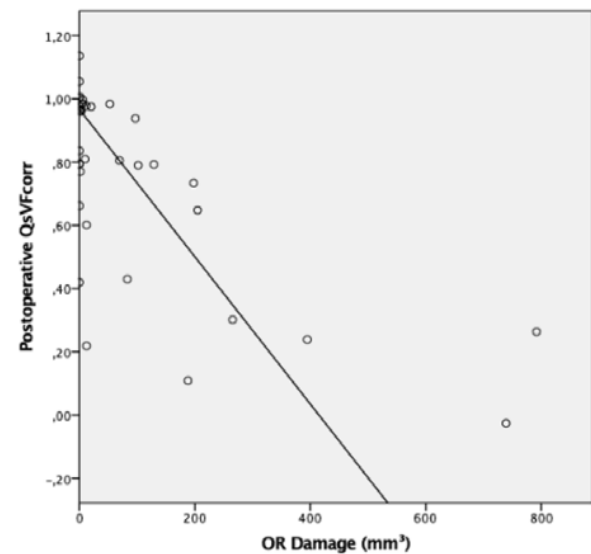
Regression plot of perimetry outcomes (QsVFcorr - corrected quadrant specific vision loss) and quantified OR damage.

Conclusion: Patients undergoing ATL are at higher risk for postoperative VFDs than those undergoing SAHE. Furthermore, VFDs tend to be more severe after ATL than after SAHE. Diffusion based tractography of the OR is a feasible method to reliably predict this morbidity in both treatment groups.

Disclosure: Nothing to disclose.

EPR-242
Abstract withdrawn.

Motor neurone diseases 2

EPR-243

Correlation between clinical phenotype and electromyographic parameters in amyotrophic lateral sclerosis

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Background and aims: Even if Electromyography (EMG) is routinely used to confirm the diagnosis of Amyotrophic Lateral Sclerosis (ALS), few studies analysed correlation between electrophysiological parameters and clinical characteristics of ALS. We assessed if the quantification of active denervation (AD) and chronic denervation (CD) provides clinicians information about phenotype, disease progression and survival in ALS patients.

Methods: We collected the following clinical parameters on a cohort of 689 ALS patients: survival, MRC scale, lower motor neuron score (LMNS), ALSFRS-R, deltaFRS, MITOS and King's Staging systems (KSS). We performed EMG and we calculated AD and CD scores for each predefined muscle analyzed in every district according to a fixed scheme (table 1); then we calculated AD and CD of the spinal region summing the partial scores for each limb.

Active denervation (spontaneus activity)*	Chronic denervation (MUAPs characteristics)**	Score
absent	Normal amplitude and duration	0
Fibrillation potentials and positive sharp waves + or insertional activity + or Presence of high frequency discharge oppure fibrillation potentials +/-	Increased duration, normal amplitude or normal duration, increased amplitude or decreased amplitude, increased/decreased/normal duration or decreased duration, normal amplitude	1
Fibrillation potentials and positive sharp waves ++	Increased duration, increased amplitude or very increased duration and amplitude	2
Fibrillation potentials and positive sharp waves +++ or ++++ or Fibrillation potentials and positive sharp waves in every site	No activity during voluntary muscle activation	3

Table 1: criteria used to score active and chronic denervation Abbreviations: MUAPS= Motor Unit Action Potentials * in case of different scores between muscles, the highest score was considered. ** in case of expression such as "slightly", "mainly".

Results: We found that spinal AD and CD were strongly directly correlated to LMNS (respectively p=4.4x1,037 and p=2.79x10-45) and inversely to MRC (respectively p=4.5x10-35 and p=2.97x10-35) Furthermore, patients with higher spinal AD and CD scores had significant lower ALSFRS-R scores, higher KSS and MITOS stages; conversely, only AD, and not CD, was directly associated to deltaFRS (p=1.0x10-6) and inversely survival (p=1.1x10-5).
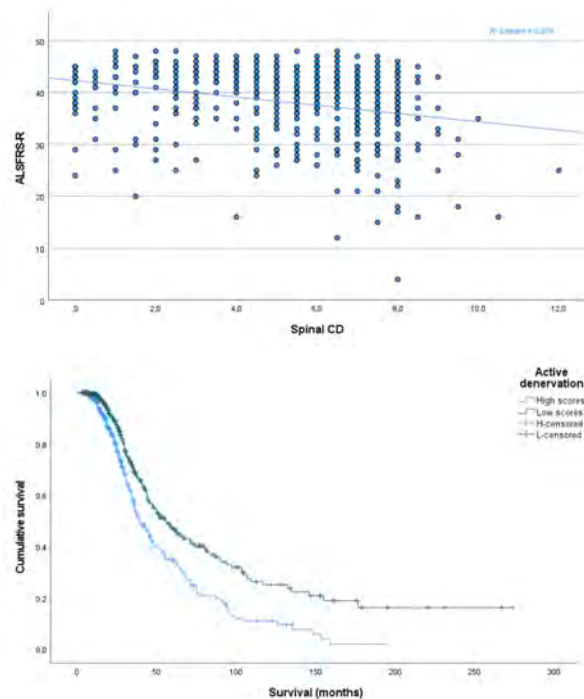
Conclusion: Our results confirmed that EMG examination represents not only a diagnostic instrument, but also a prognostic tool. In this context, AD seem to be a reliable predictor of disease's progression and survival, conversely CD seems to better describe functional disability.

Disclosure: Allergan, Eli Lilly, Neopharmed Gentili, Novartis, Piam.

EPR-244

Disease modifying treatments for Adults with Spinal-Muscular-Atrophy at Atkinson Morley Neurosciences Centre, London

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Background and aims: There are two disease modifying treatments for adults with Spinal Muscular Atrophy (SMA) in England. Nusinersen requires intrathecal (IT) administration. Risdiplam is an oral medication.

Methods: We performed retrospective analysis of medical records.

Results: 38 patients aged 17–57 years were assessed (Figure 1). All patients have baseline respiratory and motor function assessment (Table 2). We attempted IT access for nusinersen in eleven patients (Table 1). Three patients needed non-invasive ventilation (NIV) and one had swallowing difficulties. One patient with type-2 SMA with severe scoliosis had hypokalemia and urinary retention post-procedure so treatment was stopped. One biplane injection for spinal fusion was unsuccessful due to absence of CSF. In type-3 SMA, all injections were successful allowing repeated administration. Complications included transient low-pressure headache, radicular and back pain Risdiplam was prescribed for nine patients all with type 2 SMA. They had 0–5 comorbidities and 1–12 additional medications. Seven patients required NIV while two had swallowing difficulties (one with gastrostomy). Two patients had adverse effects: (i) increased weakness and treatment cessation (ii) transient transaminitis but treatment was restarted successfully.
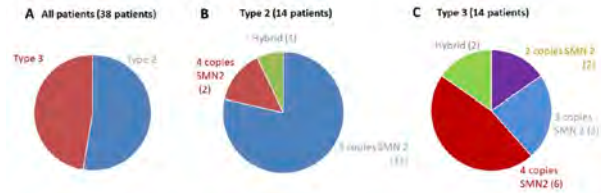
Figure 1: Patients assessed with SMA. A: 38 patients were assessed with type 2 and 3 SMA. Full genetic results with SMN2 copy number and hybrid genes were available for 28 patients: 14 with type 2 SMA (B) and 14 patients with type 3 SMA (C).

Baseline assessment	ALL	Ambulant Type 3 SMA			Non ambulant type 3 and type 2	
	Force vital capacity (FVC)	Hammersmith Functional Motor Scale Expanded (HFMSE)	Revised Hammersmith Scale (RHS)	6 minute timed walk	Children's Hospital of Philadelphia Infant Test of Neuromuscular Disorders (CHOP-ATTEND)	Revised upper limb module (RUL)
Patients Treated with Nusinersen (Type 2 and Type 3)						
	38-153%	37-60	31-67	43-492m	17-38	2-33
Patients Treated with Risdiplam (Type 2 only)						
	19% to 74%),	-	-	-	19-46	0-19

Table 1: Baseline assessment before treatment with Nusinsern and Risdiplam

Patients treated with Nusinersen	Spinal anatomy	Normal spine	Severe Scoliosis	Spinal fusion	Spinal fusion	Total attempted	Total full loading completed
	Imaging used	Single plane fluoroscopy	Biplane fluoroscopy	Biplane fluoroscopy	CT guidance		
Type 2	-	2	1	-		3	1
Type 3 – lost ambulation in childhood	-	-		2		2	2
Type 3 lost ambulation in adulthood	1	-		-		1	1
Type 3 ambulant	5	-		-		5	5
TOTAL	6	3		2		11	9

Table 2: Patients treated with Nusinersen: type of SMA, ambulation status, spinal anatomy and radiological guidance used

Conclusion: It is possible to administer IT Nusinersen with complex spinal anatomy with appropriate neuroradiological expertise. Treatment success is higher and complication rates lower in patients with type-3 SMA. We found Risdiplam a well-tolerated treatment for adults with a wider range of ages and comorbidities and contaminant medications than in clinical trials. Liver function monitoring is important. This information may inform future disease modifying treatment protocols.

Disclosure: Clare Galtrey has been on advisory board for Roche.

EPR-245

Detection of Misfolded Alpha-Synuclein in Amyotrophic Lateral Sclerosis (ALS)

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Background and aims: Neurodegenerative diseases are commonly characterized by disorders of protein folding. Misfolded alpha-synuclein, a driver of pathology in Parkinson's disease, has been implicated in ALS due to its observed interactions with SOD1 and TDP43. Further, Parkinsonian features have been reported in 30% of ALS subjects and, on pathologic exam, Lewy bodies have been observed in 11% of patients. Following up on these observations, we have explored the prevalence of misfolded alpha-synuclein in sporadic and familial ALS patients utilizing a seed amplification assay (SAA) that allows for the detection of minute amounts of aggregated alpha-synuclein in spinal fluid.

Methods: Spinal fluid samples were added to a 96-well plate with monomeric alpha-synuclein and Thioflavin T, a fluorescent dye. During cyclic shaking for seven to ten days, fluorescence labelling of amyloid structures was serially measured to determine the presence of misfolded alpha-synuclein oligomers/fibrils. When fluorescence exceeded 25,000 RFU, the sample was deemed positive.

Results: Utilizing the SAA, we detected self-aggregation of alpha-synuclein in spinal fluid from 7 of 41 cases of sporadic ALS subjects and 6 of 18 Guamanian ALS subjects. In a limited number of familial ALS subjects (n=15), we have yet to make similar observations. These results were compared with a control panel.

Sample Type		# Positive for misfolded alpha-synuclein
Sporadic ALS	n = 41	7
C9orf72 ALS	5	0
SOD1 ALS	10	0
Guamanian ALS/PDC	18	6

Table 1.

Conclusion: These finding suggest the possibility that a subgroup of ALS patients exists for which alpha-synuclein contributes to the disease pathogenesis.

Disclosure: Dr. Lebovitz is the CEO and co-founder of Amprion Inc., where the seed amplification studies were conducted.

EPR-246

Pathogenic HTT and NOTCH2NLC repeat expansions are rare in Italian amyotrophic lateral sclerosis patients

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Background and aims: By examining whole-genome sequence data from 6,116 frontotemporal dementia (FTD)/amyotrophic lateral sclerosis (ALS) patients, Dewan and colleagues reported HTT full-penetrance pathogenic repeat expansions in eight patients (0.13%), but not in healthy controls (n=3,158) nor in Lewy body dementia patients (n=2,599). Similarly, Yuan and colleagues found four carriers of abnormal GGC repeats in NOTCH2NLC in a cohort of 545 ALS patients, but none within 1,305 healthy subjects from mainland China. HTT repeat expansions are the genetic cause of Huntington's disease, whereas abnormal GGC repeats in NOTCH2NLC have been previously identified in neuronal intranuclear inclusion disease (NIID) muscle weakness-dominant subtype (NIID-M). The aim of our study was to investigate the role of pathogenic HTT and NOTCH2NLC repeat expansions in an Italian cohort of ALS patients.

Methods: A screening analysis of HTT CAG repeats and NOTCH2NLC GGC repeats was performed by repeat-primed polymerase chain reaction (RP-PCR) in a cohort of 350 probable/definite ALS Italian patients.

Results: Mean age at onset of patients was 60.7 years (SD 13.6), and 62.6% were males. Sporadic cases were 329 (94.0%). None of our patients showed the typical sawtooth tail pattern on RP-PCR, thus excluding abnormal repeat expansion in HTT and NOTCH2NLC.

Conclusion: Our results suggest that pathogenic HTT and NOTCH2NLC repeat expansions might be absent or at least extremely rare in Italian ALS patients. As limited data are available so far, further replication studies are required to confidently confirm the pathogenic role of HTT and NOTCH2NLC repeats expansions in ALS before moving to common clinical practice.

Disclosure: The authors declare no conflicts of interest.

EPR-247

Evaluation of the Penn Upper Motor Neuron score as a tool to determine the clinical phenotype and prognosis of ALS

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Background and aims: The Penn Upper Motor Neuron Score (PUMNS) has been proposed as a measure of UMN disease in amyotrophic lateral sclerosis (ALS). In our study, we evaluated the correlation between PUMNS and clinical/neurophysiological parameters to confirm whether PUMNS represents a reliable marker of UMN impairment and if it can be used as a prognostic tool.

Methods: The following clinical parameters were collected on a cohort of 875 ALS Italian patients: age and site of onset, survival, MRC scale, lower motor neuron score (LMNS), PUMNS, ALSFRS-R, deltaFRS, MITOS and King's Staging systems. Transcranial magnetic stimulation was performed on a subgroup of patients and central motor conduction time (CMCT) and cortical silent period (CSP) were calculated.

Results: We observed that patients with an earlier age at onset and bulbar onset had more UMN impairment. Higher PUMNS values were associated to lower ALSFRS-R ($p=3.5\times10^{-11}$) and to higher deltaFRS scores, as well as to higher MITOS and KSS stages, indicating that a greater UMN burden correlates with disease severity. Conversely, we did not appreciate any association between PUMNS and survival or markers of LMN disease. With regard to neurophysiological parameters, PUMNS values showed a strong direct association to CMCT ($p=3.46\times10^{-16}$) and inverse association to CSP ($p=0.011$) values.

Conclusion: Our results confirm that PUMNS represents not only a reliable measure clinical UMN dysfunction, but also a tool to better characterize phenotype, functional disability, disease progression and prognosis in patients affected by ALS. PUMNS also display a strong correlation to other markers of UMN impairment.

Disclosure: No disclosures reported.

EPR-248

Tuberculin skin test reactions in non-BGC vaccinated individuals and Amyotrophic Lateral Sclerosis risk

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Background and aims: Exposure to Mycobacterium tuberculosis or other mycobacteria rarely causes disease. It may, however, cause a latent infection, which has been suggested as a risk factor for amyotrophic lateral sclerosis (ALS). By using population-specific cutoffs in skin induration sizes, the tuberculin skin test (TST) offers a method for detecting infected individuals. We hypothesized that individuals with a positive TST had increased risk of ALS.

Methods: Using data from the Norwegian tuberculosis screening program (1963–1975), we designed a population-based cohort study and related the size of TST reactions in individuals not previously vaccinated with BCG to later ALS disease identified through validated Norwegian health registers. We fitted Cox proportional hazard models to investigate the association between a positive tuberculin skin test and ALS risk.
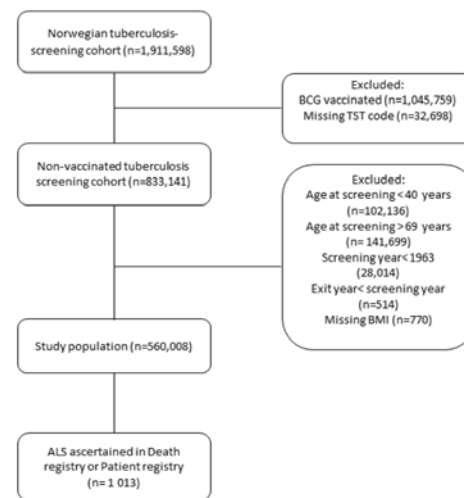
Selection of participants

Results: Among 560,008 non-BCG vaccinated participants (49% males) aged 40–70 years at screening, 1,013 (53% males) later developed ALS. Compared to those with a negative TST (0–3 mm induration size) hazard ratio was 1.21 (95% CI 1.02–1.45) for moderate positive (4–9 mm) and 1.23 (95% CI 1.01–1.49) for strong positive TST (>9 mm). The association was similar among sexes and persisted when excluding the first 5 years of follow-up.

	Cases		Noncases	
	Male	Female	Male	Female
Participants	541	472	274,373	282,622
Age (years) at screening, mean (SD)	53.9 (7.6)	54.4 (8.2)	55.6 (7.9)	55.9 (8.1)
Birth year, mean (SD)	1914 (7.8)	1914 (8.4)	1912 (8.1)	1912 (8.3)
BMI, mean kg/m2 (SD)	24.8 (2.9)	25.7 (4.1)	25.2 (3.2)	26.8 (4.5)
Exposure category, n (column %)				
Negative Tuberculin skin test (TST)	84 (15)	135 (29)	52,262 (19)	94,636 (33)
Positive TST (4-9 mm)	166 (31)	168 (36)	78,378 (29)	101,564 (36)
Strong positive TST (>9 mm)	161 (30)	80 (17)	80,698 (29)	42,551 (15)
History of prior positive TST	121 (22)	83 (18)	57,636 (21)	42,511 (15)
Possible tuberculosis	9 (2)	6 (1)	5,399 (2)	3,360 (1)

Baseline characteristics of non-BCG vaccinated individuals aged 40–69 years participating in the last stages (1963–1975) of the Norwegian tuberculosis screening program, according to ALS-status and sex

Tuberculin skin test (TST) Category	Participants	Cases	Risktime, years	Multivariable adjusted[1] HR (95% CI)
All,				
Negative TST	147,220	219	12,025,082	Baseline
TST 4-9 mm	180,276	334	14,614,334	1.21 (1.02-1.45)
TST > 9 mm	126,730	247	10,096,655	1.23 (1.01-1.49)
Male				
Negative TST	52,288	84	4,131,521	Baseline
TST 4-9 mm	78,378	166	6,150,136	1.34 (1.03-1.76)
TST > 9 mm	83,065	167	6,476,037	1.27 (0.97-1.67)
Female				
Negative TST	94,848	135	7,893,561	Baseline
TST 4-9 mm	101,732	168	8,464,198	1.12 (0.89-1.41)
TST > 9 mm	43,745	80	3,620,618	1.25 (0.94-1.66)
Born 1895-1909				
Negative TST	71,847	97	5,921,069	Baseline
TST 4-9 mm	78,444	117	6,425,874	1.14 (0.86-1.50)
TST > 9 mm	46,406	69	3,740,481	1.12 (0.81-1.55)
Born 1910-1919				
Negative TST	51,051	78	4,139,818	Baseline
TST 4-9 mm	65,379	138	5,263,990	1.36 (1.02-1.82)
TST > 9 mm	49,424	87	3,902,173	1.10 (0.80-1.52)
Born 1920-1935				
Negative TST	24,322	44	1,964,195	Baseline
TST 4-9 mm	36,453	79	2,924,469	1.16 (0.79-1.71)
TST > 9 mm	31,147	91	2,454,001	1.57 (1.07-2.31)
5 exposure categories, all				
Negative TST	147,117	219	12,016,642	Baseline
TST 4-9 mm	180,276	334	14,614,334	1.20 (1.01-1.43)
TST > 9 mm	123,490	241	9,822,265	1.21 (1.00-1.47)
Prior positive TST	100,351	204	7,998,977	1.22 (1.00-1.49)
Possible tuberculosis	8,774	15	691,737	1.05 (0.62-1.78)

Risk (hazard ratio - HR) of ALS by categories of tuberculin skin test reactivity at tuberculosis screening 1963–1975 in non-BCG vaccinated individuals. 1 Stratified by age and calendar year at screening and adjusted for sex, BMI and county of residence

Conclusion: A positive tuberculin skin test reaction in non BGC-vaccinated individuals is associated with increased ALS risk. These findings may suggest a link between mycobacteria infection and ALS risk.

Disclosure: ON and TH have received grants from ALS Norway (patient organization).

EPR-249

NEK1 variants in a cohort of Italian ALS patients

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Background and aims: NEK1 loss of function (LoF) variants are associated to amyotrophic lateral sclerosis (ALS) and the p.Arg261His missense variant has a role in disease susceptibility. The pathogenic role of other missense variants is unclear. The aim of our work was to investigate the presence and impact of NEK1 variants and to explore potential genotype-phenotype correlations in a cohort of Italian ALS patients.

Methods: We sequenced a cohort of 356 unrelated Italian ALS patients by Next Generation Sequencing (NGS). A cohort of 380 non-neurological unrelated Italian patients was selected as control group. We assessed whether the presence of NEK1 variants was associated to phenotypic features.

Results: We detected 20 different NEK1 rare variants (4 LoF and 16 missense) in 33 unrelated patients with sporadic ALS. The four LoF variants (two frameshift and two splice-site variants) were novel. The p.Arg261His missense variant, previously reported as a risk factor for ALS, was found in 13 patients and one control. Among the missense variants, nine were classified as variants of uncertain significance, including four novel variants. 15 NEK1 variant carriers harbored variants in other ALS-related genes. Flail arm phenotype was over-represented among NEK1 carriers.

Conclusion: NEK1 variants are not rare in the Italian population. The fact that we found NEK1 variants only in sporadic patients, together with the high frequency of oligogenic carriers, supports the hypothesis that some NEK1 variants confer a significant susceptibility to ALS, although they might not be sufficient per se for disease development. These variants may however act as a phenotypical modifier.

Disclosure: Nothing to disclose.

EPR-250

Serum Chloride as a respiratory failure marker in Amyotrophic Lateral Sclerosis

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Background and aims: Serum chloride is a metabolic indicator of the degree of respiratory acidosis easily obtainable by routine blood analysis. We investigated the role of serum chloride analysed at diagnosis as a prognostic factor in a population-based series of ALS patients.

Methods: We collected all the serum chloride in patients followed up in Turin ALS Centre as part of the Piemonte and Valle d'Aosta Register for ALS from January 1st, 2007 to December 31st, 2019. We also collected clinical data such as age at diagnosis, sex, date of onset, site of onset, date of death/tracheostomy, ALSFRS-r score at diagnosis, weight loss and FVC at diagnosis.

Results: 1,484 ALS patients were included in the analysis. Serum chloride showed a significant but small correlation with FVC ($R=0.149$, $p<0.001$) and respiratory symptoms at diagnosis ($R=0.179$, $p<0.001$), measured using ALSFRS-R. Survival analysis performed using both Cox proportional hazard models, adjusted for many different prognostic factors, and Kaplan-Meier curves (two groups according median value) demonstrated a significantly lower risk for death/tracheostomy for patients with high serum chloride (HR 0.982 95% CI 0.969–0.995, $p=0.007$; log rank test $p<0.001$). Stratifying patients according to NIV usage, baseline low serum chloride was associated with a shorter time-to-ventilation (median 11.5 months, 4.0–19.0 vs. 14.0 months, 8.0–26.0).

Figure 2. Kaplan Meier curves for time-to-NIV in ALS patients (adapted to NIV) with serum chloride values at diagnosis above and below median value. Survival was calculated from diagnosis to NIV start

Conclusion: Serum chloride can be used as a low cost screening test at diagnosis and during follow-up to monitor respiratory dysfunction in ALS patients.

Disclosure: No disclosures to report for the present manuscript.

Figure 1. Kaplan Meier curves for overall survival in ALS patients with serum chloride values at diagnosis above and below median value. Survival was calculated from diagnosis to death/tracheostomy

MS and related disorders 5

EPR-251

Radiologically isolated syndrome: a single-center cohort with clinical and radiological follow-up

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Background and aims: We aim to describe clinical, radiological, and biological characteristics of patients presenting with a radiologically isolated syndrome (RIS), to analyze risk factors for developing multiple sclerosis (MS) symptoms during the follow-up, and to analyze the diagnostic properties of the different criteria (Okuda 2009 and MAGNIMS 2018).

Methods: An observational study including 88 patients referred as suspected RIS. After a centralized MRI review, patients were classified as standard RIS patients (MAGNIMS criteria) or possible RIS (suspected lesions not accomplishing the MAGNIMS 2018 criteria). A Cox regression analysis and a diagnostic performance analysis of different RIS criteria were performed using in both cases MS diagnosis during follow-up as the outcome.

Results: After a clinical and radiological reevaluation, 63 patients were included. 41 patients were classified as standard RIS and 21 patients as possible RIS. After a mean time of follow-up of 72.67 months (SD 44.14), 19 patients (30.16%) were diagnosed with MS. A younger age, presence of spinal cord lesions at baseline, and presenting radiological activity during follow-up conferred a higher risk of having MS during the follow-up. Regarding diagnostic performance, compared to the Okuda 2009 criteria, the MAGNIMS 2018 RIS criteria showed greater sensitivity (0.84 vs. 0.63) with slightly lower specificity (0.59 vs. 0.43).

Conclusion: A high percentage of RIS patients will develop MS during follow-up, being more frequent in young patients, with spinal cord lesions, and radiological activity during the follow-up. Compared to the original criteria, the MAGNIMS 2018 RIS criteria have a better sensitivity and a lower specificity.

Disclosure: Nothing to disclose.

EPR-252

miR-145, miR-26a and Smoking contribute to Multiple Sclerosis exacerbation

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Background and aims: Smoking is the leading preventable risk factor for MS development and progression. Cigarette smoking promotes a chronic inflammatory state with the induction of Th17 cells. Chronic inflammation can be sustained by smoking-induced dysregulation of the epigenetic profile, especially microRNAs (miRS). We sought to quantify serum levels of miR-26a and miR-145, key players in the Th17 cells modulation, and to analyse its diagnostic performance in MS development and progression.

Methods: MiRs serum levels were quantified in 116 patients with definitive MS diagnosis accordingly to 2017 McDonald's Criteria (61 female, age=42±12 ; disease duration=13±9, 10 with Progressive MS, 29% HLA-DRB1*15 positive, mean Expanded Disability Status Scale (EDSS)=2.3±2.1, Multiple Sclerosis Severity Score (MSSS) =2.8±2.7 Age Related MSSS (ARMSSS)=3.6±2.6). 63 individuals without autoimmune and neurological pathologies were included in the control group.

Results: MS patients and control individuals had similar miR-26a and miR-145 circulating levels. Also, both miR were not influenced by clinical course nor by HLA-DRB1*15 presence. Noteworthy, miR-26a serum levels were inversely correlated with clinical outcome especially in smokers (miR-26a: EDSS - p=0.006, MSSS - p=0. 010, ARMSSS p=0.013; miR-145: MSSS - p=0.031, ARMSSS - p=0.025).

Conclusion: Our preliminary results suggest that miR-26a and miR-145 may be reliable prognostic MS biomarkers especially in smokers. The evaluation of miR-26a and miR-145 levels and smoking cessation could improve MS prognosis.

Disclosure: Financial support: BIEM

EPR-253

Immune response following vaccination against seasonal influenza in patients treated with the BTK inhibitor evobrutinib

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Background and aims: Bruton's tyrosine kinase inhibitors (BTKis) reduce oncology patients' immune responses to vaccines, but there are no data in autoimmune diseases, like systemic lupus erythematosus (SLE) or multiple sclerosis.
Objective: determine the humoral response to influenza vaccination in patients with SLE receiving evobrutinib, a BTKi, in a post-hoc analysis of a double-blind, randomised, placebo-controlled Phase II trial (NCT02975336).
Methods: Post-hoc analysis of patients with SLE treated with evobrutinib 75mg once-daily (QD; n=11), 50mg twice-daily (BID; n=21), or placebo (n=23) receiving influenza vaccination during the trial (median treatment exposure pre-vaccination: 16.4–36.4 weeks). Pre-/post-vaccine haemagglutination inhibition (HI) serum antibody titer samples were collected (median 8.1–11.6 weeks post-vaccination). Seroconversion: pre-vaccination titers of =1:10 rising to ≥1:40 or increasing >4-fold, respectively, post-vaccination. Seroprotection: serum HI titer of ≥1:40 post-vaccination. Seroconversion/seroprotection rates are percentage of patients who met these definitions.
Results: Baseline mean(±SD) age of vaccinated patients treated with placebo or evobrutinib was 41.0(±11.1) and 43.0(±11.7) years; mean(±SD) disease duration was 8.3(±7.1) and 6.9(±5.4) years, respectively; 89.1% were female. Across strains, seroconversion rates were 47.8% for placebo and 53.1% for total evobrutinib (75 mg QD and 50 mg BID; rate difference: 5.3% [95% CI -21.7;31.3]). The seroprotection rates across strains pre-/post-vaccination were 69.6%/91.3% for placebo and 56.3%/81.3% for total evobrutinib. Pre-/post-vaccination HI antibody titer geometric mean ratios were similar for evobrutinib and placebo with different strains.
Conclusion: This is the first evidence demonstrating that patients treated with a BTKi, evobrutinib, for an autoimmune disease (SLE) can mount a humoral response to seasonal influenza vaccination.

EPR-254

Extended vs standard interval dose in Ocrelizumab treated MS patients during COVID-19 pandemic: an Italian experience

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Background and aims: Ocrelizumab (OCR), a B cell–depleting therapy, has raised safety concerns during the COVID-19 pandemic era, for the alert of increased risk of infection. This has brought to the attempt of an extended interval dosing (EID) regimen.
Methods: We enrolled all Multiple Sclerosis (MS) patients who received maintenance doses of OCR from February 2020 to June 2021. Data were extracted in December 2021. We considered all infusions occurring during the index window. Standard interval dosing (SID) or EID regimen were defined according to the time-interval between infusions (equal or higher than 210 days). We built two logistic-regression models for clinical (relapses) and radiological (new lesions on T1-gadolinium or T2-weighted sequences in magnetic resonance imaging, MRI) activity along with the available follow-up.
Results:
A total cohort of 263 was enrolled (188 with EID and 75 with SID, respectively). The EID patients were younger, with a higher rate of vaccination against Sars-Cov2 (p<0.05). The SID patients were mostly on a progressive course and with a higher level of disability (all p<0.05). EID did not influence the risk of relapse occurrence nor radiological activity in the logistic models. Being female, having a progressive course, and a higher level of baseline MRI activity (p<0.05) were the highest determinants of relapse occurrence. Whilst radiological activity was influenced by the number of relapses in the previous year and by baseline disability level.
Conclusion: EID did not seem to be associated with increased disease activity. EID regimen needs to be weighed carefully in selected MS populations.
Disclosure: The authors had nothing to disclose.

EPR-255

First relapse phenotype and recovery during first-line therapies: an Italian Registry study

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Background and aims: The relapse phenotype has not been fully investigated in relapsing-remitting Multiple Sclerosis (RRMS) field as a parameter to verify a disease-modifying therapy (DMT).

Methods: A multicentre retrospective analysis of prospectively collected data from the Italian MS Registry on RRMS patients, starting first-line DMTs from January 1, 2013, to December 31, 2019.

Results: 2,676 patients fulfilled the required criteria. The first-relapse phenotype of 712 relapses was determined. Being female and higher number of relapses before diagnosis were associated with higher risk of relapse in the 5-year period (HR=1.3, 95% CI 1.07–1.46; p=0.005 and HR=1.1, 95% CI 1.06–1.15; p<0.001, respectively) whilst older age at the time of first DMT prescribed (HR=0.98, 95% CI 0.98–0.99; p<0.001) to a lower risk. The pyramidal phenotype was associated with higher age and baseline EDSS score. Older age correlated also with worse sequelae (proportional OR = 1.02, 95% CI 1.01–1.04; p=0.004), as the occurrence of a second relapse before the DMT starting (proportional OR = 1.72, 95% CI 1.01–2.92; p=0.044). The pyramidal phenotype, adjusted for age and other phenotypes was associated to a 1.95-fold higher risk of severe or moderate sequelae (proportional OR = 1.95 95%CI 1.35–2.80; p<0.001).

Conclusion: The characterization of different relapse phenotypes from early phases of RRMS and the first DMT prescribed should be considered a determinant of therapeutic choice.

Disclosure: Authors had nothing to disclose related to this abstract.

EPR-256

Safety and efficacy of parenteral cladribine used in higher doses in multiple sclerosis patients - 22 years observation

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Background and aims: Cladribine is registered as a 10 mg tablets with fixed cumulative dosing of 3,5 mg/kg of body weight. It is important to investigate if increased dosing of the drug might lead to higher efficacy with preserved safety. The aim was to compare the clinical outcomes between patients receiving different dosing parenteral cladribine regimens with up to 22 years of follow-up.

Methods: The study group consisted of 52 patients diagnosed with relapsing multiple sclerosis who received induction treatment (cumulative dose of 1.8 mg/kg s.c.;consistent with 3,5 mg/kg given orally, divided into 6 courses every 5 weeks) and were offered the maintenance treatment (repeated courses in a dose of 0.3 mg/kg s.c., over 5–22 years). EDSS scores were assessed for all patients at baseline, at the end of the cladribine induction treatment course (Year1) and during observation (in the year 5, 10, 15, 20 and 22). Disease progression was defined as change in EDSS score of ≥0,5 between baseline and last follow up.

Results: There were 41 patients who received increased cumulative dose (higher than induction of 1.8 mg/kg) and 11 who received the standard induction dose of cladribine. The risk of progression correlated with lower cumulative dose (p=0,01) and more advanced disability at baseline (p<0.05). The maintenance treatment with increased cumulative dose was safe and well tolerated.

Conclusion: Cladribine treatment with increased cumulative dosing is associated with disease stabilization and favorable safety profile over prolonged follow-up.

Disclosure: The authors report no conflicts of interest in this study.

EPR-257

Natalizumab during pregnancy in women with Multiple Sclerosis and its impact on children´s development

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Background and aims: In cases of highly active multiple sclerosis, natalizumab-treatment up to or during pregnancy might be necessary. Whereas data on pregnancy outcomes are available, though scare, data on child development are lacking.

Methods: Eligible cases (natalizumab-treatment at conception or no treatment exposure during pregnancy) from the German Multiple Sclerosis and Pregnancy Registry were identified. Data are collected with a standardized questionnaire in regular telephone-interviews during pregnancy and postpartum; data on child follow-up are derived from children's medical check-up booklets. Children will be followed-up until 5 years of age. Development outcomes will be compared between the two groups.

Results: Of the 150 exposed cases n=47 received their last natalizumab-infusion during the 1st trimester or up to 6 weeks before the last menstrual period whereas n=103 were treated also during 2nd/3rd trimester. Median number of infusions during pregnancy was 4 (range 1–8). Currently, the control group comprises 48 cases with interferon-beta or glatiramer acetate treatment before pregnancy. 1-year infant data are presented, but inclusion of controls and overall follow-up is still ongoing; updated data will be presented at the congress. Pregnancy outcomes were comparable between the groups (Table 1). Percentages of developmental delay (motoric, speech) were similar: n=4 (2.7%) in exposed cases vs. n=2 (4.2%) in controls. n=2 (1.3%) exposed infants were diagnosed with a chronic condition (spinal muscular atrophy and neurodermatitis). Body measurements were descriptively comparable between exposed and unexposed infants during the course of the year (Table 2).

Table 1: Pregnancy outcomes

	Entire Cohort n = 198	Exposed n = 150	Control n = 48
Gestational week at birth, median (range)	39.14 [28.6-42.1]	39.07 [28.6- 42.0]	39.71 [35.5- 42.1]
Gestational week at birth excluding preterm births, median (range)	39.35 [37.0-42.1]	39.14 [37.0- 42.0]	39.85 [37.0- 42.1]
Preterm births, n (%)	16 (8.08)	13 (8.67)	3 (6.25)
Cesarean section, n (%)	62 (31.31)	50 (33.33)	12 (25.00)
Breastfeeding, n (%)	147 (74.24)	104 (69.33)	43 (89.58)
Reported exclusive breastfeeding, n (%)	99 (50.00)	72 (48.00)	27 (56.25)
Breastfeeding under natalizumab treatment, n (%)		44 (29.33)	0 (0.0)
Duration natalizumab exposed breastfeeding, median (range) days		161 [14-571]	NA
Congenital anomaly, n (%)	13 (6.57 %)	8 (5.33 %)[1]	5 (10,42 %)[2]

n, number of infants; NA, not applicable
[1] atrial septal defect, hypospadias (n=2), patent foramen ovale (n=2), macrocephaly, cleft lip and palate and pectus excavatum
[2] spontaneous gene mutation and achondroplasie, atrial septal defect, ventricular septal defect, patent foramen ovale and polydakty

Body measurements at medical check-ups excluding preterm births	All n = 182	Exposed n = 137	Control n = 45
U1 body weight boys, mean (SD) grams	3391 (388)	3225 (404)	3610 (349)
U1 body length boys, mean (SD) centimeter	51.47 (2.3)	51.21 (2.4)	52.81 (1.8)
U1 head circumference boys, mean (SD) centimeter	34.93 (1.1)	34.86 (1.2)	35.37 (1.0)
U1 body weight girls, mean (SD) grams	3347 (511)	3324 (543)	3506 (319)
U1 body length girls, mean (SD) centimeter	51.20 (2.9)	51.18 (3.0)	51.37 (2.4)
U1 head circumference girls, mean (SD) centimeter	34.79 (1.7)	34.67 (1.8)	35.43 (1.3)
U2 body weight boys, mean (SD) grams	3211 (404)	3170 (404)	3393 (324)
U2 body length boys, mean (SD) centimeter	51.45 (2.4)	51.23 (2.6)	52.16 (1.8)
U2 head circumference boys, mean (SD) centimeter	34.95 (1.2)	34.84 (1.3)	35.43 (1.0)
U2 body weight girls, mean (SD) grams	3155 (485)	3141 (509)	3209 (377)
U2 body length girls, mean (SD) centimeter	51.32 (3.0)	51.20 (3.1)	51.77 (2.7)
U2 head circumference girls, mean (SD) centimeter	34.82 (1.6)	34.70 (1.7)	35.33 (1.1)
U3 body weight boys, mean (SD) grams	4468 (645)	4473 (683)	4617 (526)
U3 body length boys, mean (SD) centimeter	55.00 (2.4)	55.07 (2.6)	54.72 (2.4)
U3 head circumference boys, mean (SD) centimeter	37.85 (1.2)	37.85 (1.2)	37.29 (1.2)
U3 body weight girls, mean (SD) grams	4232 (579)	4249 (609)	4326 (454)
U3 body length girls, mean (SD) centimeter	54.66 (2.5)	54.65 (2.6)	54.70 (2.5)
U3 head circumference girls, mean (SD) centimeter	37.22 (1.3)	37.20 (1.3)	37.29 (1.2)
U4 body weight boys, mean (SD) grams	6645 (827)	6627 (790)	6953 (871)
U4 body length boys, mean (SD) centimeter	63.53 (3.0)	63.32 (3.3)	64.00 (2.4)
U4 head circumference boys, mean (SD) centimeter	41.72 (1.4)	41.65 (1.3)	41.80 (1.5)
U4 body weight girls, mean (SD) grams	6104 (862)	6170 (907)	5950 (705)
U4 body length girls, mean (SD) centimeter	61.56 (2.9)	61.94 (3.3)	60.55 (2.3)
U4 head circumference girls, mean (SD) centimeter	40 50 (1.4)	40.42 (1.4)	40.83 (1.3)
U5 body weight boys, mean (SD) grams	8443 (853)	8396 (834)	8528 (916)
U5 body length boys, mean (SD) centimeter	69.67 (2.9)	69.77 (3.2)	69.67 (2.3)
U5 head circumference boys, mean (SD) centimeter	44.52 (1.2)	44.55 (1.2)	44.42 (1.4)
U5 body weight girls, mean (SD) grams	8443 (853)	8396 (834)	7512 (879)
U5 body length girls, mean (SD) centimeter	67.92 (3.0)	68.26 (3.0)	67.16 (2.9)
U5 head circumference girls, mean (SD) centimeter	43.12 (1.5)	43.29 (1.6)	43.05 (1.5)
U6 body weight boys, mean (SD) grams	10142 (1097)	10110 (1086)	10192 (1111)
U6 body length boys, mean (SD) centimeter	77.14 (3.3)	77.38 (3.4)	76.85 (3.1)
U6 head circumference boys, mean (SD) centimeter	47.14 (1.4)	46.11 (1.4)	46.92 (1.4)
U6 body weight girls, mean (SD) grams	9238 (1354)	9297 (1402)	9099 (1310)
U6 body length girls, mean (SD) centimeter	74.46 (3.0)	74.65 (2.4)	74.05 (4.1)
U6 head circumference girls, mean (SD) centimeter	45.67 (1.6)	45.55 (1.4)	45.94 (1.8)

BMI, body mass index; NA, not applicable, SD, standard deviation; U1: Medical check-up at birth, U2: Medical check-up at 3-10 days of age; U3: Medical check-up at 4-5 weeks of age; U4: Medical check-up at 3-4 months of age; U5: Medical check-up at 6-7 months of age; U6: Medical check-up at 10-12 months of age

Conclusion: 1-year infant data show no signs that natalizumab exposure during pregnancy adversely affected children's development.

EPR-258

AMASIA study: Real World Insights on Siponimod Treated Patients with Secondary Progressive Multiple Sclerosis in Germany

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Background and aims: Progressive motor dysfunction and cognitive decline are typical hallmarks of secondary progressive multiple sclerosis (SPMS). Siponimod, a selective sphingosine-1-phosphate receptor modulator, is approved for the treatment of active SPMS. The non-interventional AMASIA study will provide real-world evidence on the long-term effectiveness and safety of siponimod as well as its impact on quality of life.

Methods: Siponimod treated SPMS patients will be followed over 3 years. Every 6 months, disability progression and cognitive changes are evaluated by the expanded disability status scale (EDSS) and the symbol digit modalities test (SDMT). Questionnaires from the perspective of patients, physicians, and relatives on disability progression, cognitive worsening and quality of life are documented.

Results: A previous interim analysis including 435 patients with active SPMS presents an average AMASIA patient of 54.6 years, an EDSS of 5.3 and a SDMT score of 39.2 when starting Siponimod. Prior to siponimod, 47.9 % of the patients had received baseline disease-modifying therapies (DMT). Treatment satisfaction with siponimod as measured with the treatment satisfaction questionnaire (TSQM-9) remained high after six months of treatment. Here, we expand the previous analysis and present a patient population of ca. 530 patients with baseline and ca. 190 patients with 12-month follow-up data, including patient-reported outcome questionnaires on disability progression, cognitive worsening, and quality of life.

Conclusion: AMASIA encompasses a large cohort of active SPMS patients and will enable a comparison of clinical trial data to the actual treatment context in real-world clinical practice.

EPR-259

Serum cytokines and alemtuzumab infusion-related adverse events in Multiple Sclerosis: preliminary results

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Background and aims: Alemtuzumab (AL) is an anti-CD52 antibody approved for the treatment of highly active relapsing-remitting Multiple Sclerosis (MS). During AL administration, infusion-related adverse events (IRAE) are common and often associated with the cytokines release syndrome (CRS) caused by AL-mediated lymphocyte depletion. Limited evidence exists about the association between cytokine release and IRAEs. Our objective is to explore the relationship between serum cytokines modifications during AL infusions and the occurrence of IRAEs.

Methods: We evaluated IRAEs during AL infusions in MS patients followed at our centre from 2015 to 2021. Blood was collected daily before infusion. Cytokines were dosed with Bio-Plex 27-plex in a patient subset in the first 3 days of infusion. Comparisons were performed with Kruskal-Wallis or ANOVA tests.

Results: A total of 50 patients and 379 infusions were analysed. The most frequent IRAEs were bradycardia (82.0% and 52.1%,), rash (80.0% and 45.8%,), and CRS (54.0% and 35.4%,) during the first and second course, respectively. The cytokines analysis was performed for 23 patients, measured in the first (18 patients) and the second (9 patients) course (total of 27 single courses). A significant increase in FGF in patients with bradycardia, of IL-9, IL-10, and IFN-gamma in patients with rash and of IL-10 and IL-12 in those with CRS was found (Figure 1).
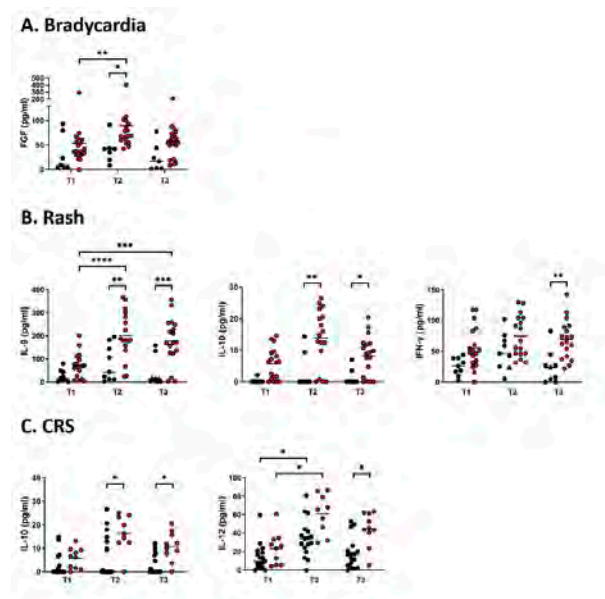
Figure 1: Red and black circles indicate patients with or without the IRAE, respectively. T1, T2, and T3 correspond to the first 3 days of AL infusion during the two courses. Asterisks indicate significance (* p<0.0001)

Conclusion: In our cohort, the increase of different cytokines was associated with different IRAEs during AL infusion. It will be worthy to expand our analysis to deepen the biological mechanisms underlying AL-related IRAEs.

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Neurogenetics, Neuroepidemiology, & Neurological manifestation of systemic diseases 2

EPR-260

Genetic leukoencephalopathies diagnosed in adulthood: clinical characterization of a tertiary center cohort

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Background and aims: Genetic leukoencephalopathies are a heterogeneous group of disorders primarily affecting white matter. In the era of gene therapies, its recognition/characterization gains greater relevance. Our objective was to characterize a cohort with definite/probable genetic leukoencephalopathy diagnosed in adulthood.
Methods: We identified all patients with a genetic test for leukoencephalopathies or with reference to white matter disease (WMD), from our database for genetic tests (period 2016–2020). Demographic, clinical, complementary investigation data were collected.
Results: The cohort was formed by 69 patients (58% females), 46.4% with pediatric-onset. In the pediatric-onset subgroup, the most frequent presentations were cognitive delay (62.5%) and movement disorders (37.5%); in the adult-onset subgroup it were cognitive deterioration (37.8%) and movement disorders (35.1%). The genetic strategy was as follows: 78.3% NGS panels, 13% Sanger sequencing, 7.2% biochemical studies, 1.5% array-CGH. A definite diagnosis was obtained in 46.9% of pediatric-onset and 24.3% of adult-onset cases. Pelizaeus-Merbacher disease and Aicardi-Goutières syndrome were exclusively diagnosed in pediatric-onset (20% each); HTRA1-related WMD in adult-onset (33.3%). Vanishing WMD (6.7% pediatric-onset, 22.2% adult-onset), and mitochondrial disease (13.3% pediatric, 11.1% adult-onset) were diagnosed in both subgroups. Average time from onset to diagnosis was 35.9 years (17–54) in pediatric-onset, and 9.6 years (2–19) in adult-onset subgroup.
Conclusion: The high prevalence of pediatric-onset forms reflects not only the epidemiology of genetic leukoencephalopathies but also the delayed diagnose until adulthood. Although the vast majority of patients has been studied through NGS, an elevated percentage remains without diagnosis. A WES/WGS approach would probably improve the diagnostic rate of these genetically heterogeneous disorders.
Disclosure: Nothing to disclose.

EPR-261

Loss of C-terminal Mediator Complex subunit-11 impairs brain development and causes severe progressive neurodegeneration

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Background and aims: The Mediator (MED) is an evolutionarily conserved multi-subunit protein complex that modulates the activity of several transcription factors as the activity of different critical components of the overall transcriptional machinery. Genetic defects of different MED subunits, such as MED17 or MED27 have been implicated in severe brain developmental disorders with microcephaly and neurodegeneration.

Methods: Exome or genome sequencing were performed in four unrelated families identified via different research networks and Matchmaker Exchanges. The functional impact of the candidate variant on both MED11 RNA and protein was assessed by RT-PCR and Western Blotting using fibroblast cell lines derived from patients and controls and by computational approaches.

Results: A recurrent, segregating homozygous variant in MED11 (c.325 C>T; p.Arg109Ter) was identified in all the affected children. The variant results in a premature stop codon and a putative protein lacking the last nine residues of MED11 C-terminal. The phenotype was characterized by congenital microcephaly, profound neurodevelopmental delay, exaggerated startle reaction since neonatal age, refractory myoclonic epilepsy and a diffuse and severely aggressive brain degeneration with premature death. Semi-quantitative RT-PCR and Western blot on patient-derived fibroblasts revealed levels of protein and transcript similar to healthy carriers and age- and sex-matched controls, suggesting the variant does not cause non-sense mediated decay (NMD) but instead disrupts the C-terminal domain of MED11.
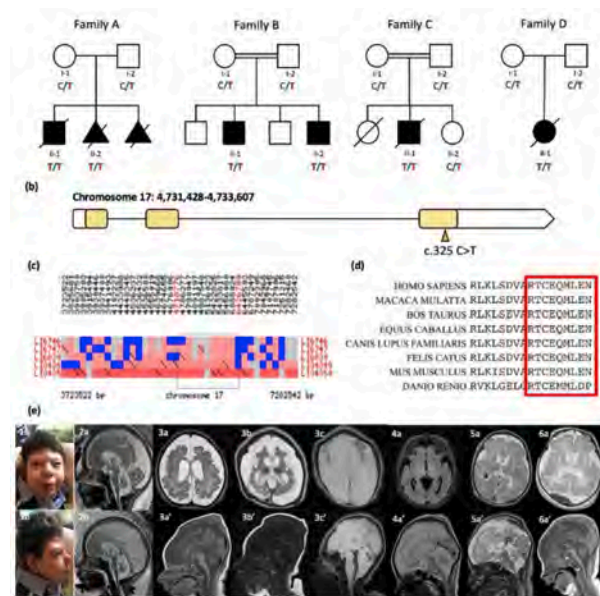
Figure 1: Clinical, genetic and neuroradiological features of the affected individuals.
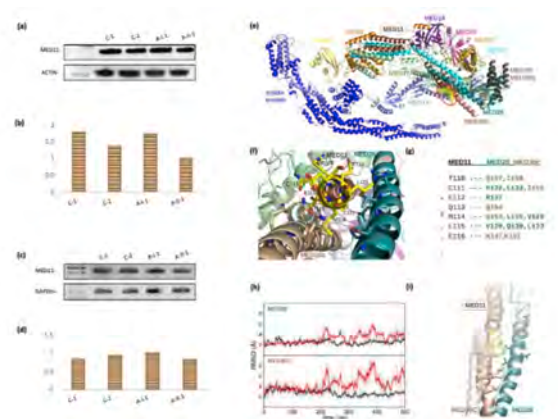
Figure 2: Cellular studies and computational analysis of the impact of the med11 C-terminal region.

Conclusion: Loss of the C-terminal of MED subunit 11 may affect its binding efficiency to other MED subunits, thus impacting the complex stability and function and leading to a rare and severe prenatal-onset developmental and degenerative neurological condition.

Disclosure: C.B. is employer of CENTOGENE. The remaining authors declare no competing interests.

EPR-262

Whole Exome Sequencing yield across heterogeneous neurologic phenotypes

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Background and aims: Next generation sequencing methodologies, including whole exome sequencing (WES), are becoming part of the clinical practice of neurology. Our aim here was to describe the use of WES for heterogeneous neurological phenotypes in a cohort of Greek patients.

Methods: In our study we included patients presenting with neurological phenotypes deemed of genetic origin. After obtaining informed consent, WES was performed on 238 patients (108 females, 130 males, median age 21 years, range 1–83 years). Sequencing was performed at either Otogenetics, Norcross, GA, USA or Macrogen, Seoul, Korea, using the Illumina HiSeq2000/25000 or the HiSeq4000 platform aiming at a >50x coverage. Variant annotation was performed in the Neurogenetics Laboratory, University of Crete, Greece, using the Ingenuity Clinical Insight (Qiagen, USA) software.

Results: The most common indications for ordering WES were muscle disorders (28.5%), epilepsy/epileptic encephalopathies (25.2%), developmental disorders (9.6%), motor neuron disease/spastic paraparesis (7.5%) and cerebellar ataxia (6.3%). The overall diagnostic rate of WES was 36.9% (causative genetic defects identified in 88 patients). Per diagnostic category, the diagnostic rate was: muscle disorders 45.6% (31/68), epileptic syndromes 28.3% (17/60), developmental disorders 39.1% (9/23), motor neuron disease/spastic paraparesis 44.4% (8/18), and cerebellar ataxia 26.7% (4/15).

Conclusion: In our cohort of patients with heterogeneous neurological phenotypes, WES showed high diagnostic efficiency across a wide age range. Our results offer support to the applicability of WES in clinical practice to end the diagnostic Odyssey of patients with heterogeneous neurogenetic disorders.

Disclosure: Nothing to disclose.

EPR-263

Genotype-Phenotype Correlations in Neurofibromatosis Type 1: identification of novel and recurrent NF1 gene variants

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Background and aims: Neurofibromatosis type 1 (NF1, OMIM #162200), is a complex tumor predisposition syndrome caused by loss of function mutations in the NF1 gene. To date, no clear genotype-phenotype correlation has been discerned in NF1. We aimed to study the genotype–phenotype correlations in a monocentric study cohort of adult NF1 patients.

Methods: Our series includes 85 familial/sporadic NF1 patients, enrolled at Division of Neurology, Neurofibromatosis and Rare Diseases Center of AOU Luigi Vanvitelli. The clinical data were collected at the time of mutation analysis and a combination of targeted next-generation sequencing and multiplex ligation-dependent probe amplification was performed for molecular analysis. Correlation study was performed using the Spearman rank correlation test; Odds ratio with 95% confidence intervals was estimated to evaluate prevalence of clinical features in the different mutation subtypes.

Results: We reported 66 different NF1 mutations, including 11 novel variants, distributed along the entire gene. The 94% of patients shown a more severe phenotype presenting at least one systemic complication. Spine deformities were the most common complications in our series. Odds ratio with 95% CI analysis revealed that the probability to have learning disabilities was higher in NF1 patients carrying frameshift mutations.

Conclusion: This study offered an important contribution to a better definition of genotype–phenotype correlation in the NF1 pathogenesis and may improve the management of NF1 patients.

Disclosure: The authors declare that the research was conduct in the absence of any commercial or financial relationship that could be construed as a potential conflict of interest.

EPR-264

Risk factors of post-stroke epilepsy in a prospective hospital-based study

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Background and aims: Stroke is a leading cause of acquired epilepsy in the elderly. About 10% of all strokes result in post-stroke epilepsy (PSE) within several years after the event. However, risk factors and mechanism of post-stroke epileptogenesis is still to be elucidated.

Methods: We performed a single-hospital prospective study of 424 post-stroke patients. Clinical and demographic data, data about pre-admission seizures were collected at admission; neurological state and seizures were observed dynamically during the hospital stay. Patients were followed for two years after discharge or until death. Data about seizures, neurological recovery and recurrent stroke during the follow up period was obtained by a neurologist.

Results: Acute symptomatic seizures within a week after the stroke occurred in 97 (23%) of patients. Post-stroke epilepsy was diagnosed in 30 patients with a cumulative risk of developing PSE within two years after stroke of 9.7% in Kaplan-Meier analysis. Presence of hemorrhage significantly increased risk for PSE (log-rank test, p=0.01). The neurological recovery was significantly delayed in patients who subsequently developed PSE (ANOVA rm, p=0.01). Watershed infarction (HR 2.2, 95% Confidence Interval (CI) 1.6–3.1, p<0.005) and increased activated thromboplastin time at admission (HR 1.02, CI 1.1–1.04, p=0.01) were independent risk factors for developing PSE in multivariate Cox regression.

Conclusion: Watershed stroke and increased activated thromboplastin time were identified as independent risk factors for PSE. Early post-stroke dynamic is revealed to be crucial for epileptogenesis and acute post-stroke complications may increase the risk for developing PSE.

Disclosure: Nothing to disclose.

EPR-265

Cytochrome oxidase activity in Wilson patients on decoppering therapy

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Background and aims: Wilson´s disease is caused by mutations in ATP7B, the hepatic copper transporter, which leads to copper deposition in several organs, particularly the liver and brain. Treatment involves the use of chelating agents to remove copper and thus achieve a negative copper balance. However, copper is an essential cofactor of many enzymes, including the mitochondrial enzyme cytochrome C oxidase (COX) and its overdepletion could potentially impair mitochondrial respiratory chain activity, which is likely a key component in the pathophysiology of the neurological damage associated with copper deficiency.

Methods: Plasma copper levels and platelet mitochondrial COX and complex II activities were measured in healthy controls and 36 patients with Wilson`s disease undergoing treatment with chelating agents. Hypocupraemic myeloneuropathy, the neurological manifestation of copper deficiency, was assessed clinically and by neurophysiological testing.

Results: Plasma copper levels in treated Wilson patients were on average only 30% of those in the control group. COX activities were significantly lower in platelets from the Wilson patients, whilst the activity of complex II, a copper-independent respiratory chain enzyme, was similar in controls and Wilson patients. No myeloneuropathies were found, even in patients with very low copper levels.

Conclusion: Decoppering therapy is difficult to control and frequently produces hypocupraemia in Wilson patients, which in turn significantly lowers the activities of mitochondrial cuproenzymes, particularly COX. Although several Wilson patients from our study had plasma copper levels in the same range as published patients with hypocupraemic myeloneuropathy, none of our patients showed evidence of neurological damage.

Disclosure: Nothing to disclose.

EPR-266

Mitochondrial DNA, optic neuropathy, and dystonia

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Background and aims: Mitochondrial DNA (mtDNA) point-mutations causing Leber Hereditary Optic Neuropathy (LHON) are usually described to only affect the optic nerves. Reports of LHON plus syndromes are uncommon and dystonia is exceedingly rare.

Methods: We review the clinical, radiological, muscle biopsy and molecular genetic data of three patients (two pedigrees) attending our centre. We have an extensive video collection documenting their semiology.

Results: Two siblings presented with early childhood onset of progressive generalised dystonia, including oromandibular involvement, and became wheelchair dependent since mid-teens. They do not have optic neuropathy. Investigations showed symmetrical lentiform nuclei necrosis on MRI head (see figure), elevated CSF lactate, and complex I deficiency on muscle biopsy. Their overall phenotype is consistent with Leigh-like syndrome. Our third patient presented with failure to thrive, developmental delay, optic atrophy, progressive generalised dystonia and requires gastrostomy feeding. His MRI head showed overall delayed myelination of cerebral hemispheres and hypoplastic cerebellar vermis at two years of age and he had elevated CSF lactate. Mitochondrial Complex I to IV showed low activity on muscle biopsy but this may be artefactual. Whole exome sequencing did not identify a cause. All patients have non-consanguineous parents and unremarkable family histories. Full mtDNA genome sequencing identified the m.11,778G>A, in MT-ND4 gene, affecting the mitochondrial complex I subunit, in all patients.

MRI head of siblings showing symmetrical lentiform nuclei lesions without other significant changes. Axial T2, T2-FLAIR and T2-GRE, coronal T1 and sagittal T2 (left to right). Top is proband at 21 years of age and bottom is her brother at 17 years of age.

Conclusion: Mitochondrial DNA diseases should be considered in cases of dystonia and have significant implications for genetic counselling of maternal relatives. Equally, "LHON" mutations should not be discarded based on a multisystemic phenotype or absence of optic neuropathy.

Disclosure: No conflicts of interest. The authors would like to raise that some details of the siblings have been included as part of the following publication by Prof McFarland, R., et al. (2007). "Homoplasmy, heteroplasmy, and mitochondrial dystonia." Neurology 69(9): 911–916. DOI: 10.1212/01.wnl.0000267843.10977.4a. However, we now have new imagery and an extensive video collection documenting their semiology which is novel and we believe to be a greater learning opportunity.

Neuroimmunology 3

EPR-267

Interleukin 6 SNP rs1818879 regulates radiological and in-flammatory activity in multiple sclerosis

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Background and aims: The clinical course of multiple sclerosis (MS) is critically influenced by interplay between in-flammatory cytokines. Interleukin 6 (IL-6) rs1818879 single-nucleotide polymorphisms (SNPs) has been reported as a factor capable of influencing clinical course of several inflammatory and infective diseases. However, the role of this polymorphism has never been evaluated in MS.

Methods: We explored in 205 MS patients at the time of diagnosis the associations between rs1818879 polymorphism, clinical characteristics, and the cerebrospinal fluid (CSF) levels of a large set of proinflammatory and anti-inflammatory molecules.

Results: Using principal component analysis and logistic regression analysis we identified an association between rs1818879, radiological activity and a combination of cytokines, including the Il-1, IL-9, IL-5, IL-10 and vascular endothelial growth factor (VEGF).

Conclusion: Our results suggest a possible association between rs1818879 polymorphism and inflammatory activity in MS.

Disclosure: I declare no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

EPR-268

Encephalitis with Autoantibodies against the Glutamate Kainate Receptor (GluK2)

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Background and aims: We report the identification of antibodies against the glutamate kainate receptor subunit 2 (GluK2-abs) in patients with autoimmune encephalitis and describe the clinical-immunological features and antibody effects.

Methods: Rat neuronal cultures were used to precipitate the antigen of two sera from 8 patients with similar brain immunohistochemistry staining. Samples from 596 patients with different neurological disorders and 23 healthy controls were screened by cell-based assay (CBA) with GluK2-expressing HEK293 cells. GluK2-ab effects were determined by confocal microscopy in cultured neurons and electrophysiology in GluK2-expressing HEK293 cells.

Results: Patients' antibodies precipitated GluK2. GluK2 antibody-specificity was confirmed by CBA, immunoprecipitation, GluK2-immunoabsorption, and GluK2 knockout brain immunohistochemistry. 2/8 samples showed reactivity with GluK1 or GluK3 subunits that was abrogated after GluK2 immunoabsorption. 6/8 patients developed acute encephalitis and clinical or MRI features of predominant cerebellar involvement (4 presenting as cerebellitis, which in 2 patients caused obstructive hydrocephalus), and 2 patients had other syndromes (1 with cerebellar symptoms). One of 8 samples showed mild reactivity with non-kainate glutamate receptors (AMPAR and NMDAR) leading to identify 6 additional patients with GluK2-abs among anti-AMPAR (5/71) or anti-NMDAR encephalitis (1/73) patients. Patients' antibodies internalized

GluK2-containing receptors in HEK293 cells and neurons; these effects were reversible in neurons. A significant reduction of GluK2-mediated currents was observed in cells treated with patients' GluK2 serum; these functional effects were not mediated by receptor blocking but by antibody-mediated receptor internalization.

Conclusion: GluK2-abs associate with an encephalitis with prominent clinic-radiological cerebellar involvement. The antibody effects are predominantly mediated by internalization of GluK2-containing receptors.

Disclosure: I have no disclosures to report.

EPR-269

Immune-related neurological disorders in patients with renal and bladder cancer

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Background and aims: Renal cell cancer (RCC) and bladder cancer (BC) are rarely linked to paraneoplastic neurological syndromes (PNS). Recently, there has been an increase in neurologic immune related adverse events (n-irAEs) secondary to immune checkpoint inhibitors (ICI), some of them resembling PNS. Our aim was to evaluate the potential paraneoplastic origin in a cohort of patients with RCC or BC and neurological symptoms.

Methods: Retrospective nationwide study of patients with RCC or BC and suspected PNS or n-irAEs and application of the updated PNS criteria.

Results: We identified a total of 18 patients with RCC (10/18) or BC (8/18) and suspected PNS between 2007–2021, and 17 patients with RCC (14/17) or BC (3/17) and n-irAEs after ICI between 2017–2021. Among patients with suspected PNS, there was a predominance of encephalitis in patients with RCC (6/10) and encephalomyelitis/sensory neuronopathy in patients with BC (3/8), followed by cerebellar ataxias in both (3/10 with RCC, 3/8 with BC). Within this group, only three cases scored for definite PNS, all with neuroendocrine BC and high-risk antibodies. Patients with n-irAEs presented with encephalitis (6/17), meningitis (1/17), cerebellitis (1/17), cranial neuropathy (2/17), peripheral neuropathy (3/17), myasthenia gravis (2/17), myositis (1/17), overlapped meningoencephalitis and neuropathy (1/17). None of them fulfilled critera for definite PNS (Figure).
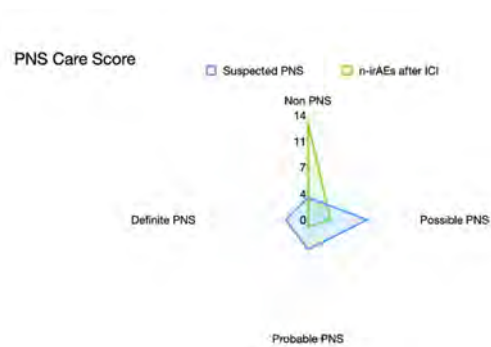
Figure: PNS Care Score applied to patients with RCC or BC and suspected PNS or n-irAE

Conclusion: PNS associated to RCC or BC are rare and the nature of neurological disorders linked to these cancers remains controversial. Even though n-irAEs after ICI are more commonly expected in these tumors, they do not probably respond to a paraneoplastic mechanism in most cases.

Disclosure: Macarena Villagrán-García received a fellowship grant from the Spanish Society of Neurology.

EPR-270

Prognostic relevance of quantitative and longitudinal MOG-Abs testing in patients with MOGAD

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Background and aims: MOG antibodies (MOG-Abs) associated disorders (MOGAD) are autoimmune conditionsat high risk of relapse. MOG-Abs testing has diagnostic implication, but the relevance of quantitative titration and longitudinal testing is debated. We aimed to define the prognostic relevance of MOG-Abs titres at onset and during follow-up.

Methods: Multicentric study including patients with MOGAD with at least one follow-up sample collected 3 months after disease onset. MOG-Abs were tested with a live cell-based assay with IgG1 confirmation and titred. The cut-off for positivity was 1:160.

Results: We analyzed 355 samples (16.9% from relapses and 83.1% from remission phases) from 102 patients with MOGAD, 56.9% of which were aged >16 years. A relapsing course was found in 44/102 patients(43.1%). Attack samples had higher titres (median: 1:1,280, range: 40–40,960) compared to remission (median: 1:640, range:0–81,920, p=0.001). Patients with relapsing vs monophasic disease courses had higher remission titres (median 1:640, range: 0–1:81,920; IQR: 1:160–1:5,120 vs median 1:480; range: 0–22,280, p=0.02), but comparable relapse titres. Paired onset and remission titres showed a significant trend towards reduction (p<0.001). Only 4/72 patients tested at 3–18 months since onset became negative, and none of them experienced relapses. Considering the first available remission sample for each patient, patients with remission titres ≥1:2,560 had more frequently a relapsing course (log rank, p<0.001). No differences were observed according to onset titres.

Conclusion: MOG-Abs titres correlate with disease phases. Longitudinal testing with titration could be useful to define the relapse risk.

Disclosure: Nothing to disclose.

EPR-271

Safety and humoral response to mRNA SARS-CoV-2 vaccines in autoimmune neurological disorders: the ANCOVAX study

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Background and aims: Assessing the safety of SARS-CoV-2 mRNA vaccines and the effect of immunotherapies on the seroconversion rate in patients with autoimmune neurological conditions (ANC) is relevant to clinical practice. Our aim was to assess the antibody response to and safety of SARS-CoV-2 mRNA vaccines in ANC.

Methods: This longitudinal study included ANC patients vaccinated with 2 doses of BNT162b2 or mRNA-1273 between March and August 2021. Side effects were assessed 2–10 days after each dose. Neurological status and anti-spike receptor binding domain antibody levels were evaluated before vaccination and 4 weeks after the second dose. Healthcare-workers served as controls for antibody levels.

Results: We included 300 ANC patients (median age 52, IQR 40–65), and 347 healthcare– workers (median age 45, IQR 34–54). mRNA–1273 vaccine was associated with an increased risk of both local (OR 2.52 95% CI 1.45–4.39, p=0.001) and systemic reactions (OR 2.51 95% CI 1.49–4.23, p=0.001). The incidence of relapse was not different before and after vaccine (Incidence rate ratio 0.72, 95% CI 0.29–1.83). Anti–SARS–CoV– 2 IgG were detected in 268 (89.9%) patients and in all controls (p<0.0001). BNT162b2 vaccine (OR 8.84 95% CI 2.32–33.65, p=0.001), anti-CD20 mAb (OR 0.004 95% CI 0.0007–0.026, p<0.0001) and fingolimod (OR 0.036 95% CI 0.002–0.628, p=0.023) were associated with an increased risk of not developing anti-SARS-CoV-2 IgG.

Conclusion: SARS-CoV-2 mRNA vaccines were safe in a large group of ANC patients. Anti-CD20 and fingolimod treatment, as well as vaccination with the BNT162b2 vaccine, led to a reduced humoral response. These findings could inform vaccine policies in ANC patients undergoing immunotherapy.

Disclosure: Nothing to disclose.

EPR-272

Clinical and immunological characterization of paraneoplastic neurological syndromes related to merkel cell carcinomas

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Background and aims: Merkel cell carcinomas (MCC) are rare neuroendocrine malignancies with a high immunogenic background that may contribute to the immune tolerance breakdown that defines paraneoplastic neurological syndromes (PNS). However, the clinical and paraclinical features of MCC-related PNS have been poorly defined.

Methods: Retrospective analysis of patients with suspected MCC-related PNS and systematic review of the literature.

Results: 14 patients were identified in our center, and 41 in the systematic review, for an overall cohort of 55 patients. The median age was 68 years (range 41–90), and 35/54 (64%) were men. Lambert-Eaton myasthenic syndrome (LEMS), paraneoplastic cerebellar degeneration (PCD), encephalitis, and other neuromuscular disorders were observed in a similar proportion. The median PNS-Care Score was 7 (range 1–10), although lower scores were found among patients with neuromuscular disorders. Fourteen patients (25%) had neurological immune-related adverse events (NirAE) after immune checkpoint-inhibitors (ICI). At PNS onset, 1/46 (2%) patient had a localized MCC, while 24/46 (52%) had lymph node involvement with spontaneous primary tumor regression, predominantly in patients with LEMS (9/14, 64%). Regarding the immunological profile, 38/51 (74%) of the patients had neural antibodies (Abs): 12/38 (31%) had high-risk Abs, while 16/38 (42%) had intermediate-risk Abs.

Conclusion: LEMS, PCD, and encephalitis in the context of MCC are likely paraneoplastic, while this causal association is variable for neuromuscular disorders. Furthermore, NirAE after ICI for MCC may have in some cases PNS-like pathogenesis due to the frequent identification of classic paraneoplastic clinical phenotypes and neural Abs.

Disclosure: Nothing to disclose.

EPR-273

Clinical and radiological correlates of apathy in Multiple Sclerosis

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Background and aims: Apathy has been recognized as a frequent behavioral symptom in patients with multiple sclerosis (pMS) but their clinical and MRI correlates have been poorly investigated and resulted the aim of our study.

Methods: 123 pMS (mean age 40.25±11.5; female 60.9%; RRMS 75.6%) were prospectively enrolled and underwent examination with Expanded Disability Status Scale (EDSS), Apathy Evaluation Scale (AES), Hospital Anxiety and Depression Scale (HADS-A and HADS-D), Brief International Cognitive Assessment for MS (BICAMS), MS Neuropsychological Screening Questionnaire Self Report Form (MSNQ-S) and brain MRI at 3T. Total brain and grey matter (GM) volumes were obtained using SIENAX and Freesurfer parcellation software. Diffusion Tensor Imaging (DTI) and Spherical Mean Techinque (SMT) metrics were extracted from GM structures and White matter (WM) tracts.

Results: Apathetic pMS (40, 32,5%), in comparison with non-apathetic pMS, showed lower education level (p=<0,001), higher EDSS (p=0.05), HADS-D (p=<0.001) and HADS-A scores (p=0.025), and worse MSNQ-p score (p=<0,001). The two groups were not different in normalized brain, GM and WM volumes. However, occipital lobe (p=0,002), pericalcarine (p=0,006), lingual (p=0,002), lateroccipital (p=0,023) and cuneus cortices (p=0,019) resulted more atrophic. We identified significant microstructural differences in several DTI and SMT parameters of frontal, cingolate and parietal lobes and their sub-areas as well as of right cingulate, inferior longitudinal (IFL), inferior fronto-occipital (IFOF) and left superior longitudinal (SLF-III) fascicles (p range 0,013–0,05).

Microstructural abnormal brain areas betweem apathetic and non-apathetic pMS in our cohort
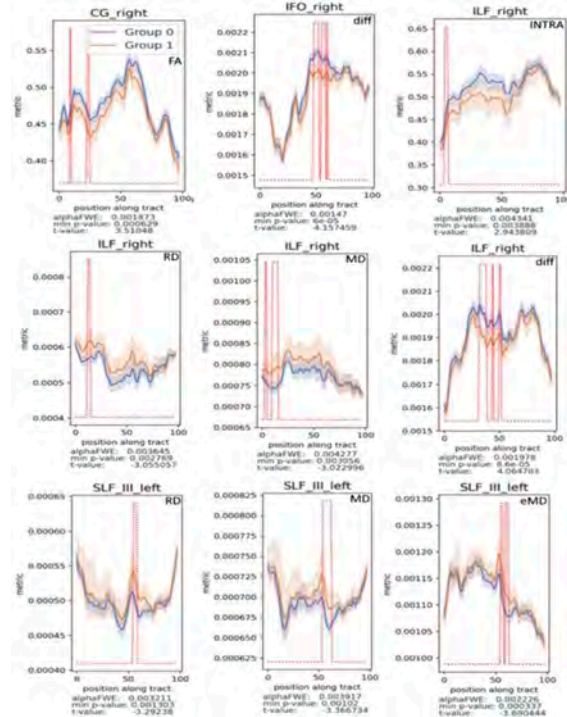
Significant microstructural abnormal parameters of white matter tracts comparing apathetic and non-apathetic pMS in our cohort

Conclusion: Our results suggest that posterior brain atrophy and microstructural changes in anterior cortex and in several WM tracts seem to play a relevant role in explaining apathy in MS.

Disclosure: Nothing to disclose.

Neuro-oncology, Neuroimaging, & Clinical neurophysiology 2

EPR-274

MRI biomarkers for disease progression in SMA

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Background and aims: This study assesses the utility of a multiparametric magnetic resonance imaging (MRI) protocol, including water T2 mapping, Dixon based Proton Density Fat Fraction (PDFF) estimation, and diffusion tensor imaging (DTI), for detecting loss of spinal motor neurons and subsequent damage in adult SMA patients to optimise disease monitoring.

Methods: 16 patients (mean age 39.6±2.8 years, six females, ten males) and 13 age-matched controls (mean age 49.4±3.7 years, four females, nine males) underwent MRI imaging, including measurements of Dixon based PDFF and muscle water T2 (T2w) of the biceps femoris (BFM) and quadriceps femoris muscle (QFM) and diffusion tensor imaging of the sciatic nerve. Participants returned for a second scan 6 months later. MRI parameters were correlated with clinical data.

Results: We found significantly higher intramuscular fat fractions in thigh muscles, the BFM and QFM, of SMA patients, compared to healthy controls, at baseline and after six months. Additionally, T2 values significantly correlated positively with intramuscular PDFF ($p<0.05$). Hammersmith functional motor scale significantly correlated with the intramuscular PDFF of QFM. No significant differences in the DTI scans of the sciatic nerve were seen between the two groups.

Conclusion: This study demonstrates that the suggested multiparametric MRI protocol including water T2 mapping and Dixon based PDFF distinguishes between adult SMA patients and controls due to massive intramuscular fat accumulation in SMA. Further long-term studies are warranted to evaluate Dixon based PDFF and water T2 mapping as surrogate markers in SMA patients during treatment.

Disclosure: This study was funded by Biogen.

EPR-275

Holmes-Adie syndrome associated to anti-Hu antibodies, a key finding for the diagnosis of lung carcinoma. A case report.

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Background and aims: Adie's pupil is an infrequent neuro-ophthalmological disorder caused by parasympathetic denervation, usually idiopathic and benign. It has also been described in paraneoplastic syndromes (PNS), especially when associated with areflexia, conforming the so-called Holmes-Adie syndrome (HAS).

Methods: We present a patient diagnosed with lung carcinoma during the study of HAS.

Results: A 78-year-old female without relevant clinical history is hospitalized due to intestinal occlusion (post-surgical adhesions), when anisocoria is detected. We observed left mydriasis, slowly reactive to light, preserved accommodation, achieving constriction with pilocarpine 0.1%, suggesting Adie's pupil (Figure 1, 2). Also, generalized areflexia stands out. The patient referred progressive 6-month evolution of distal sensory deficit involving all limbs. CSF-study showed slight hyperproteinorraquia. Blood analysis (autoimmune, endocrinological profile) and brain-MRI found non-significant alterations. EMG was compatible with axonal, sensory-motor, severe polyradiculoneuropathy (Figure-3). Given HAS suspicion (Adie's pupil and areflexia, probably related to the polyradiculoneuropathy), requested onconeural study was positive for anti-Hu antibodies. Hypothesising a PNS, thoracic-abdominal CT-scan was performed showing a pulmonary nodule, with pathological result of small-cell lung carcinoma. Final diagnostic judgement was HAS, probable paraneoplastic aetiology.
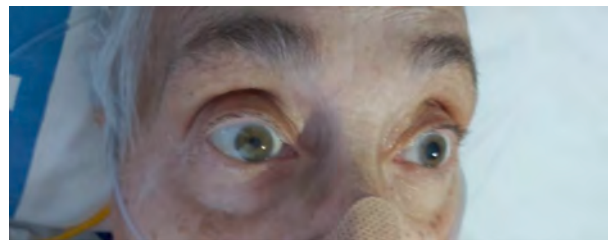
Figure 1: Left Left mydriasis slowly reactive to light stimulation, accommodation preserved.

Figure 2: After administration of pilocarpine 0.1%, a greater left pupillary contraction is observed compared to the contralateral one, findings suggestive of Adie's pupil.

Table 1: On EMG, neurography shows findings suggestive of severe sensory-motor demyelinating polyradiculoneuropathy

Conclusion: Anti-Hu antibodies are frequently associated with small-cell lung carcinoma (among other neoplasms), usually manifested as PNS, especially sensory neuronopathy. HAS is a rare manifestation of anti-Hu antibodies, described only in few case-reports. As in our case, it might be the first manifestation of an underlying neoplasm, presenting a diagnostic challenge. When finding of Adie's pupil, an extensive physical examination should be performed, paying special attention to signs suggesting polyneuropathy, emphasizing the study of onconeural antibodies/underlying neoplasm when found.

Disclosure: Nothing to disclose.

EPR-276

Improved suvr calculation for [18f]-AV45 amyloid pet imaging using a novel reference region approach

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Background and aims: Utilization of a data-driven approach to find an optimal reference region for [18F]-AV45 PET imaging that differentiates the spectrum of Alzheimer's disease (AD) in both cross-sectional and longitudinal study designs.

Methods: Data of 283 participants (135 amyloid-negative cognitively normal (CN), and 148 amyloid-positive AD) from the ADNI database (http://adni.loni.usc.edu/) was used. All [18F]-AV45 scans were co-registered, normalized, and skull-stripped. The dataset was split into a training-and test-dataset. Voxel-wise group comparisons were performed in the training-set (75 CNs, 77 ADs) to identify a reference region that is void off on-target tracer uptake. Potential clusters were used to extract mean global SUVRs in the test-dataset (60 CNs, 70 ADs). Effect sizes between novel clusters and commonly used reference regions were compared. Baseline and follow-up data of 19 CNs, 36 participants with mild cognitive impairment, and 24 ADs was used to test whether the newly identified cluster is more sensitive to assess longitudinal change than common reference regions. Effect sizes of change in SUVR between baseline and follow-up were used as metric of sensitivity.

Results: The training dataset yielded two novel clusters in the brainstem and the cerebellar white matter. These new reference regions showed higher effect sizes compared with commonly used reference regions. Significant differences in the effect sizes were observed when examining longitudinal change in SUVR computation compared with previously used reference regions.

Conclusion: The data-driven approach using cross-sectional and longitudinal study designs improved SUVR measurements for [18]-AV45 imaging. Additionally, longitudinal SUVR quantification benefited from this method, with implications for clinical trial designs.

Disclosure: Nothing to disclose.

EPR-277

Magnetic resonance imaging of the spinal cord provides a marker of the rate of progression in ALS patients

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Background and aims: Amyotrophic lateral sclerosis (ALS) is a progressive motor neuron disorder. Neuroimaging seems to be a reliable potential biomarker, not only for better diagnosis but also to provide a reliable assessment of disease progression. Therefore, the aim of this study is to measure the change of spinal cord MRI metrics over time based on a prospective, longitudinal, multipoint study.

Methods: We included 40 ALS patients who underwent a structural and diffusion MRI. MRI scans were acquired on a 3T Siemens scanner, and clinical variables were collected over three-time points. Spinal cord toolbox (SCT) was used to treat the structural and diffusion images to compute cross-sectional area (CSA) per-level and DTI parameters at the LCSTs and the DCs at the cervical level. Clinical and demographic data were evaluated for correlations with cervical spinal cord damage parameters.

Figure: Region of interest (ROI) definition and the multiparametric MRI analysis.

Results: At the inclusion timepoint, MRI damage parameters, including CSA per-level and the DTI parameters at the lateral corticospinal tract and posterior dorsal columns at the cervical level, showed significant differences within the cohorts when we divided them regarding age at onset and site of onset. A significant difference in the MRI damage parameters was found within subgroups regarding the rate of progression as measured by the ALSFRS.

Conclusion: This study demonstrates different scales of damage, indicated by the damage parameters at the MRI, in ALS patients based on the site of onset and the age at onset. And there was a tendency to show more prominent differences with the use of DTI damage parameters.

Disclosure: Nothing to disclose.

EPR-278

Impact of cancer type on the temporal association with ischemic stroke

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Background and aims: Cancer and acute ischemic stroke (AIS) are common causes of death worldwide. We studied the temporal association with stroke of different types of cancer.

Methods: Longitudinal retrospective study of the acute revascularization registry of AIS (May 2009 to December 2019) at a Comprehensive Stroke Center. Patients were followed until death or December 2021. Cancer diagnoses were obtained from patients' medical records. Active cancer was defined as new cancer diagnosis or metastasis or recurrence of known cancer within 12 months before or after the index stroke.

Results: Cancer was diagnosed in 169 (16%) of 1,059 AIS patients. Mean follow-up time was 6.8 (2–12) years. The prevalence of each cancer at any time (Figure 1) and within the active group were, respectively: colorectal (18% and 15%), prostate (16% and 13%), breast (15% and only 7%), bladder (10% and 11%), lung (5.9% and 13%), and pancreas (3% and 5.6%). Lung, bladder, and pancreas were more common in the active group and alongside kidney, all had a median distribution of stroke nested around a new cancer diagnosis (Figure 2) with the opposite being true for breast cancer. The proportion of strokes with undetermined etiology was also related to the interval to cancer diagnosis, with the greatest percentage in those diagnosed within 5y after the index stroke (Figure 3).
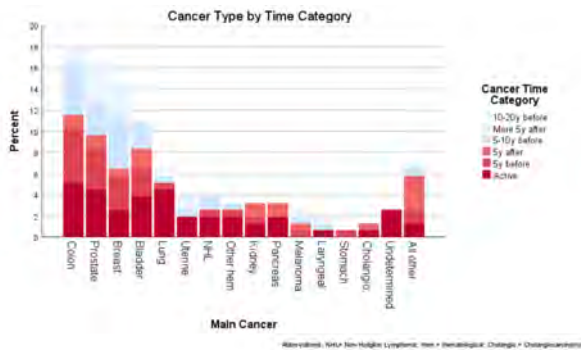
Figure 1
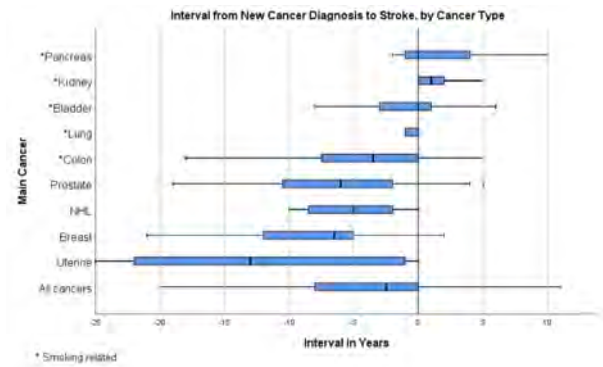
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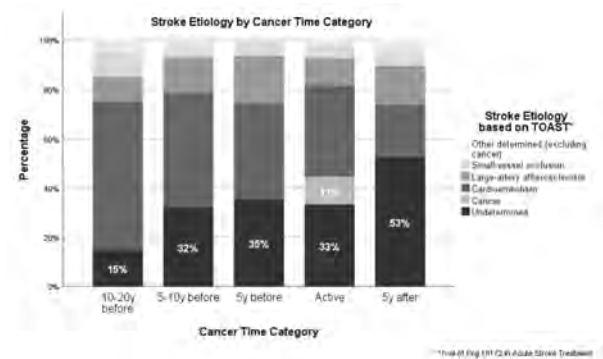
Figure 3

Conclusion: Stroke is mostly associated with uncontrolled cancer. Smoking-related cancers were more frequent in the active group suggesting greater prothrombotic tendency. Occult cancer may be involved in a significant proportion of AIS with undetermined etiology.

Disclosure: The authors have no financial disclosures or conflicts of interest.

EPR-279

Pretreatment Peripheral Immune Cell Ratios as Prognostic Biomarkers in Glioma Patients

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Background and aims: In the glioma microenvironment, elevated immune cell ratios are posited to reflect systemic response to malignancy. Given the dearth in clinically significant molecular markers to predict prognosis, there is potential for immune cell ratios to serve as low-cost and readily available prognostic markers. This study evaluated the ability for pretreatment peripheral immune cell ratios (Neutrophil-to-Lymphocyte Ratio, NLR, and Monocyte-to-Lymphocyte Ratio, MLR) to predict overall survival (OS) and modified Rankin Scale (mRS) at admission, 6 months and 12 months post-diagnosis. It also explored relationships between immune cell ratios and clinicopathological parameters (tumour location, tumour size, tumour grade, IDH-1 mutation, MGMT promoter methylation status).

Methods: Pretreatment NLR and MLR were analysed retrospectively in 64 glioma patients from Royal Melbourne Hospital. OS was evaluated with the Kaplan-Meier method. Prognostic factors for OS and mRS were evaluated with univariate and multivariable regression analyses.

Results: Higher pretreatment NLR (>4.7), compared to lower pretreatment NLR (≤4.7), predicted higher mean admission mRS (p<0.001) and 6-month mRS (p=0.02). Higher NLR was associated with poor functional outcome (mRS 3–6) at admission (p<0.001) and 6 months (p=0.001). Higher pretreatment MLR (>0.35) predicted poorer OS (p=0.02). Higher NLR was associated with larger tumour diameter (≥5cm) (p=0.02).

Fig. 1. Kaplan-Meier OS analysis of pretreatment MLR. Abbreviations: OS, overall survival; MLR, monocyte-to-lymphocyte ratio

Table 1. Association between pretreatment NLR and mRS

	All cases		≤4.7		>4.7		p
	Mean ± SD	Range	Mean ± SD	Range	Mean ± SD	Range	
mRS at admission	2.73 ± 0.98	1-5	2.40 ± 0.78	1-4	3.31 ± 1.03	1-5	<0.001
mRS at 6 months	2.87 ± 1.98	0-6	2.44 ± 1.94	0-6	3.6 ± 1.88	1-6	0.02
mRS at 12 months	3.74 ± 2.16	0-6	3.45 ± 2.20	0-6	4.11 ± 2.08	1-6	0.31

Abbreviations: NLR, neutrophil-to-lymphocyte ratio; MLR, monocyte-to-lymphocyte ratio; mRS, modified Rankin Scale; SD, standard deviation

Conclusion: To our knowledge, this was the first study to evaluate the association between immune cell ratios and mRS. This study demonstrated that NLR and MLR can serve as prognostic markers to predict functional outcomes and OS in glioma patients, which allows us to identify high-risk patients in need of further treatment.

Disclosure: No potential competing interest was reported by the authors.

EPR-280

Association of Atrial Fibrillation with Outcomes in Stroke Patients receiving Intravenous Thrombolysis: A Meta-Analysis

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Background and aims: Atrial fibrillation (AF) is the most common arrhythmia and one of the leading causes of ischemic stroke. Previous studies have indicated that stroke patients with AF have a worse neurological outcome profile than stroke patients without AF. This meta-analysis studied the impact of AF on clinical and safety outcomes in acute stroke patients treated with intravenous thrombolysis (IVT).

Methods: A random-effects meta-analysis was undertaken to estimate the association of AF with outcomes after acute ischemic stroke, namely functional outcome & mortality at 90 days, post-IVT angiographic reperfusion, symptomatic intracerebral hemorrhage (sICH), hemorrhagic transformation (HT), and onset to reperfusion therapy time (OTRT). Studies involving AIS patients treated with IVT, and relevant outcomes data grouped by AF and no-AF were included.

Results: This meta-analysis included 16 studies with a total cohort of 11,070 AIS patients who underwent IVT. AF was significantly associated with worse 90-day functional outcomes (OR 0.50, 95% CI 0.39–0.63; $p<0.0001$), increased mortality (OR 2.13, 95% CI 1.44–3.14; $p<0.0001$), increased rates of sICH (OR 2.03, 95% CI 1.61–2.56; $p\leq0.0001$) and ICH of any cause (OR 2.98, 95% CI 1.06–8.40; $p<0.0001$). Notably, no significant difference in OTRT was observed between AF and no-AF groups.

Conclusion: This meta-analysis demonstrated, in AIS patients undergoing IVT, AF is linked with markedly poorer clinical and safety profile after treatment.

Disclosure: Nothing to disclose.

Neuro-ophthalmology/ neuro-otology & Coma and chronic disorders of consciousness

EPR-281

BEEGO: a Rasch-built scale for visual analysis of clinical EEG in the diagnostic evaluation of disorder of consciousness

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Background and aims: Visual analysis of clinical standard EEG in patients with disorders of consciousness (DoC) has recently been recognized by the European and American Academy of Neurology as an important diagnostic tool for distinguishing between vegetative state (VS) and minimally conscious state (MCS). Although conventional EEG assessment is strongly recommended in current guidelines, available EEG scales for DoC were never validated. Here, using Rasch Analysis we aimed at developing and validating a novel scale (BEEGO, Background EEG Organization) for the analysis of wakeful EEG in DoC based on the American Clinical Neurophysiology Society (ACNS) Standardized Critical Care Terminology.

Methods: We enrolled 175 brain-injured patients with a prolonged or chronic DoC in rehabilitation settings. Clinical variables were collected and EEG were analyzed according to the standardized ACNS descriptors of EEG background by two independent trained neurophysiologists. Rasch methodology was used to develop the BEEGO scale and to explore the extent to which BEEGO's items met Rasch-based criteria of successful measurement of wakeful EEG activity.

Results: By applying Rasch analysis, we were able to identify and validate the set of 5 descriptors of ACNS Critical Care terminology that best measured the level of physiological arousal as expressed by wakeful EEG activity. Rasch analysis indicated that the BEEGO scale successfully measured the latent variable and thus the degree of recovery of thalamo-cortical activity in DoC patients.

Conclusion: The Rasch-based approach allowed us to develop a linearly-weighted scale which may be included in a diagnostic work-flow to complement conventional and advanced neurophysiological assessment in DoC.

Disclosure: This work was supported by ERA PerMed JTC2019 "PerBrain".

EPR-282

Coma Recovery Scale-Revised sub-scores improve prognostic accuracy in prolonged Disorders of Consciousness

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Background and aims: The Coma Recovery Scale-Revised (CRS-R) is the most sensitive and validated clinical tool for an accurate diagnosis of patients with prolonged disorders of consciousness (pDoC: unresponsive wakefulness syndrome, UWS, and minimally conscious state, MCS). The CRS-R is composed by six sub-scales that are evaluated independently from each other for diagnostic purposes, but its total score, together with clinical diagnosis, can help to predict recovery of consciousness. Here we investigated whether a novel index, based on the scores of the single CRS-R sub-scales, could have a prognostic value higher than that provided by clinical diagnosis at admission (CDA).

Methods: 190 patients with pDoC (130 males; median age=58.5 years [IQR=21.6]; time post-onset=1–6 months; VS/UWS=93, MCS=97) were enrolled in 23 Italian intensive neurorehabilitation units. Patients' clinical diagnosis and CRS-R were collected at admission and 6 months after the injury. Via unsupervised machine learning approach, patients were divided into two clusters based on their CRS-R sub-scores. The prognostic value of this Consciousness-Domains Index (CDI) was evaluated.

Results: At the six-month follow-up, 86 (45.3%) patients recovered full consciousness. The visual, motor and auditory CRS-R sub-scales were found to be the most strongly associated with good outcome. For 11/190 patients (5.8%), the CDI showed higher prediction accuracy with respect to clinical diagnosis at admission, resulting in an improved classification accuracy (CDI=77.9% vs. CDA=74.2%; p<.001).

Conclusion: These findings suggest that single CRS-R sub-scales should be considered also for prognostication in patients with pDoC. The data-driven CDI presented here could help clinicians in prognostication and guide caregiver in decision-making.

Disclosure: No conflict of interests to be declared.

EPR-283

Self-rating of caloric-induced vestibular perception in common vestibular disorders

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Background and aims: Vestibular perception depends both on the intensity of the vestibular stimulus coded by inner ear sensors, and cognitive and emotional post-processing in higher vestibular networks. Clinical experience suggests differences in vestibular perception between common vestibular disorders. However, easy tools for its assessment and quantification are missing.

Methods: In this prospective study, 828 consecutive patients were recruited at the German Center for Vertigo and Balance Disorders (LMU Munich). All patients underwent routine caloric testing with warm (44°) and cold (30°) water for both ears. Slow phase velocity (SPV) of caloric-induced nystagmus was documented, respectively. Subjectively perceived vertigo sensation was rated by a numeric rating scale (NRS, 1–10), after each testing condition and in total. Mean NRS values and ratios of NRS per caloric-induced SPV were calculated for patient subgroups with different vestibular disorders (defined by established diagnostic classification criteria).

Results: NRS showed a good correlation with the mean caloric-induced SPV across all patients. Patients with functional dizziness and vestibular migraine had the highest mean NRS values (7.1 both groups), while patients with bilateral vestibulopathy had the lowest (2.7). A NRS-threshold of ≥ 7 had a ROC-AUC of 0.67 for functional dizziness, a NRS-threshold of ≤ 4 a ROC-AUC of 0.77 for bilateral vestibulopathy. Ratios of NRS per mean caloric-induced SPV were highest for patients with bilateral and unilateral vestibulopathy.

Conclusion: Subjective rating of vertigo sensation induced by a standardized caloric stimulus is a clinically suitable tool to quantify vestibular perception, which can support differential diagnosis in common vestibular disorders.

Disclosure: Nothing to disclose.

EPR-284

Sector-to-Channel Correlation of mfVEP and OCT: a Potential Method to Screen Inflammatory Neurodegeneration Drugs for MS

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Background and aims: Smoldering inflammation is a major factor of the accumulated neurodegeneration and disability in the progressive phase of multiple sclerosis(MS). Advances in neuro-ophthalmology suggest that neuronal/dendritic loss can be measured as atrophy of ganglion cell layer/inner plexiform layer (GCIPL) under optical coherence tomography (OCT), while inflammation/demyelination as prolonged latency in multi-focal visual evoked potential (mfVEP). Together with voxel-based morphometry (VBM), the GCIPL map can be divided into sectors corresponding to the mfVEP channels based on their topological relationship and perform sector-to-channel correlations, which enables detailed investigations of the interaction.

Methods: 32 newly diagnosed progressive patients were enrolled(16 primary-PPMS and 16 secondary-SPMS). OCT Macula volume scans were scanned and mfVEPs were recorded. The GCIPL maps were divided into sectors that correspond to the channels of the mfVEP topologically. Sector-to-channel correlations were performed between the GCIPL thickness calculated from OCT and the mfVEP parameters (amplitude and latency).
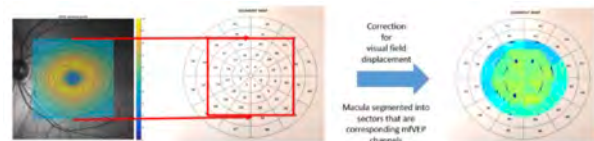
Sector-to-channel correlation between OCT and mfVEP

Results: The amplitude of the PPMS group was positively correlated with the GCIPL thickness in sectors located in the central and nasal macula. On the other hand, the latencies in both PPMS and SPMS groups were negatively correlated with the GCIPL thickness, in both central and peripheral sectors.

Sector-to-channel correlation results of PPMS and SPMS. Positive correlations betweem mfVEP amplitude and GCIPL thickness was found in PPMS group, while both groups showed negative correlations between mfVEP latency and the GCIPL thickness

Conclusion: Our results showed that even in progressive MS that without acute inflammatory attack, longer latency of VEP was still found, implying smoldering neuroinflammation. The delayed VEPs negatively correlated with the neuronal/dendritic loss, suggesting the inflammation leads to neurodegeneration. The sector-to-channel correlation can be used to monitor inflammatory neurodegeneration in vivo and to screen for potential drugs targeting this aspect.

Disclosure: The author has nothing to disclose.

EPR-285
Apraclonidine, an eye opener

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Background and aims: Pharmacological testing with apraclonidine eye drops aids the diagnosis of Horner syndrome by inducing a typical reversal of anisocoria. We investigated the effect of apraclonidine on eyelid position in patients with Horner syndrome compared to physiological anisocoria based on infrared video recordings.

Methods: 37 adult patients underwent binocular pupillometry before and after instillation of 1% apraclonidine eye drops for evaluation of anisocoria. The test paradigm consisted of 4 cycles of 5 seconds light-on and 15 seconds light-off. A positive apraclonidine test indicating Horner syndrome was defined by enlargement of the smaller pupil and (slight) constriction of the larger pupil after 30 minutes. To measure the palpebral aperture, custom-made software was used to analyze the infrared images recorded during pupillometry (Fig. 1). The mean was calculated from 3–4 measurements taken from individual cycles within 5 seconds after light-off by setting a vertical line centered at the pupil from the upper to the lower eyelid margin.
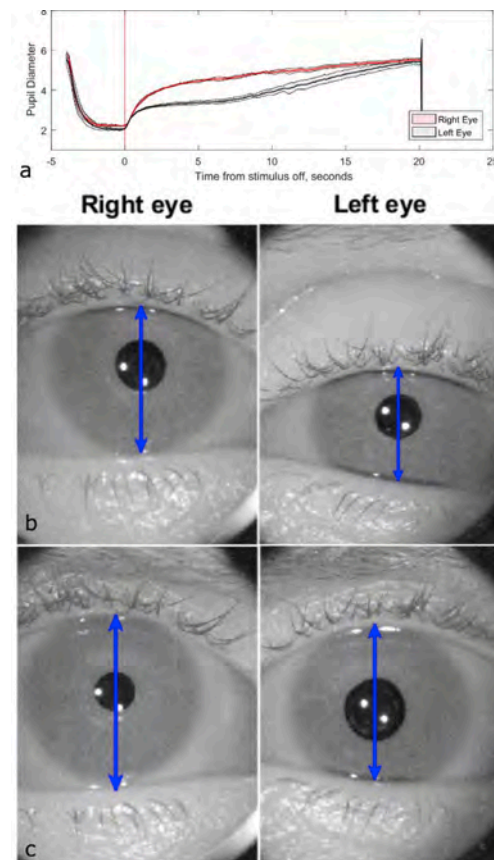
Figure 1: a)Pupillometry confirming left Horner syndrome. b) Ptosis and miosis on affected left side. c) Reversal of anisocoria and resolution of ptosis 30 minutes after apraclonidine 1% eye drops..

Results: The baseline inter-eye difference of eyelid opening was 0.98±0.88mm in Horner syndrome (21 patients) and 0.11±0.81mm in physiological anisocoria (16 patients). Following apraclonidine application, the inter-eye difference decreased significantly in Horner syndrome to 0.28±1.07mm (p<0.005) and remained similar in physiological anisocoria (-0.01±0.83mm, p=0.40).

Conclusion: The eyelid elevating effect of apraclonidine eye drops was significantly more pronounced in eyes with a sympathetic denervation deficit compared to eyes with physiological anisocoria. Measuring the eyelid opening may therefore enhance the diagnostic accuracy of apraclonidine testing combined with pupillometry to differentiate Horner syndrome from physiological anisocoria.

Disclosure: Fabienne C. Fierz has received the career development grant Filling the Gap 2020-2021 from the University of Zurich, Switzerland.

EPR-286

Benign Paroxysmal Positional Vertigo: Comparision of the "SémontPLUS Maneuver" with the Epley Maneuver – an RCT

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Background and aims: In a previous study we demonstrated that the SemontPLUS Maneuver (SM+) is superior to the regular SM. In the current study we compared the efficacy of the new SM+ with the Epley maneuver in patients with posterior canal BPPV (pcBPPV).

Methods: In a prospective multinational (Germany, Italy, Belgium) RCT, patients with pcBPPV were randomly assigned (1:1) to "SM+" or Epley treatment. The SM+ is characterized by an overextension of the head/body by at least 60° below earth horizontal line during step 2 of the maneuver. Each morning after the first maneuver of each day the patient documented in a standardized evaluation sheet whether vertigo occurred. The primary endpoint was: "How long (in days) does it take until no attacks can be induced "in the morning" by the maneuvers?"

Results: In the 142 patients so far analysed (interim analysis), it took a mean of 3.55 days (range 1–20 days) and a median 1 day for the Epley maneuver; for the SM+ it took a mean 2.06 days (range 1–8 days) and a median 1 day for recovery. Statistical analysis with the two-sided Mann-Whitney-u-test revealed a p-value of 0.06.

Conclusion: This interim analysis suggests that the SémontPLUS maneuver is evidently superior to the Epley maneuver in terms of the time it takes until recovery. Final statistical inference will be drawn, once the planned number of patients are recruited and analysed.

Disclosure: M. Strupp is Joint Chief Editor of the Journal of Neurology, Editor in Chief of Frontiers of Neuro-otology and Section Editor of F1000. He has received speaker's honoraria from Abbott, Auris Medical, Biogen, Eisai, Grünenthal, GSK, Henning Pharma, Interacoustics, J&J, MSD, NeuroUpdate, Otometrics, Pierre-Fabre, TEVA, UCB, and Viatris. He receives support for clinical studies from Decibel, U.S.A., Cure within Reach, U.S.A. and Heel, Germany. He distributes "M-glasses" and "Positional vertigo App". He acts as a consultant for Abbott, AurisMedical, Heel, IntraBio and Sensorion.

EPR-287

The use of optical coherence tomography (OCT) in retrochiasmal lesions.

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Background and aims: Trans-synaptic degeneration (TD) may present as thinning of the peripapillary retinal nerve fiber layer and/or the ganglion cell-inner plexiform layer (GCL-IPL) in optical coherence tomography (OCT). We aimed to analyse OCT sensitivity in patients with retrochiasmal lesions.

Methods: Retrospective analysis of patients referred to our clinic with retrochiasmal tumor or stroke who had a complete neuro-ophthalmologic, perimetric, and OCT assessment. Patients with unrelated ophthalmological disease were excluded. We collected demographic, clinical and visual data. OCT was considered abnormal if any of the following criteria were met in at least one eye: presence of visible thinning in at least one sextant based on color-coded thickness maps (visible thinning, VT); normalized asymmetry score (NAS) ratio between temporal and nasal GCL-IPL thickness >0.092 (2SD, 16 healthy controls); Subjective visual analysis of color-coded thickness maps (SUBJ).

Results: We included 25 patients, mean age of 57.6 ± 16.5 years old, 36% (n=9) were females. Perimetry showed homonymous defects in all patients. Up to 80% (n=20) of patients showed an abnormal OCT. Depending on VT, NAS, or SUBJ criteria, the OCT was considered abnormal in 11 (44%), 11 (44%), and 16 (64%) of patients, respectively. An abnormal SUBJ was associated with longer disease duration. SUBJ was the best method to detect OCT-related TD (area under the curve, 0.889 [95% CI, 0.756–1,000]).

Conclusion: OCT was able to detect TD following a retrochiasmal lesion in the majority of patients, particularly when using SUBJ. Disease duration is crucial for OCT-related TD to develop.

Disclosure: Nothing to disclose.

ePosters

Saturday, June 25 2022
Ageing and dementia 1

EPO-001

Default-Mode Network in Corticobasal Syndrome

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Background and aims: Default-mode network (DMN) plays an important role in the pathogenesis of neurodegenerative disorders, but its activity remains underevaluated in corticobasal syndrome (CBS) with only few studies conducted to date. We used resting-state fMRI to assess DMN changes in CBS and to determine whether its volume is associated with clinical characteristics of the disease.

Methods: Resting-state fMRI was performed in 13 patients with CBS (mean age 63.0±11.,0; 4 males/9 females), 15 with Alzheimer's disease (AD) dementia (73.3±8.62, 3/12), 16 with behavioral variant frontotemporal dementia (bvFTD) (63.9±7.30; 8/8) and 20 healthy controls (HC) (54.4±9,23; 8/12). DMN volume differences between groups were evaluated with correction for age and sex. Multiple regression was used to assess correlations between DMN volume in CBS and clinical data: disease duration, total Addenbrooke's Cognitive Examination and Frontal Assessment Battery (FAB) scores and Trail Making Test part B.

Results: In comparison with HC, the CBS group showed statistically significant DMN volume reduction in posterior cingulate cortex bilaterally. The CBS group compared to AD showed larger DMN volume in left precuneus (pFDR<0.05, fig.) whereas no difference were found between CBS and bvFTD. Among clinical data only FAB scores were positively correlated with DMN volume in left precuneus (p<0.001).
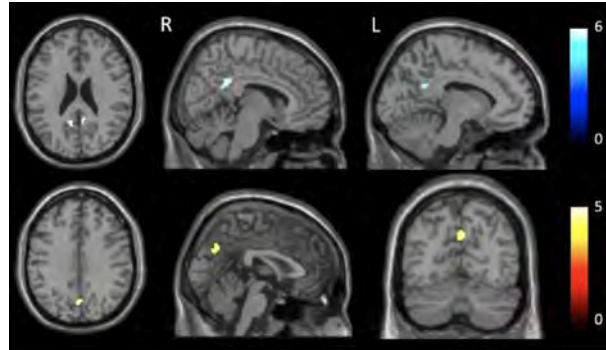
Localization of significant (pFDR-corr <0.05) DMN volume alterations in CBS compared with other groups. Upper row: decline of DMN volume in CBS group compared with healthy controls. Lower row: increase of DMN volume in CBS group compared with AD.

Conclusion: Our findings demonstrate that DMN volume is reduced in CBS compared with HC and correlates with the severity of cognitive impairment, which may indicate the importance of its role in the pathogenesis of CBS. DMN volume may potentially be used in differential diagnosis of CBS with AD but not with bvFTD.

Disclosure: Nothing to disclose.

EPO-002

Development of seizures reduces survival in patients with Alzheimer's Disease

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Background and aims: Patients with Alzheimer's Disease (AD) have an increased risk rate of epilepsy, especially in early-onset cases, compared with age-matched healthy-controls. AD mouse models have showed that AD mice have an increased risk of death. We aimed to investigate if seizure development was associated with an increased risk of death.

Methods: We conducted a retrospective study in a cohort of AD patients with CSF biomarkers. We identified patients who developed seizures. We collected demographic and clinical variables (development of seizures, time of death, sex, years of education, CSF biomarkers, baseline Mini–Mental State Examination score, comorbidities and apolipoprotein E status).

Results: We included 415 AD patients. The development of seizures was associated with younger age of dementia's onset, lower baseline Mini–Mental State Examination and higher CSF total tau protein levels. In multivariate analysis, developing seizures was the only variable associated with a reduced survival (β=0.538, 95% CI=[0.032, 1.045], p=0.037).

Conclusion: Patients with AD who develop seizures are at an increased risk of death, independent of other variables, namely CSF biomarkers.

Disclosure: Nothing to disclose.

EPO-003

Abstract withdrawn

EPO-004

Effect of Plasma Exchange with Albumin replacement on cognition in Alzheimer's disease: a Latent Growth Mixture Model

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Background and aims: Alzheimer Management By Albumin Replacement (AMBAR) trial evaluated efficacy and safety of Plasma Exchange with Albumin replacement (PE-A) in mild-to-moderate Alzheimer's disease patients. PE-A-treated patients performed significantly better than placebo on Alzheimer's Disease Cooperative Study-Activities of Daily Living (ADCS-ADL) score [Least-Square Mean Difference (LSMD): 3.5, p=0.030], but significance was not reached on Alzheimer Disease Assessment Scale-Cognitive subscale (ADAS-Cog) score (LSMD: -2.1; p=0.063). In post-hoc analysis we evaluated whether unobserved heterogeneity in cognitive change could explain discordant PE-A treatment effect on ADCS-ADL vs. ADAS-Cog.

Methods: We used Latent Growth Mixture-Model (LGMM) to identify sub-groups ("classes") among pooled PE-A-treated patients who differed in their longitudinal cognitive function trends. Logistic regression was used to predict LGMM-identified class membership, and a Mixed-Model for Repeated Measures (MMRM) was used to evaluate PE-A efficacy for LGMM-identified class vs. placebo in the Full Analysis Set (FAS).

Results: A cognitive-erratic (n=48, 22%) and cognitive-stable (n=175, 78%; Figure 1) class of patients were identified. Predictors of cognitive-stable class membership were baseline Mini-Mental State Examination score (OR=1.29, p=0.003), baseline Clinical Dementia Rating-sum of boxes (OR=0.75, p=0.006), and female sex (OR=2.34, p=0.037). MMRM showed significant improvements for the cognitive-stable PE-A class vs. FAS placebo in ADAS-Cog (LSMD -2.7, p=0.007) and ADCS-ADL (LSMD 4.9, p=0.001; Figure 2).

CFBL: Change from baseline; LGMM: Latent Growth Mixture Model
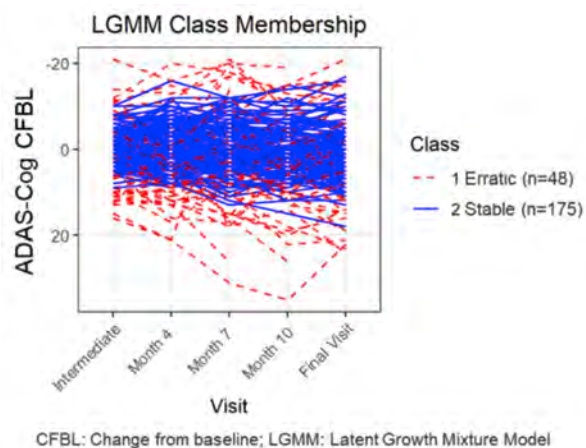
Figure 1: Latent Growth Mixture-Model

CFBL: Change from baseline; FAS: Full Analysis Set; LGMM: Latent Growth Mixture Model
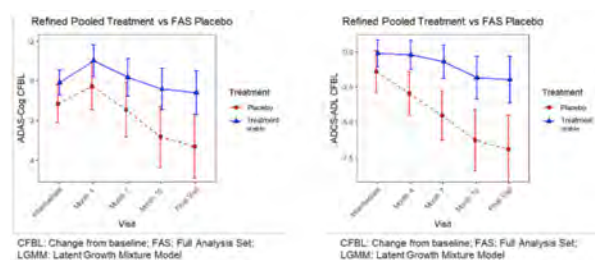
Figure 2: Mixed-Models for Repeated Measures on ADAS-Cog and ADCS-ADL in Refined Pooled Treatment Sample from LGMM-Identified Classes vs FAS placebo

Conclusion: Compared to placebo, a large subgroup of PE-A-treated patients with stable cognitive trajectory and more likely mild and females, had a statistically significant effect of PE-A on co-primary endpoints ADCS-ADL and ADAS-Cog, suggesting that unobserved heterogeneity may have had a masking effect in the AMBAR trial.

Disclosure: This study was funded by Grifols SSNA a maker of Albutein®.

EPO-005

Spatial navigation distinguishes Alzheimer's disease and non Alzheimer's pathologic change and relates to CSF biomarkers

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Background and aims: We assessed the differences in spatial navigation performance between older adults with amnestic mild cognitive impairment (aMCI) with AD, aMCI with non Alzheimer's pathologic change (non-AD), mild AD dementia, and cognitively normal (CN) older adults. The associations between spatial navigation performance and biomarkers in cerebrospinal fluid (CSF) were also examined.

Methods: 118 older adults with AD aMCI (n=33), non-AD aMCI (n=31), mild AD dementia (n=28) and CN older adults (n=30) underwent clinical and laboratory evaluations, comprehensive cognitive assessment, brain magnetic resonance imaging and spatial navigation testing in the egocentric Route repetition task, where participants repeated the route through a virtual city, and the allocentric Route retracing task, where participants indicated their way back. Cognitively impaired participants underwent analysis of amyloid-β1-42, total tau and phosphorylated tau181 (p-tau181) in CSF and/or amyloid PET imaging.

Results: In the Route repetition task, AD aMCI had worse performance than non-AD aMCI and CN (p<.001), and did not differ from mild AD dementia. Non-AD aMCI did not differ from CN and had better performance than mild AD dementia (p<0.001). In the Route retracing task, AD aMCI and non-AD MCI had worse performance than CN (p≤0.009) and did not differ from dementia. Lower amyloid-?1-42 was associated with worse performance in the Route repetition task (ß=0.39, p=0.005) and higher p-tau181 was associated with worse performance in the Route-retracing task (ß=-0.28, p=.041).

Conclusion: Egocentric spatial navigation performance differentiates aMCI older adults with AD and non-AD. CSF amyloid-β1-42 and p-tau181 are associated with egocentric and allocentric spatial navigation performance, respectively.

Disclosure: European Regional Development Fund–Project ENOCH no. CZ.02.1.01/0.0/0.0/16_019/0000868; the Institutional Support of Excellence 2. LF UK grant no. 6990332; and the Grant Agency of Charles University grant no. 327821.

EPO-006

Awareness in neurodegenerative disorders: a systematic MRI review

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Background and aims: This systematic review investigated awareness and related disturbances in Alzheimer's disease (AD) and behavioural variant of frontotemporal dementia (bvFTD), and explored common and specific structural and functional brain correlates of awareness in the two conditions.

Methods: A literature review was performed targeting these areas: awareness, neurological condition, MRI. Inclusion criteria were: (a) studies on awareness; (b) use of structural and/or functional MRI; (b) on humans; (c) English language and full-text; (d) on AD and bvFTD. 1,340 articles were obtained for title/abstract screening. Subsequently, 43 articles were selected for full-text screening and, at last, inclusion consensus was reached on 36 papers. Included studies regarded different aspects of awareness: anosognosia, insight, social cognition, including theory of mind (ToM) and emotional processing, free-will and autonoetic awareness.

Results: In bvFTD, anosognosia occurs since early disease stages and is associated to medial prefrontal regions alterations; in AD, anosognosia appears later and is linked to difficulties in evaluating one's capacities. This difficulty is secondary to memory deficits in AD, and, as for autonoetic awareness, it is associated with temporal (hippocampal) alterations. In bvFTD, insight loss is often present and related to limbic (amygdala) alterations, while lack of free-will (expressed as environmental dependency) is related to orbitofrontal alterations. Finally, ToM impairment is present in both bvFTD and AD patients since the early phases, and is associated with fronto-striatal and limbic circuits' involvement.

Conclusion: Awareness is characterized by multiple aspects, which are affected at different stages of AD and bvFTD, and are subtended by either common or distinct brain circuits.

Disclosure: Nothing to disclose.

EPO-007

New biomarker of cognitive decline

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Background and aims: Amnestic mild cognitive impairment (aMCI) is predementia condition of Alzheimer's disease, while non amnestic Mild cognitive impairment (nMCI) is not defeniltly finishing dementia. EEG-coherence is a sensitive marker of functional connectivity, whereas fMRI detects activation patterns ,which could be coupled. The aim was to correlate fMRI activation patterns and EEG-coherence in aMCI, nMCI and age-matched controls.

Methods: 80 aMCI, 85 nMCI and 85 age-matched controls underwent fMRI (3 Tesla ,TRIO, Siemens) and resting EEG-recordings (NeuroScan Synamps System). EEGs were recorded using a standard protocol and montage. Coherences between regions of interest, based on fMRI activation patterns were calculated.

Results: aMCI-subjects showed reduced coherence compared with controls between ACC and left frontal superior gyrus within delta, theta and alpha1-band. Theta coherence was significantly lower between anterior and posterior cingulate gyrus, between right and LTG (aMCI < controls, p<0,001), fig1,2. There were not found significant differences between nMCI and controls between ACC in theta anf delta bands (nMCI < controls, p<0,05).

Conclusion: EEG coherence seems to be a useful approach, which helps to detect the early stage of cognitive decline in neurodegeneration process.

Disclosure: Nothing to disclose.

EPO-008

Characterising the prodromal phase of dementia with Lewy bodies

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Background and aims: Three subtypes of prodromal dementia with Lewy bodies (DLB) have recently been proposed. This study investigates the prodromal phase in DLB and the frequency of these subtypes.

Methods: Patients diagnosed with DLB from the 1st of February 2017 to the 1st of February 2021 were retrospectively identified and matched to a group of patients with Alzheimer's disease (AD). Patient case files were reviewed with regards to first symptoms and symptoms in the prodromal phase (cognitive impairment, psychiatric symptoms, delirium/acute confusional episodes, RBD, motorsymptoms indicative of Parkinson's disease, anosmia, and autonomic dysfunction).

Results: A cohort of 166 DLB patient and 168 AD patients was included. Of the proposed subtypes in patients with DLB 30% presented with cognitive impairment at onset in isolation, 6% with psychiatric symptoms, and 2% with delirium/acute confusional episodes. Eighty-three percent of patients with DLB had two or more non-cognitive symptoms in the prodromal phase. Further, 82 % had at least one psychiatric symptom, and 33 % had an episode with delirium/acute confusional episode in the prodromal phase. Of other possible subtypes, Rapid eye movement sleep Behavior Disorder was found at onset in 22% with a mean prodromal length of 8.4 years (as opposed to 4.3 years in DLB generally).

Conclusion: We found no clear evidence to support a high prevalence of the three subtypes of prodromal DLB. Our findings indicate that an RBD subtype may exist, but more research is needed.

Disclosure: Nothing to disclose.

EPO-009

Regional cerebral blood flow and brain structural changes in mild cognitive impairment and Alzheimer's disease

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Background and aims: Brain atrophy and structural changes due to aging contribute strongly to the pathophysiology of mild cognitive impairment (MCI) and Alzheimer's disease (AD). Regional cerebral blood flow (CBF) impairment is believed to be one of the initial changes in the AD continuum. In this study, we investigated the association between CBF and brain structural changes associated with aging and neurodegeneration.

Methods: Data from three groups of participants including 39 control normal (CN), 82 MCI, and 28 AD subjects were downloaded from the Alzheimer's disease Neuroimaging Initiative (ADNI). Magnetic resonance images (MRI) of participants were automatically segmented by FreeSurfer V 4.3 and 5.1 software and arterial spin labeling (ASL) MRI was applied to measure CBF and investigate the effect of aging and structural changes on CBF in experimental groups. One-way ANOVA and linear regression were used to compare data and find a correlation between CBF and structural changes in the brain.

Results: AD patients had significantly lower Mini-Mental State Examination (MMSE) score (p=0.001) and more APOE-ε4 carriers (p=0.001) as compared to the MCI and CN groups. Our findings revealed a widespread significant correlation between the CBF and structural changes, including cortical volume, subcortical volume, surface area, and thickness in all participants, particularly AD patients after adjusting for age, sex, and APOE genotyping status.
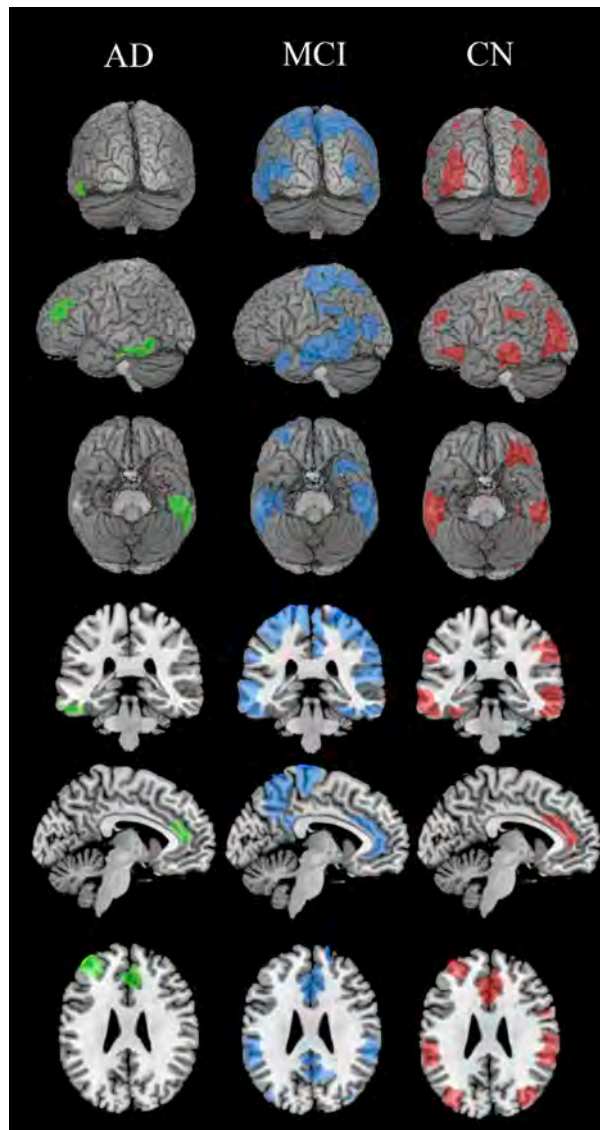
Regions of interest are shown for significant correlation between structural change values and regional cerebral blood flow. AD (green), MCI (blue), CN (red). Alzheimer's Disease (AD), mild cognitive impairment (MCI), control normal (CN).

Conclusion: CBF decline may be a useful biomarker for MCI and AD and accurately reflect the structural changes related to AD.

Disclosure: Funding: We do not have any financial support for this study. Conflict of interest: The authors declare no conflict of interest regarding the publication of this paper.

EPO-010

A case of depressive pseudodementia with reversible severe brain hypometabolism mimicking Alzheimer's disease

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Background and aims: Differential diagnosis between Alzheimer's disease (AD) and depressive pseudodementia (DP) may be challenging. Recent EANM-EAN guidelines recommended using brain FDG-PET to differentiate between neurodegenerative dementias and DP, with specific hypometabolism patterns across the former group, and typically normal or frontal hypometabolism in the latter. We report the case of a 74 year-old man with reversible DP, whose FDG-PET closely mimicked the typical AD pattern.

Methods: The patient underwent yearly neuropsychological (NPS) testing, while brain FDG-PET and MRI were done at presentation and after two years.

Results: At referral, the patient was severely depressed, complained of memory deficits, and his MMSE was 16/30. Brain MRI showed mild diffuse atrophy, while PET visual rating and semiquantitative analysis revealed severe hypometabolism in bilateral precuneus, parietal, and temporal lobes, sparing frontal areas, consistent with moderate AD. Shortly after starting therapy with duloxetine, trazodone, quetiapine and delorazepam he underwent formal NPS testing, which revealed moderate impairment of episodic memory and mild impairment on executive and visuospatial tests, judged consistent with neurodegenerative dementia and concomitant depression. Two years later his MMSE improved up to 30/30, MRI was unchanged, NPS assessment did not show significant deficits, and FDG-PET was reverted to normal.
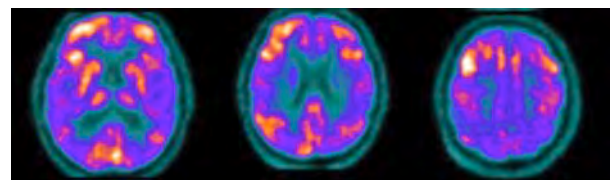
FDG-PET at referral, before antidepressant therapy
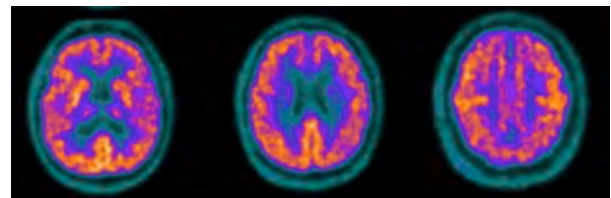
FDG-PET two years after the start of antidepressant therapy
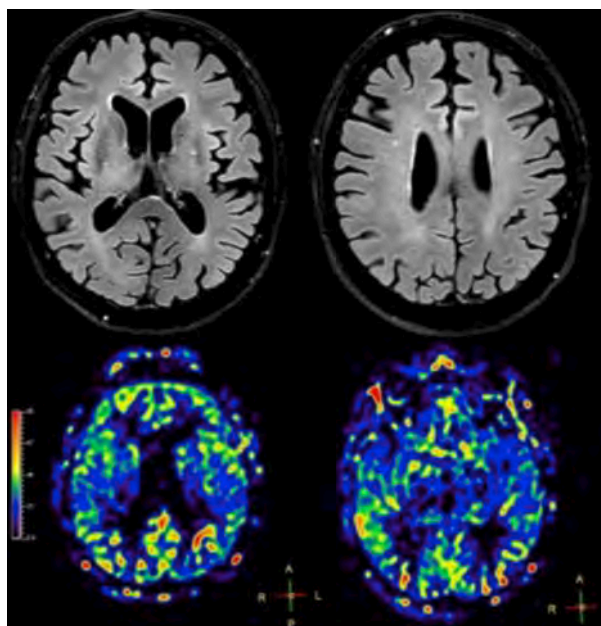
Brain MRI at two year follow-up (T2 and pCASL sequences)

Conclusion: The peculiarity of our case lies in the distribution of FDG-PET abnormalities: lack of the usual frontal hypometabolism of DP, but involvement of precuneus and temporo-parietal regions, corresponding to the metabolic signature of AD. Confirmation of PET findings via semiquantitative analysis and their reversion to normality with antidepressant treatment proved the non-neurodegenerative origin of such abnormalities.

Disclosure: The authors have no conflict of interest or funding to declare.

EPO-011

Language impairment and Antidepressant use are associated with a poor response to Acetylcholinesterase Inhibitors in AD

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Background and aims: Waiting for new disease modifying drugs, Acetylcholinesterase Inhibitors (AchEI) represent the only therapeutic option for Alzheimer's disease (AD), showing a wide variability in individual response. Knowing factors affecting response to treatment can be useful to administer a tailored therapy or to avoid an early discontinuation. Here, we aimed at detecting factors associated with a poor response to AD treatment.

Methods: In this retrospective study we enrolled 157 patients with a biomarker confirmed AD diagnosis. All the patients were assuming an AD treatment and had a follow up evaluation in a time ranging 5–19 months after baseline. Patients were labelled "non responders" if they lost equal or more than the average decline observed in AD at MMSE (2.2 points lost per year). We adopted logistic regression models to search for independent associations with the "AD response" outcome.

Results: 57% of patients were "responders". We found no significant differences in demographic parameters, cerebrospinal fluid (CSF) AD biomarkers' levels and neuropsychiatric inventory (NPI) scores between responders and non-responders. After adjustment for age, education, sex and disease severity, a poor response to AD treatment was associated with worse baseline cognitive scores at Token Test ($p=0.02$), Phonemic ($p=0.032$) and Semantic ($p<0.001$) Verbal Fluency and with the assumption of an anti-depressant drug ($p=0.058$).

Conclusion: Non-responders to AD treatment showed slight but wider deficits in cognitive domains other than memory, in particular language. Furthermore, anti-depressants are associated with a poor response to AD treatment, thus possibly suggesting a prominent role of "mood" symptoms on cognitive worsening.

Disclosure: Nothing to disclose.

EPO-012

Normal Pressure Hydrocephalus: Longitudinal Observations

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Background and aims: Patients with normal pressure hydrocephalus (NPH) and changes of neurodegenerative biomarkers in cerebrospinal fluid (CSF) suggestive of Alzheimer's disease (AD+) benefit from a spinal tap, while patients with NPH and no CSF changes (AD-) do not (Müller-Schmitz et al. 2020, Ann Neurol 88: 703–711). In this prospective study we followed patients with NPH over time.

Methods: Between 2016 and 2021, 41 consecutive patients with imaging changes indicative of NPH were studied on at least two admissions. Patients with NPH and AD+ (n=25; 76±5 years) and AD- (n=16; 77±5 years) were subjected to clinical, motor and cognitive tests before and after a spinal tap of 40–50 ml. The CSF biomarkers included S100-Protein, Neuron-specific Enolase (NSE), β-Amyloid 1–42, Tau-Protein and Phospho-Tau. Data were estimated using a repeated analysis of variance (ANOVA), the post-hoc student t-test and correlation analysis.

Results: Motor and neuropsychological data differed between the AD+ and AD- patients with NPH over time. The AD- patients showed an improvement after the spinal tap in short-term memory, while the AD+ patients showed a long-term improvement of memory tests. However, their motor functions deteriorated. In both groups, a decrease in patients' urinary incontinence to 50 percent was recorded. Over time ß-Amyloid decreased in the AD- patients to the level of the AD+ patients, while the CSF pressure and the NSE increased in both groups.

Conclusion: Our data supports the association of Alzheimer's disease and NPH and questions the dichotomy of a neurodegenerative and idiopathic NPH.

Disclosure: Nothing to disclose.

EPO-013

Transcranial Pulse Stimulation in Alzheimer´s Disease – Short and long-term clinical results

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Background and aims: Transcranial Pulse Stimulation (TPS) is a non-invasive therapy that uses shockwaves. There is first evidence for beneficial clinical effects in Alzheimer´s Disease (AD). Long-term results and controlled trials are not yet reported. We report first clinical experience from a center in Germany.

Methods: A consecutive number of ten TPS-treated AD-patients was examined retrospectively (heterogeneous group with MMST from 2 to 27). Patients received 4–12 sessions of 3,000-6,000 pulses per session with 4 Hz of 0.2 mJ/mm^2 (MRI navigated bifrontal biparietal, bitemporal and praecuneus) with six initial sessions over two weeks plus one booster every four weeks. Cognitive and affective scores were assessed (e.g. ADAS, MMST, MoCa, BDI).

Results: Treatment was well tolerable with low number of side effects (transient headache, nausea restless feeling). All patients improved at least transiently in one neuropsychological test. Significant mean improvement was best detected in the ADAS sum score with 18% after the first treatment cycle. Best improvement in a patient was 40%. Marked improvement of mood was seen in some patients. Longitudinal data of first treated individuals up to 1 year will be presented.

Conclusion: These pilot results confirm the recently published results. The sample was heterogeneous but some patients showed a marked improvement of mood and cognition. Long-term data of individuals should be completed within the next months. More data and subgroups need to be analyzed. Prospective controlled trials would be the next step to proof the efficacy of this new technique.

Disclosure: LW receives consultancy honoraria and travel payments from Storz Medical.

Cerebrovascular diseases 1

EPO-014

See it to believe it

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Background and aims: INO is a recognized manifestation of medial longitudal fasciculus (MLF) lesions, most typically caused by brain demyelinating disorders. It is rarely a consequence of unilateral FEF lesion.

Methods: Case report and review of literature.

Results: An 82-year-old female, with a history of type 2 diabetes mellitus, presented with sudden vertical oscillopsia and instability. Neurologic examination revealed impaired adduction of the right eye associated with horizontal and torsional nystagmus of the left abducting eye, and preserved convergence (suggesting a right INO). Brain MRI showed a hyperintense T2 lesion with diffusion restriction and low apparent diffusion coefficient in the right middle frontal gyrus, likely representing acute ischemic stroke in right FEF; the remaining of the neuroimaging was normal. We found no potential cardioembolic causes for the stroke, therefore the patient was discharged with single antiplatelet therapy.
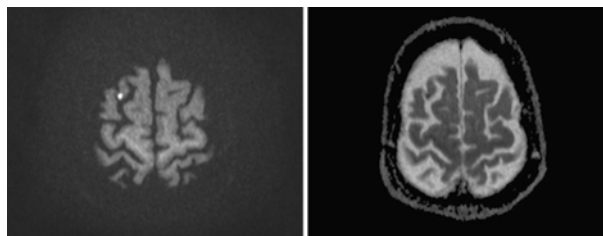
Brain MRI showing a lesion with diffusion restriction and low apparent diffusion coefficient in the right middle frontal gyrus, likely representing acute ischemic stroke in right FEF.

Conclusion: The FEF is the cortical area considered responsible for horizontal gaze movements, connected indirectly to the extraocular muscles via the paramedian pontine reticular formation (PPRF); thus, its lesion causes deviation of the eyes ipsilateral to the side affected. INO has been classically associated with pontine MLF lesions, being stroke and demyelinating diseases the two main etiologies, usually demostable by brain MRI. Recently, a new pathway connecting the FEF and the ipsilateral MLF bypassing PPRF has been proposed, pointing out lesions of FEF as additional causes of INO. We believe that this case report further supports the existence of the aforementioned unique bundle originating from FEF that projects directly to ipsilateral MLF.

Disclosure: There are no financial conflicts of interest to disclose.

EPO-015

Can d-dimer level predict functional outcome after acute ischemic stroke treated with mechanical thrombectomy?

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Background and aims: D-dimers are products of fibrin degradation. In acute ischemic stroke (AIS), higher d-dimer levels have been associated with cardioembolic sources, occult cancer, larger and more severe infarcts. To date, only one study has evaluated d-dimer level as a predictor of functional outcome after mechanical thrombectomy (MT) – however, it addressed patients with AIS related to cancer only. We aimed to evaluate the relationship between d-dimer level in the first 24 hours after hospital admission and short-term functional outcome in patients with AIS treated with MT.

Methods: We retrospectively reviewed patients with AIS treated with MT in our hospital center from May 2020 to April 2021. Patients treated with intravenous thrombolysis were excluded. Demographic, clinical and neuroradiological characteristics, d-dimer level within 24 hours of admission, and functional status (modified Rankin scale) at 3 months of follow-up. Patients were categorized into quartiles according to d-dimer values. Odds ratio of unfavorable functional outcome were obtained for each quartile and adjusted for confounders.

Results: 109 patients were included. Patients with higher d-dimer levels obtained a worse short-term functional outcome (OR=4.037, CI 95% 1.295–12.585 for Quartile 3; OR=5.950, CI 95% 1.797–19.699 for Quartile 4). After adjusting for age and sex, our results maintained significance for Quartile 4 (OR=4.163, CI 95% 1.168–14.831).

Conclusion: Our results suggest a potential role for d-dimer level as a predictor of functional outcome after AIS treated with MT. Limitations of this study include its small sample size and inclusion of patients irrespective of the mTICI (modified Treatment in Cerebral Infarctions) grade obtained.

Disclosure: The authors have nothing to disclose.

EPO-016

Long-term outcome in stroke: the need of individualized follow-up

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Background and aims: The ideal length of follow-up in a specialized consultation after ischemic stroke has not been established. In the long-term, many stroke patients potentially have relevant functional incapacity related to deficits in domains other than motor.

Methods: We evaluated long-term stroke patients who underwent endovascular treatment of anterior circulation in our stroke center and that were classified as "therapeutic success" (modified Rankin scale – mRS<3) at 3 months. Participants underwent a comprehensive interview and examination using validated standard questionnaires for Portuguese population to assess different life aspects after stroke as Post-Stroke Checklist, EQ-5D-3L scale, mRS, Barthel Index (BI), Burden Scale for Family Caregivers and Hamilton scale.

Results: We evaluated 20 patients. The mean age was 68.6 years old (±12,4) and the mean time for the interview was 53 (±6,6) months after the stroke. Most patients were independent, with a mean mRS of 1 (ranging from 0–3) and BI 96 (70–100). Seventy percent had a clinically significant deficit in at least one domain. On the Post Stroke Checklist (PSC), 80% of participants demonstrated a not good perceived health status. EuroQoL index value was 0.749 (0.117–1.00). The two major disability parameters identified were in cognition (65%) and depression (30%).

Conclusion: These results highlight the prevalence and importance of non-motor disabilities in long-term stroke patients, even after short-term classification as "therapeutic success". These patients may benefit from a more global assessment and extended follow-up. Future larger studies are needed to redefine therapeutic success in stroke.

Disclosure: Nothing to disclose.

EPO-017

Remote Cerebellar Hemorrhage – a rare complication of spinal surgery

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Background and aims: Remote cerebellar is a complication most often associated with supratentorial neurosurgical procedures. It can also occur as a distant complication of other types of surgical interventions, such as spinal surgery.

Methods: Clinical case.

Results: A 77-year-old woman with a history of degenerative osteoarthritis, arterial hypertension, diabetes mellitus and atrial fibrillation (hypocoagulated with apixaban 5 mg bid, suspended before surgery), underwent intersomatic arthrodesis for lumbar spine stenosis at the level of L4-L5. The procedure was complicated by a tear in the dura mater of 3 mm in length, repaired with a synthetic patch. Following the surgery, the patient developed movement-triggered nausea/vomiting as well as non-preferential imbalance. No headache was referred. The neurological examination revealed bilateral ataxia in the finger-nose and heel-knee tests, most evident on the left-side, and astasia-abasia. NCCT of the head revealed bilateral cerebellar hemorrhage, predominantly layered along the cerebellar folia ("zebra sign"), with adjacent edema and minimal mass effect, and the diagnosis of remote cerebellar hemorrhage was put forth. CT-angiography excluded arterial-venous malformations or venous sinus thrombosis. Patient was submitted to conservative treatment, and follow-up imaging showed progressive reabsorption of the hematic component. Hypocoagulation was resumed without complications 14-days after the hemorrhagic event, and the patient was referred to a rehabilitation clinic.

Conclusion: Remote cerebellar hemorrhage is a rare complication of spinal surgery. Its occurrence may be related to iatrogenic CSF hypotension with thrombosis of the penetrating veins and resultant hemorrhage. This unusual etiology should be considered in patients with neurological deficits after surgical procedures complicated with dural tears.

Disclosure: The authors have no disclosures.

EPO-018

Psychiatric status during hospitalization is a strong predictor of post-stroke anxiety: a prospective study

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Background and aims: Acute ischemic stroke (AIS) is an important cause of mortality worldwide. Psychiatric comorbidities associated with this condition as well as post-stroke depression and anxiety are frequent. Its early recognition might contribute to the recovery of the functional status of these patients. The present research aims to investigate the frequency and predictors of anxiety 90 days after AIS.

Methods: A prospective cohort study was conducted in a tertiary center of neurology in southern Brazil, including 148 patients with AIS who were interviewed between January 2020 and February 2021. The first interview, during hospitalization, included the investigation of clinical variables and the application of the Hospital Anxiety and Depression Scale (HADS). Subsequently, the HADS was reapplied 90 days after stroke. Predictor variables were investigated by univariate and multivariate linear regression.

Results: The frequencies of anxiety during hospitalization and 90 days after stroke were 33.8% and 23.7%, respectively. Anxiety and depressive disorder during hospitalization (B: 0.441; p<0.01 and B: 0.241; p<0.01, respectively) and depression 90 days after stroke (B: 0.394; p<0.01) were strong predictors of anxiety 90 days after AIS. Other clinical variables were not associated with the study outcome.

Conclusion: This study identified a high frequency of anxiety 90 days after AIS. Psychiatric status during hospitalization was demonstrated to be a strong predictor of anxiety 90 days after AIS. This highlights the importance of the early diagnosis of psychiatric conditions, even during hospitalization, to prompt treatment of those patients who might experience a positive impact on their recovery.

Disclosure: Nothing to disclose.

EPO-019

Predictors of post-stroke depression in the acute phase of ischemic stroke: a cross-sectional study

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Background and aims: Ischemic stroke is a remarkable cause of death and disability worldwide. Post-stroke depression (PSD) is the most common psychiatric disturbance after stroke. Despite PSD being a potentially treatable condition, it still requires approaches to improve the early diagnosis. The present study aims to investigate the predictors and correlated variables associated with PSD during hospitalization.

Methods: A cross-sectional study was carried out in a specialized center of neurology situated at Santa Catarina, Brazil. 148 patients with acute ischemic stroke hospitalized between January 2020 and February 2021 were included. Sociodemographic, clinical and radiological variables were assessed during hospitalization. The Hospital Anxiety and Depression Scale (HADS) was applied, as well as the National Institute of Health Stroke Scale (NIHSS) and modified Rankin Scale (mRS). Predictors factors were investigated through binary logistic regression and continuous variables through correlation tests.

Results: The prevalence of PSD during hospitalization was 31.1%. Predictors of PSD in the acute phase of the stroke were female sex (OR: 2.6; CI 95%: 1.3 to 5.4; p<0.01) and post-stroke anxiety during hospitalization (OR: 4.9; CI 95%: 2.3 to 10.3; p<0.01). The variables NIHSS, mRS, and stroke area were positively correlated with HADS – depression values.

Conclusion: This research evidenced a high prevalence of PSD in the acute phase of stroke. Despite the study being conducted during the COVID-19 pandemic, the data found is similar to the non-pandemic periods. The research provided clues to identify and early treat patients at greater risk of developing PSD during hospitalization.

Disclosure: Nothing to disclose.

EPO-020

Lesion probability map in cerebral venous sinus thrombosis due to Behçet's disease

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Background and aims: Behcet's disease(BD) is a multisystemic inflammatory disease. The second most common clinical form of Neuro-BD is cerebral venous sinus thrombosis(CVST). In previous studies, affected cerebral venous sinuses were classified categorically. In our study, we aimed to create thrombus probability maps of patients with BD and CVST to visually present and compare patient subgroups.

Methods: Seventeen patients with a diagnosis of BD-related CVST(BD-CVST) and 23 patients with a diagnosis of CVST related to other etiologies(non-BD-CVST) were included. Demographic data, disease symptoms, neurological examination findings, and etiologies were recorded. High-resolution MR venography examinations obtained during CVST were used to mark and digitalize thrombosed areas using computer-aided design software. Thrombus probability and subtraction maps were created to reveal the differences between the subgroups.

Results: Focal neurological findings were only found in the non-BD-CVST. Brain MRIs were within normal limits except for one patient with BD, while parenchymal pathology was observed in 13 patients(56.5%) in the non-BD-CVST. Transverse sinus(TS) was the most common location of thrombosis in BD-CVST and TS thrombosis was significantly higher than the frequency of superior sagittal sinus(SSS) thrombosis($p<0.01$). In the non-BD-CVST, thrombus developed mostly in the SSS and TS. Interestingly, TS was affected in all patients with BD, while it was not affected in 22% of the non-BD-CVST. The frequency of SSS thrombosis was more common in the non-BD-CVST (Figure 1).
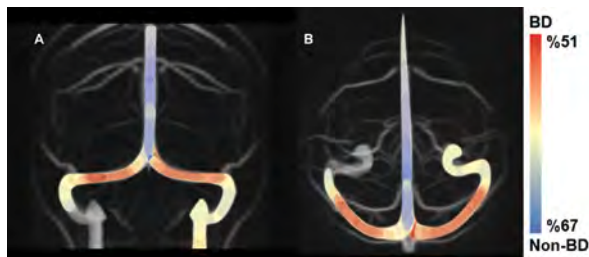
Figure 1: Thrombus probability difference map of patients with and without BD. A: Anterior-posterior view. B: Superior-inferior view. The level of the thrombus probability difference is shown on the red-blue color scale.

Conclusion: We observed a decreased risk of venous infarction and hemorrhage in BD-CVST. Interestingly, non-BD-CVST patients had a higher rate of SSS thrombosis, while BD-CVST patients had a higher rate of TS thrombosis.

Disclosure: The authors have no conflicts of interest to declare.

EPO-021

Isolated SAH is a good prognostic sign in cerebral venous thrombosis

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Background and aims: Cerebral venous thrombosis (CVT) is a rare cerebral vascular disease however, presentation of CVT is highly variable clinically and radiologically. A recent study has shown that isolated subarachnoid hemorrhage (iSAH) in CVT is not so rare as thought previously and may have a good prognostic significance. Hemorrhagic venous infarction however is a factor of unfavorable outcome mostly associated to multiple cerebral sinuses/veins occlusion. We hypothesized that our patients who initially suffered iSAH will have a better clinical outcome than those who suffered hemorrhagic cerebral infarction.

Methods: We selected the patients hospitalized due to CVT and presented either isolated SAH or cerebral hemorrhagic infarction at admission time or during the next 24 hours. They were 23 (10 men) aged 22–73 years. The data was extracted from hospital admission records, our computer data system and radiological database system.

Results: The iSAH group were 8 (6 men) aged 49.3 ± 16.2 and haemorrhagic infarction group were 15 (4 men) aged 47.9 ± 16.8. The isolated SAH group had significantly better outcome regarding mRS score than haemorrhagic infarction group (Mann-Whitney Rank Sum Test, $p=0.026$) despite significantly greater number of thrombosed venous sinuses/deep veins. (Mann-Whitney Rank Sum Test, $p=0.002$). Additional variables of significant impact were oedema formation ($p=0.004$) and sulcal obliteration ($p=0.014$).
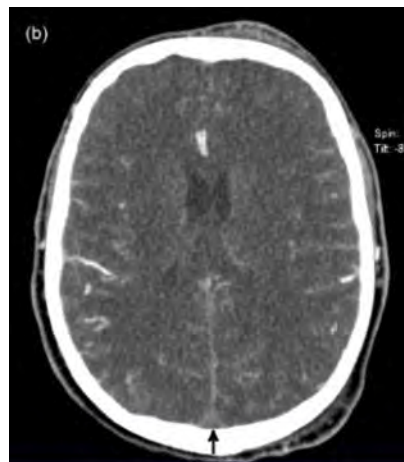
Isolated SAH
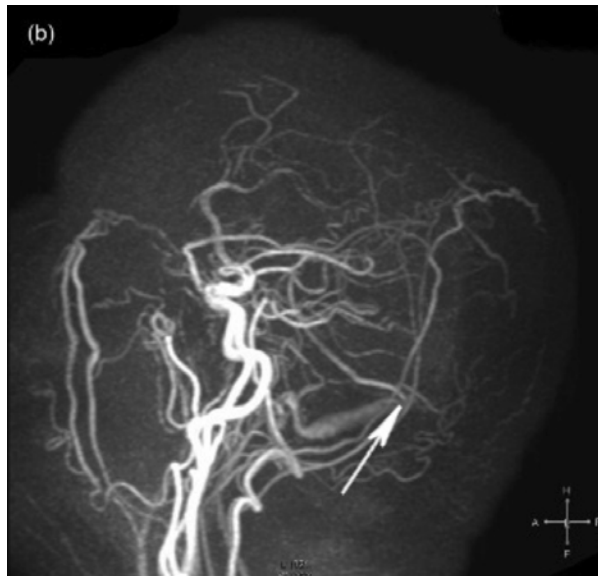
Lateral sinus patent from the Labbe vein inflow
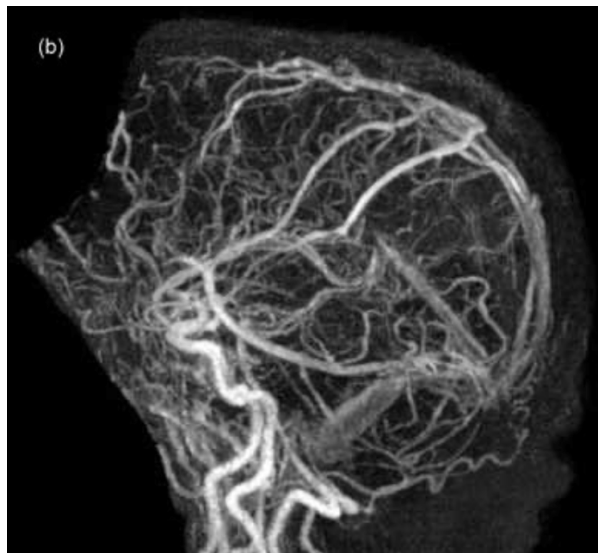
Complete recanalisation

Conclusion: The patients who suffer iSAH initially have significantly better outcome prognosis than haemorrhagic infarction patients despite of greater number of thrombosed sinuses/veins. A possible explanation might include patent superficial cerebral communicating veins.
Disclosure: Nothing to disclose.

EPO-022

Association between neighbourhood deprivation and stroke survival: A 20-year follow-up study in Sweden

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Background and aims: Neighborhood deprivation effects on survival of stroke patients is lacking, better understanding of association may would help identify stroke patients deemed to be at an increased risk of mortality. Our aim was to study the potential effect of neighbourhood deprivation on rates of mortality in patients with stroke, a 20-years nationwide follow-up study.

Methods: The association between neighbourhood deprivation and the outcome was explored using Cox regression analysis, with hazard ratios (HRs) and 95% confidence intervals (95% CIs). All models were conducted in both men and women and adjusted for individual variables and co-morbidities.

Results: There was an association between level of neighbourhood deprivation and total mortality in stroke patients. The HRs were 1.61, 95% CI 1.158–1.63 and 1.66, 95% CI 1.64–1.69 for total mortality among men and women patients living in high deprivation neighbourhoods compared to those from low deprivation neighbourhoods, after adjustments for potential confounders. For stroke patients, psychiatric disorders and diabetes, the HRs increased by increasing neighborhood deprivation and reached 1.35 (95% CI 1.26–1.45), 1.52 (95% CI 1.38–1.67) in men, and 1.24 (95% CI 1.18–1.31) and 1.62 (95% CI 1.47–1.79) in women, respectively, in high deprivation neighborhoods, after adjustments.

Conclusion: This study shows that neighbourhood deprivation is an important factor for total and cause-specific mortality among stroke patients. These findings could serve as an aid to policy-makers when allocating resources in primary health care settings as well as to clinicians who encounter patients in deprived neighbourhoods.

Disclosure: Nothing to disclose.

EPO-023

The Harlequin sign as an atypical manifestation in internal carotid artery dissection

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Background and aims: Harlequin phenomenon is characterized by hemifacial flushing and hyperhidrosis resulting from contralateral sympathetic denervation. It can occur as an isolated manifestation (Harlequin syndrome) or accompanied by other signs of autonomic dysfunction (Harlequin sign) (HS).

Methods: A healthy 40-year-old man presented severe left-sided headache after a training run. Two weeks later he went to the emergency room for persistent left-sided headache and physical examination showed ipsilateral eye ptosis and miosis as the only findings. He also showed a photo taken shortly after the headache started, presenting left forehead and nose pallor and right hemifacial flushing. Magnetic resonance angiography of the neck and brain revealed a narrowing and semi-circular wall hematoma of the left internal carotid artery (ICA) at the cervical segment, consistent with ICA dissection.
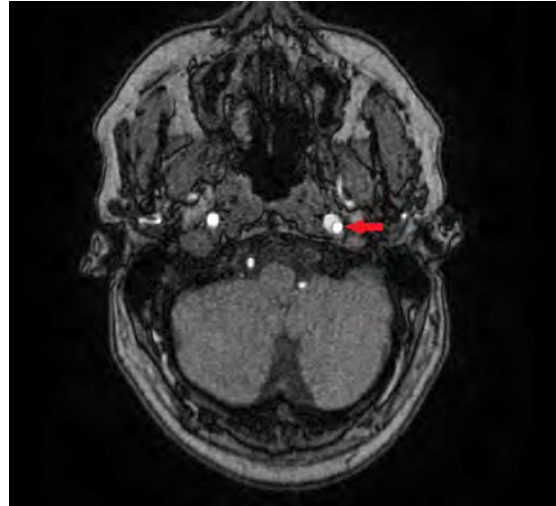
Magnetic resonance angiography showing left internal carotid artery dissection (arrow)

Results: Sympathetic innervation of the face depends on a three-neuron pathway. The third-order neuron originates in the superior cervical ganglion and projects its fibres along the carotid system. The ICA carries oculosympathetic and vaso/sudomotor fibres of the forehead and nose, whereas sympathetic fibres of the remaining facial areas proceed along the external carotid artery. Therefore, ICA dissection in this patient can explain both ipsilateral Horner syndrome and HS with pallor restricted to the forehead and nose. Since the Harlequin phenomenon was described in 1988 multiple causes have been reported, but we have found only two reports of HS secondary to ICA dissection.

Conclusion: HS should be considered as a possible manifestation of ICA dissection, especially when pallor affects only the forehead and nose.

Disclosure: The authors declare that there are no conflicts of interest.

Harlequin sign

EPO-024

Myocardial injury after acute stroke

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Background and aims: Patients with acute stroke frequently show signs of myocardial injury. Pathophysiology and exact incidence are not fully known yet. We aimed to investigate laboratory markers, ECG changes and echocardiographic variables.

Methods: 47 consecutive patients after acute ischemic stroke and 11 patients after intracerebral hemorrhage were enrolled. At admission, 24h and 48h later, 12lead ECG and laboratory markers, high-sensitive Troponin I(hscTnI), NT-proB-type Natriuretic Peptide(NTproBNP) and tumor necrosis factor-related apoptosis-inducing ligand(TRAIL), were obtained. Within first 5 days, echocardiographic examination was performed in 47 patients.

Results: The mean age of patients was 69.6 years, 35 were men. 21% of patients presented with TRAIL levels below 30 pg/ml. Increased hs-cTnI levels and NT-proBNP were presented in 24% of the patients. We found negative correlation between TRAIL and hs-cTnI levels, both after 24 hours(p=0,05) and 48 hours (p=0,03). There was a significant association between hs-cTnI and NT-proBNP levels at admission(p=0,02) and after 48 hours(p=0,0002). Ten patients (17%) presented with ST segment depression on ECG. Five patients had new regional wall motion abnormalities. Two patients had NSTEMI, one subacute MI and two patients had Takotsubo cardiomyopathy.

Conclusion: Although myocardial infarction or Takotsubo cardiomyopathy were present only in 7% of patients, we detected subclinical myocardial injury in another 16% of patients. Patients after acute stroke should undergo a detailed cardiac examination and should be considered for long-term cardiology follow-up care.

Disclosure: Nothing to disclose.

EPO-025

Sudden loss of visual acuity in a patient with CADASIL

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Background and aims: CADASIL is an arteriopathy that manifests with recurrent cerebral ischemic events, subcortical dementia, migraine, and mood disorders. Despite being considered a cerebrovascular disease, this hereditary arteriopathy is more widespread, and the involvement of other vessels, like those of retina and optic nerve, is currently demonstrated, by the deposition of granular osmiophilic material.

Methods: A 72-year-old female, with a history of depression, presented in August 2015 with a sudden, painless, left's eye monocular vision loss, upon awakening. After one year, she had a similar episode in the contralateral eye. She underwent an ophthalmology examination and the diagnosis of nonarteritic anterior ischemic optic neuropathy (NAION) was admitted. She was also referred to a neurology appointment, where the neurological examination revealed mild cognitive decline, significant emotional lability and reduced visual acuity bilaterally. She had a family history of cognitive decline and psychiatric symptoms affecting her mother and sister. MRI revealed extensive subcortical T2 hyperintensities of both hemispheres, including with external capsule involvement. In this context, a search for mutations in the NOTCH3 gene revealed a pathogenic mutation.
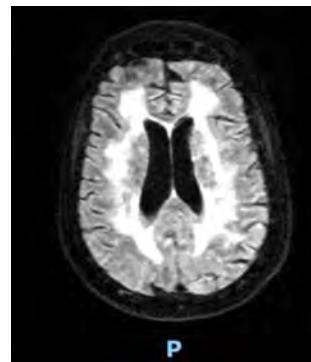
MRI (axial FLAIR) showing extensive subcortical T2 hyperintensities of both hemispheres
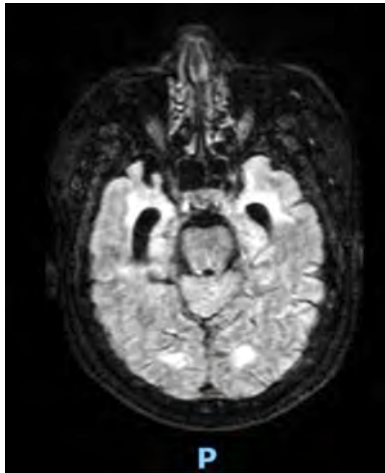
MRI (axial FLAIR) showing subcortical T2 hyperintensities, including with temporal involvement
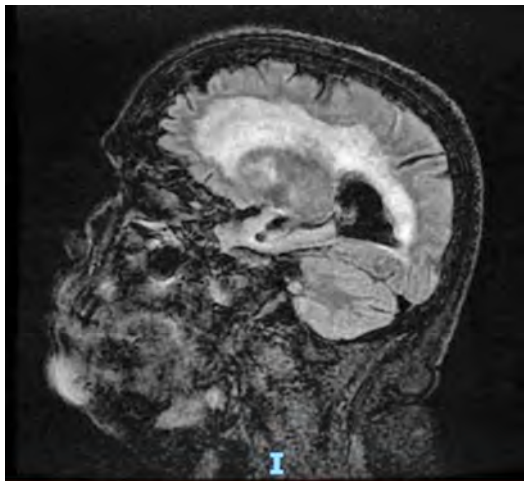
MRI (sagittal FLAIR) evidencing extensive subcortical T2 hyperintensities of both hemispheres

Results: N/A

Conclusion: We present a case of sudden vision loss as a form of CADASIL presentation. We intend to demonstrate that NAION may be part of the CADASIL phenotype and may represent a complementary marker of this arteriopathy. Therefore, we consider that the diagnosis of CADASIL should be hypothesized in these cases, particularly in patients with NAION and with other paradigmatic symptoms of this entity.

Disclosure: Nothing to disclose.

EPO-026

A Descriptive Retrospective Review of Cervical Artery Dissection

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Background and aims: Given the low incidence of cervical arterial dissection (CAD), the knowledge regarding the natural course, better acute treatment and and secondary prevention is limited.

Methods: Retrospective cohort study of CAD admitted to our hospital between Jan-2017-Dec-2021. Descriptive analysis and univariate comparative study with t-test, chi-square and ANOVA when applicable.

Results: 23 patients (74% with carotid (CD) and 26% vertebral (VD) dissection), 44% female, with a mean age of 55 years. 67% had at least one vascular risk factor. The mean previous mRS was 1. All underwent CTA and/or MR angiography with classic findings. 70% reported headache, 22% trauma/preceding vigorous exercise and 13% tinnitus. 35% had Horner syndrome. Mean admission NiHSS was 6. 1 patient underwent intravenous thrombolysis and 3 thrombectomy. As secondary prevention, 43% were monoantiaggregated, 35% double antiaggregated and 19% were hypocoagulated. The mean discharge NiHSS was 2, mRS at 3 months of 1. Imaging normalization documented in 92%. 1 patient had stroke recurrence. Previous mRS and baseline NIHSS were significantly lower in DV compared to DC. Patients with thrombus did not have a significantly different NIHSS at discharge, however mRS at 3 months was worse with a trend towards higher NIHSS. No differences in functional status were identified between patients with different secondary prevention regimens.

Conclusion: Clinical severity and functional status were worse in CD and dissections with arterial occlusion had a worse long-term outcome. The follow-up of these patients in cohorts after hospitalization is essential for the optimization of vascular risk factors and individualized imaging surveillance.

Disclosure: Nothing to disclose.

EPO-027

Evaluation of stroke prognostication using age and NIH Stroke Scale index (SPAN-100) in delayed thrombolysis

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Background and aims: The efficacy of delayed intravenous tissue plasminogen activator (tPA), beyond the 4.5 hours window, is evolving. Advanced age and high admission National Institutes of Health Stroke Scale (NIHSS) score are proposed to adversely affect the outcome of delayed thrombolysis and limit the inclusion criteria. The summation of patient age and admission NIHSS score was introduced as the SPAN-100 index as a tool of prediction of the clinical outcome after acute ischemic stroke (AIS). We aimed to assess the SPAN-100 index in AIS thrombolysed patients after 4.5 hours.
Methods: The SPAN-100 index was applied to AIS patients receiving delayed IV thrombolysis (IVT) after 4.5 hours. Patients demographics, risk factors, clinical, laboratory and radiological data, mismatch evidence, treatment onset and modality, NIHSS score at baseline and at discharge, and 3 months follow-up modified Rankin Scale (mRS) were reviewed. SPAN-100 score ≥ 100 is classified as SPAN-100 positive while score <100 is SPAN-100 negative. Clinical outcomes, death and intracerebral hemorrhage (ICH) incidences were compared between SPAN100 positive and negative groups.
Results: SPAN-100-positive delayed IVT-patients (11/136) had a 6-fold increased risk for unfavorable outcome compared to SPAN-negative patients (OR 6.34; 95% CI 1.59–25.24 p=0.004), however there was no relation between the SPAN-100 positivity and mortality or ICH.
Disclosure: The authors have nothing to disclose.

EPO-028

Comparison of the inflammatory parameters between the patients with stroke and OSAS-stroke comorbidity

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Background and aims: It was planned to evaluate and compare the inflammatory parameters in the patients with ischemic stroke and those with association of ischemic stroke and OSAS. Our other objective was to evaluate the relationship between these parameters separately evaluated in both groups of patients with etiology, prognosis, and severity of disease.
Methods: The study included 100 patients with diagnosis of ischemic stroke, 70 patients with association of ischemic stroke and OSAS, and 100 healthy individual as the control group. All patients underwent detailed examination and their NIHSS was estimated. The inflammatory parameters were compared among all these subgroups.
Results: The parameters showing significant difference in the comparison between the general disease groups (OSAS, Stroke-OSAS) and the control group included leukocytes, hemoglobin, platelets, neutrophyles, monocytes, HDL, RDW, ferritin, CRP, fibrinogen, and ratios of neutrophyles/lymphocytes, lymphocytes/monocytes, platelets/lymphocytes, and monocytes/HDL. D-dimer, fibrinogen, and RDW value were found to be significantly different according to the degree of sleep-related respiratory disorders in the Stroke-OSAS group.
Conclusion: As a result: D-dimer, fibrinogen, and RDW value were found to be significantly different according to the degree of sleep-related respiratory disorders in the Stroke-OSAS group. In the evaluation of the ratios, the neutrophyles/lymphocytes ratio as well as lymphocytes/monocytes ratio were found to be the ratios being helpful to determine size of the infarction (by means of NIHSS), and extent of the disease especially in the Stroke-OSAS association.
Disclosure: There is no conflict of interest regarding this abstract.

COVID-19 1

EPO-029

Sex differences in risk factors and outcomes among patients with COVID-19 related ischemic strokes

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Background and aims: Stroke in the course of coronavirus disease (COVID-19) has been shown to be associated with more severe respiratory symptoms and higher mortality. The aim of this study was to evaluate for sex differences in patients with acute stroke and atrial fibrillation, regarding risk factors and outcomes.

Methods: A monocentric retrospective study of 130 patients (76 women and 54 men), aged 45 to 92 years with COVID-19 and ischemic stroke was performed. Comprehensive examination included analysis of the baseline characteristics, risk factors; assessment of neurological status with NIHSS scale. Disability was measured by the modified Rankin scale and Barthel index. Pearson's chi-square test was used to compare categorized proportions. A comparison of discrete variables was conducted using a Mann-Whitney test. A 2-sided p-value <0.05 was considered significant for all statistical tests.

Results: Women were older compared to men (76.7 vs 62.5years, p<0.05). Smoking (p<0.001) was more frequent in men, while atrial fibrillation (p=0.007) and obesity (p=0.045) were more frequent in women. We did not reveal any significant differences of stroke subtypes between genders. At admission and the 14-day from stroke onset, women had higher NIHSS scores compared to men (16.34±3.64 vs 12.1±3.21 and 7.21±2.55 vs 6.1±4.39, respectively, p<0.05). Barthel index score was also higher in women compared to men at 14-day (62.55±16.83 vs 75.21±9.05; p<0.003). At 21-day, 65.8% of women were disabled or deceased, compared to 42.4% of men (p<0.001).

Conclusion: Women with COVID-19 related ischemic strokes were older, with more severe strokes and worse functional outcomes.

Disclosure: Nothing to disclose.

EPO-030

COVID-19 worry among stroke patients during and after the second Nagorno-Karabakh War

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Background and aims: In 2020, the Armenian healthcare system faced a humanitarian crisis because of war along with COVID-19 pandemic. During the 44-day war period the number of COVID-19 patients increased almost 8-fold. The study aimed to determine the level of COVID-19 worry among patients who had acute stroke during and after the war in Armenia.

Methods: An independent sample pre-post design in which the pre-period included the period of war, and the post-period included the post-war period was used. Adult stroke patients from a tertiary care center were enrolled in phone surveys. Descriptive and inferential statistics were used.

Results: We included 122 patients (n=66 for each period), mean age 64.3 years (10.2), 57% male, and reperfusion therapy received by 34.1%. We found no differences in the overall level of current worry for COVID-19 and COVID-19 worry while at the hospital between war and post-war groups (p>0.05). About 28.0% and 26.4% of participants perceived themselves at higher risk of being infected with COVID-19, whereas 34.0% and 39.6% did not know their risk level of being infected (p=0.773) in war and post-war groups respectively. COVID-19 pandemic had worse impact on employment status and health seeking behaviors during war than post-war period (p<0.05).

Conclusion: The overall rating of COVID-19 worry and the perceived risk was low among stroke patients in both periods. Because only a quarter of patients perceived a higher risk for COVID-19, we suggest improving public education on COVID-19 risks, particularly for patients with comorbidities like stroke.

Disclosure: Nothing to disclose.

EPO-031

Dementia does not lead to a worse prognosis for patients with COVID-19: Results from a large Brazilian cohort

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Background and aims: Dementia increases the severity and mortality risk in COVID-19 patients. Scientific data regarding dementia as a risk factor for COVID-19 in Latin America countries is still lacking. Therefore, the study aims to evaluate the clinical characteristics and outcomes of patients with dementia infected with SARS-CoV-2, in a cohort of Brazilian patients.

Methods: This study is part of the Brazilian COVID-19 Registry, a multicentric COVID-19 cohort, with data from 37 Brazilian hospitals. For the analysis, patients were grouped according to the presence or not of dementia, by age, sex, number of comorbidities, hospital, ad year. The following variables were collected: (1) demographics data; (2) clinical characteristics at admission; (3) laboratory findings; and (4) outcomes.

Results: This study involved a total of 590 patients. The median age was 82 (76-87) years and 43.7% were female. The dementia group presented a high prevalence of stroke (14.9% vs 8.1%; p=0.014) and delirium (51.2% vs 25.1%; p<0.001) when compared to controls. Moreover, the patients with dementia presented a lower duration of symptoms (4.0 vs 6.0 days) when compared to the control group. And still, patients with dementia were fewer for intensive care unit (99.7% vs 43.3%, p=0.020) and lower mechanical ventilation requirement (23.4% vs 33.6%, p=0.003) when compared to controls. Despite tendency, the in-hospital mortality did not differ between groups.

Disclosure: The authors declare no competing interests.

EPO-032

Gender differences in stroke during the 4 waves of COVID-19

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Background and aims: The aim of this study was to compare the differences in the number and type of strokes depending on gender and COVID-19 infection status (positive or negative).

Methods: Retrospective study based on Hospital registry of Clinical County Hospital of Brasov, Romania. We evaluated all patients with stroke hospitalized during the fourth waves of COVID-19 pandemic: first wave (14.03.2020–14.05.2020), the second wave (01.10.2020–15.01.2021), the third wave (01.03.2021–15.04.2021) and the fourth wave (10.10.2021–20.11.2021).

Results: During the fourth waves there were 421 patients (54.4% males) with stroke: 341 with ischemic stroke, 68 with hemorrhagic stroke and 12 with TIA. In the first wave there were 63.8% males (4.48% COVID+) and 36.2% females (13.18% COVID+) with stroke. In the second wave there were 51.11% males with stroke (28.26% COVID +) and 48.89% females with stroke (30.68% COVID +). In the third wave 54.29% males with stroke (15.79% COVID+) and 45.71% females with stroke (31.25% COVID+). In the fourth wave there were 48.48% males (34.38% COVID+) and 51.52% females (20.59% COVID+). In every wave. the most common type was ischemic stroke.

Conclusion: In the first 3 waves the incidence of stroke was higher among males. The incidence of stroke in COVID+ patients was higher among females in the firsts 3 waves.

Disclosure: Nothing to disclose.

EPO-033

Approach to the treatment of fatigue and brain fog in long-COVID-19 with hyperbaric oxygen therapy: a case series

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Background and aims: Long COVID-19 is a complication of SARS-Cov-2 infection that can affect 10–20% of infected patients. The most frequent and disabling symptom is fatigue, but patients also report cognitive impairment (brain fog) and depression. There is no specific or effective treatment for these symptoms. Assuming the hypothesis that there is an alteration at the level of mitochondrial metabolism (an energy dysfunction), we have carried out a study using hyperbaric oxygen therapy (HBOT).

Methods: We have studied 5 patients with long COVID-19 affected by severe fatigue, dyspnea and brain fog. Patients received HBOT sessions at 2.4–2.8 ATA, for 90 minutes. Before and one month after HBOT, the patients completed several scales: fatigue severity Scale (FSS) and Modified Fatigue Impact Scale (MFIS), quality of life related to health (EuroQol-5D, Visual Analog Scale (VAS) score), symbol digit modalities test (SDMT), and an episodic memory test (Memory Alteration Test, M@T). Previously, patients gave their written informed consent. The normality of the variables was checked with the Shapiro-Wilk test and comparisons were made using Student's t test for paired samples.

Results: The mean age of the patients was 43.4±5.8 years. The duration of symptoms ranged from 12 to 24 weeks. Patients received between 19 and 50 sessions of HBOT. All patients markedly improved in their physical condition and showed a statistically significant clinical improvement in fatigue, cognitive impairment and quality of life (see table).

Items	BASAL	POST – HBOT	p
FSS score (maximum 63)	55.2 ±8.1	43.2 ±15.9	0.034
MFIS score (maximum 84)	63.2 ±20.2	47.6 ± 21.0	0.033
SDMT score	42.2 ±13.5	47.8 ±16.7	0.040
M@T score (maximum 50)	45.0 ± 2.7	47.4 ± 3.6	0.153
BDI score (maximum 63)	26.0 ± 12.0	20.4 ± 15.9	0.227
Euro-Qol-5D score (maximum 15)	9.0 ± 1.6	7.8 ± 1.9	0.004
VAS score (%)	42.8 ± 24.0	52.4 ± 26.6	0.002

Conclusion: HBOT is an effective treatment for the management of the neurological symptoms of long-COVID, especially for fatigue and brain fog.

Disclosure: The authors declare that there are no conflicts of interest in relation to this abstract.

EPO-034

Unravelling Post-COVID-Symptoms in a Neurological Out-Patient-Clinic

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Background and aims: Following an influx of patients with new neurological symptoms after infection with SARS CoV-2, the department of Neurology at the Medical University of Vienna has established a new outpatient clinic for post-COVID neurological symptoms.

Methods: The data presented here include the first 113 outpatients and were collected from May 2021 to December 2021. All patients signed informed consent prior to semi-standardized interviewing, neurological examination, and referral for further examinations. Interviews focused on new-onset neurological symptoms after SARS CoV-2 infection. Patients with hyposmia were tested with "SNIFFIN sticks".

Results: The majority of patients were female (72.6%) and the mean age was 41.2 years. The median time between infection and onset of symptoms was 1 week (IQR 1–4). Most patients had a mild COVID-19 disease course under home isolation (91.0%), 8.1% were hospitalized, 0.9% required intensive care during infection. The majority of patients (77.0%) reported comorbidities, the most frequent were psychiatric disorders (38.0%). New-onset symptoms after infection included fatigue (75.0%), subjective cognitive impairment and "brain fog" (69.6%), headache (45.5%), and sleep disturbances (36.9%) and were not associated with age, sex or disease course. At the time of presentation, 45.3% of patients reported persistent hyposmia and were tested with "SNIFFIN sticks": thereof 48.3% had no impairment, 44.8% had hyposmia, and 6.9% showed anosmia.

Conclusion: Descriptive data collected in our outpatient clinic showed similar results as previous publications, namely fatigue, cognitive impairment, and headache as the most frequently persistent symptoms up to 19 months after SARS CoV-2 infection.

Disclosure: There is nothing to disclose in regard to the content of this publication.

EPO-035

Impact Of The Lockdown Due To COVID-19 Pandemic In Kyrgyzstan On Logistical Approaches Applied To Stroke Patients

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Background and aims: COVID-19 pandemic has significantly impacted stroke management in Kyrgyzstan, mostly worsening stroke logistics. We aimed to analyze how the lockdown during COVID-19 pandemic affected stroke care in Bishkek.

Methods: We analyzed demographic and logistical parameters in medical records of stroke patients, filled out by specialists of the Emergency Center of Bishkek, Kyrgyzstan in 4 periods (prepandemic, beginning of pandemic, lockdown (March 22, 2020 to May 1, 2020) and the height of the pandemic).

Results: In 478 patients with stroke 80.6% were hospitalized and the rest were refused to be admitted to stroke centers or were triaged due to the shortage of the stroke beds. The median time from the stroke onset till the time of admission in the hospital during lockdown was 7.95 (3.03; 25) while before the pandemic was 6.67 (3.56; 24.8) hours, p=0.001. Stroke patients during lockdown were 2.85 times more likely to develop moderate to severe neurological deficits on the NIHSS (OR= 2.85, 95% CI) and were 1.4 times more likely not to receive antihypertensive therapy with a systolic blood pressure >180 mmHg (OR =1.4, 95% CI) due to the absence of the medicaments in emergency services.
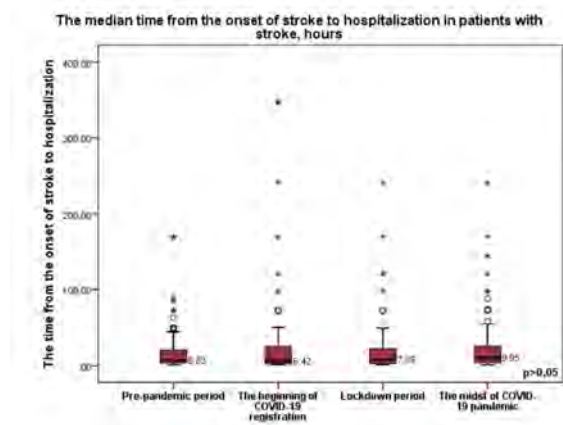
The median time from the stroke onset till the hospitalization in patients with stroke, hours

Conclusion: During the lockdown time of the emergency services arrival to stroke patients significantly shortened due to absence of traffic but time from the stroke onset till the admission to hospitals increased due to the prolonged time in the seek of help.

Disclosure: Nothing to disclose.

EPO-036

A one-year follow-up cohort study of cognitive sequelae of COVID-19 infection in Lombardia

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Background and aims: As the coronavirus pandemic spreads, there is a lot of concern on the extent of the occurrence of the long-COVID syndrome, a long-lasting disorder that arises following infection with SARS-CoV-2.

Methods: Patients healed from COVID-19 from February 2020 to May 2020 were considered for inclusion in this study, regardless of the severity of the disease. Semi-structured phone-interview focused on neurological and cognitive sequelae was administered between February and March 2021 by trained medical staff to guarantee a 1-year follow-up.

Results: Three hundred seventeen patients (mean age 52.9 years, 54.3% female) were eligible. A set of 6 questions asking the occurrence of memory loss, mental slowing, difficulty in attention, errors in naming of words, ability to evaluate meaning difference between two words and self-assessment of cognitive status was used as pre-screening of a second interview in which mental capacity perception assessed by the patient and by a caregiver were asked together with an ItelMMSE questionnaire. A subset of 12.3% did a second interview, of whom only 3/40 tested scored below 24 after adjusting MMSE. Correlation between mental capacity perceived by the proband and caregiver was higher for executive function and orientation (0.98 and 0.91) and lower for language, memory and attention (0.79, 0.73 and 0.71).

Conclusion: At 12 months after acute infection, COVID-19 survivors seem to experience at a low percentage the issue of cognitive dysfunction as compared to other studies. Reasons are timing of the interview, features of included patients or used methodology. A larger cohort of patients is under examination.

Disclosure: Nothing to disclose.

EPO-037

Neurological, cognitive and psychoemotional disorders profile in patients recovered from COVID-19 in Ukraine

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Background and aims: The COVID-19's pandemic leads to increasing of prevalence of new neurological disorders (ND) and an exacerbation of existing once, so it is important to define ND features in patients, recovered from COVID-19.

Methods: 60 patients recovered from COVID-19 (3-5 month after acute period) were assessed by neurological, cognitive (Montreal Cognitive Assessment (MoCA)) and psychoemotional (State-Trait Anxiety Inventory (STAI), Hospital Anxiety and Depression Scale (HADS), Multidimensional Fatigue Inventory (MFI-20)) parameters and quality of life (QoL) (EQ-5D scale). Also, in patients and healthy persons (n=30) interleukin-6 (IL-6) and vascular endothelial growth factor (VEGF) blood levels were observed.

Results: The mean age of patients was 39.8±2.1 years. Most of patients reported symptoms in 1-2 months after the acute period of COVID-19 [Figure 1]. According MFI-20, mean fatigue level was 49.38±1.66 points. According to MoCA, 53.3% patients had cognitive impairment (mean score 25.8±0.3 points). Attention and executive functions, speed of information processing, short-term memory impairments were most frequent. According STAI, most patients had moderate state anxiety and high trait anxiety levels. According HADS, 33.33% of patients had clinical signs of depression (mean score 11.23±0.52 points). All described impairments led to QoL level reduction (EQ-5D mean score 69.76±2.33 points). As compared to healthy persons, patients had elevated IL-6 and VEGF levels, especially after severe COVID-19.
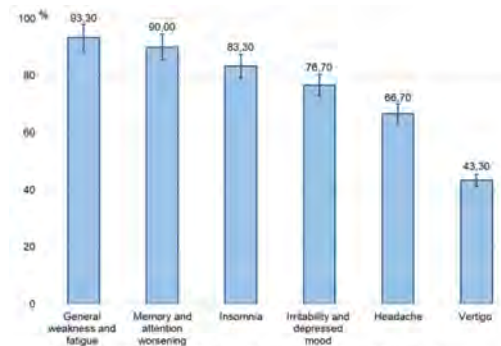
Figure 1. Prevalence of reported psychoneurological symptoms in patients recovered from COVID-19

Conclusion: Insomnia, asthenia, cephalalgia, cognitive and psychoemotional disorders are long termed consequences of COVID-19. They impact QoL and need to be identified and corrected as soon as possible.

Disclosure: Nothing to disclose.

EPO-038

Recall response to COVID-19 antigen is preserved in people with multiple sclerosis on anti-CD20 medications

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Background and aims: Antibody responses to SARS-CoV-2 vaccination are impaired in people with multiple sclerosis (MS) under anti-CD20 therapies. It is however unclear, whether patients who received the basic immunization prior to anti-B cell medication start respond to the COVID-19 booster dose, once B cells are depleted. Aim: To investigate the humoral response to recall antigen by COVID-19 booster vaccines in people with MS (pwMS), who recently started an anti-CD20 therapy compared to people with long-term B-cell depletion.

Methods: We enrolled 15 pwMS who had received booster vaccination on anti-CD20 therapy. Of these, 11 had established anti-CD20 medications and were therefore vaccinated during a continuous state of B-cell depletion (CD20-vaccine cohort). Four pwMS had received the basic immunization prior to anti-CD20 therapy commencement and only the booster dose (vaccine-CD20-vaccine cohort) under conditions of B cell depletion. We assessed SARS-CoV-2 specific antibody responses after booster vaccination.

Results: The booster dose of SARS-CoV-2 vaccination elicited measurable antibody responses in 18% of individuals from the CD20-vaccine cohort compared to 100% from the vaccine-CD20-vaccine cohort. Antibody-levels were significantly higher among patients from the vaccine-CD20-vaccine cohort compared to the CD20-vaccine cohort (mean 951.25±1137.96 BAU/ml, vs mean 12.36±11.94 BAU/ml; mean difference 938 BAU/ml (95% CI: 249–1629 BAU/ml), p <0.0001). Among the vaccine-CD20-vaccine cohort, the booster immunization led to augmentation of spike antibody levels in 75% despite concomitant B cell depletion, and values increased by 3.8–9.4-fold compared to basic immunization.

Conclusion: Our study suggests that antibody production to recall COVID-19 antigens is preserved in pwMS despite concomitant anti-CD20 therapy.

Disclosure: Nothing to disclose in regard to this abstract.

EPO-039

Impact of Covid-19 pandemic in patients with Huntington Disease

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F. Saccà

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Background and aims: If Huntington disease (HD) may represent a risk factor for COVID-19 is debated. The aim of our work was to assess the impact of COVID-19 pandemic on HD disease patients.

Methods: We conducted a telephone interview directed to patients or caregivers, using an ad hoc developed semi-structured questionnaire, composed of two sections (Table 1).

Table 1

Section one: telephone interview to HD patients

Questions	Responses
Patient's Age	
Patient's Gender	o Male o Female
Year of HD diagnosis	
Are you experiencing a decline in your clinical condition since the beginning of the pandemic?	o Yes o No
If yes, which are the domains affected?	
Are you experiencing new sleep disturbances?	o Yes o No
Did you have to stop physiotherapy and speech therapy because of the pandemic?	o Yes o No o I never started them
Did you have to miss medical visits because of the pandemic?	o Yes o No
Did you ever tested positive for COVID19?	o Yes o No

Section two: telephone interview to HD patients who tested positive for COVID19

Questions	Responses
Date of the first positive nasopharyngeal swab	
Date of the first negative nasopharyngeal swab	
Did you experience symptoms?	o Yes o No
If yes o Which type of symptoms?	
o How long did these symptoms last?	
o Did you achieve clinical resolution?	o Yes o No
o If you didn't achieve clinical resolution, which symptoms are you still experiencing?	
Did you start a medical therapy?	o Yes o No
If yes, which drugs did you use? Did you require hospitalization?	o Yes o No
If yes o in which type of hospital unit did you receive care?	o Non-intensive Care unit o Intensive Care unit
o Did you require respiratory support?	o Yes o No
o If yes, which type of respiratory support did you use?	o Yes o No
Did you undergo any radiological examination?	o Yes o No
If yes, which type of examination did you undergo?	

Results: We interviewed a total of 112 HD patients. Since the beginning of the pandemic, 72.3% of patients experienced a progression of the basal clinical condition (Figure 1). 31% of patients changed their pre-existing psychiatric therapy or started a new one. Interestingly, 50% described the onset of a new sleep disorder. Analysis of the standards of care showed that 78% of the patients missed their scheduled medical visit and 64.7% stopped physiotherapy. Within the observed cohort 10.8% of patients tested positive for COVID-19 infection, 6 experienced symptoms and 5 of them had comorbidities. Despite resolution of the infection 3 patients underwent a rapid progressive and generalized clinical worsening.

Figure 1
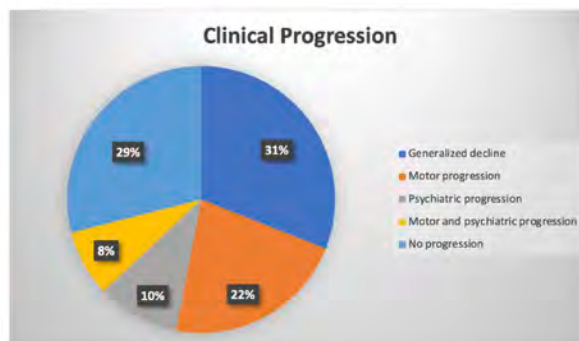
Conclusion: Our study was among one of the first to investigate the impact of the COVID-19 pandemic on HD patients. Our results shown that most patients experienced a global clinical worsening since the beginning of the pandemic. Despite the more severe confinement measure adopted by HD patients, the incidence, and the morbidity of COVID-19 infection seemed to be higher than the general population. Whether HD represents per se a risk factor for COVID-19 is unclear. However, a negative impact of HD on the immune system has been described, and difficulties in swallowing and clearing secretions may have negatively impacted the disease course.

Disclosure: Nothing to disclose.

EPO-040

Specific neurologic nomplications of hospitalized patients with COVID-19 infection – retrospective study

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Background and aims: Various neurologic manifestations of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) have been reported, ranging from anosmia to severe encephalomyelitis. Hereby we aimed to investigate epidemiology of specific neurologic diagnoses in patients with COVID-19 and analyze them statistically.

Methods: Data of all patients with PCR confirmed SARS-CoV-2 infection at First University Clinic of Tbilisi State Medical University have been collected and investigated retrospectively. We included all patients who were hospitalized from 01/01/2021 until 31/12/2021. Patients with prior history of neurologic disorders were excluded.

Results: In selected timeline, 8,447 patients were hospitalized. Out of total cases, 50 (0.59%) patients were diagnosed with following neurologic complications: Encephalopathy – 25 (0.29%), mean age – 74,45, 55% female; Seizure – 12 (0.14%), mean age – 57.41, 58.3% male; Ischemic stroke – 9 (0.11%), mean age – 67.7, 55% male; Anoxic injury –1 (0.01%), 79 year old male and Brain edema – 3 (0.03%), mean age – 69, 66.7% male. Mean age of totally reported 50 patients is 64.17 (47–90), 53.33% of them being male and 46.67% Female.

Percentage Of Selected Neurologic Complications In Hospitalized Patients With COVID-19
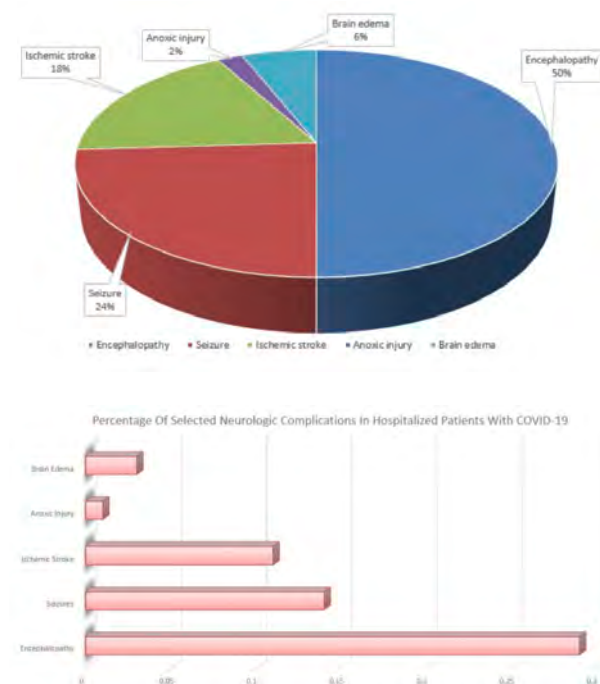
Conclusion: It must be emphasized that, specific neurologic diagnoses are relatively rare but are associated with poor prognosis. While, it is true that SARS-CoV-2 exerts its effects on nervous system, exact mechanisms of described devastating complications are still to be explained.

Disclosure: Nothing to disclose.

EPO-041

Bell's palsy occurrence during COVID-19 outbreaks, a monocentric retrospective observational study

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Background and aims: Bell's Palsy (BP) has been associated with both COVID-19 infection and COVID-19 vaccination. We aimed to evaluate the impact of the COVID-19 pandemic on real-world BP epidemiology.

Methods: We retrospectively collected data from patients admitted for BP to San Raffaele Hospital Emergency Department from January 2008 to October 2021. We divided cases into three different cohorts: 1) before March 2020 (before the pandemic), 2) from March 2020 to March 2021 (first year of the pandemic) and 3) after March 2021 (during the extensive vaccination plan implemented in Italy). Exact Poisson test was used to analyze the BP admission frequency and Chi-square was used to examine the clinical and epidemiological differences between the cohorts.

Results: We observed a significant increase in BP accesses during the first year of the COVID-19 pandemic compared with the previous years (95 vs 75.8±9.35; p=0.018). These data were confirmed after correcting for accesses for any reason, accesses for neurological reasons, and suspected stroke cases. Patients affected by BP during the COVID-19 pandemic had an increased autoimmune comorbidity (p=0.007). During the first summer trimester after the implementation of the vaccination plan, a substantial decrease in BP admission was detected.

Conclusion: Our monocentric data showed an increase in hospital accesses for BP during the first year of pandemic, and a rescue of the historical frequency in the first trimester after the implementation of the vaccination plan. Additional studies are needed to determine the epidemiolocal link between COVID-19 and BP.

Disclosure: The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

EPO-042

COVID-19 infection and vaccinations – An analysis of 51 infected and 561 completely vaccinated out-patients

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Background and aims: From the beginning of the SARS-COVID-19 pandemic on and during the course of the vaccination program people with epilepsy (PWE) were concerned about a potentially elevated risk of the infection or the vaccinations.

Methods: We collected consecutive out-patients with approved diagnosis of epilepsy, followed them until the end of 2021 and assesses the outcome of proven infections or complete vaccinations.

Results: At data cut-off 612 PWE had undergone an infection (n=51) or full vaccination (n=561). Infected PWE: 39 (75%) presented with symptoms. 5 (9.8%) had a severe course with one death. The most frequent symptoms comprised influenza-like symptoms (48.7% of infected PWE with symptoms), anosmia (28.2%) and ageusia (20.5%). The mean duration of symptoms was 20 days. Unequivocal seizure increases of seizure relapses after sustained seizure freedom during the infection occurred in 4 PWE (7.8%). Vaccinated PWE: A total of 105 PWE reported adverse events (AEs) (18.7% of all vaccinated PWE). The leading AEs comprised fatigue (50.5%% of the vaccinated PWE with symptoms), fever and headache (21.0% each). 93.3% of the reported AEs lasted ≤1 week. Unequivocal seizure increases or seizure relapses after sustained seizure freedom occurred in 8 PWE (1.4%). The comparison between infected and vaccinated PWE revealed a statistically significant higher seizure risk in the infected group (p=0.0016).

Conclusion: We did not find a different course of the infections compared with the general population. The vaccinations were generally well tolerated. Seizure aggravations occurred significantly more frequently in the infected group.

Disclosure: No conflicts of interest.

EPO-043

Antibody Response after COVID-19 Vaccination in IVIg Dependent Immune Neuropathies: an Observational Study

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Background and aims: This study aimed to assess the prevalence of anti-SARS-CoV-2 antibodies in therapeutic immunoglobulin and their impact on the immune response to COVID-19 mRNA vaccine in patients with intravenous immunoglobulin (IVIg) dependent immune neuropathies.

Methods: 46 different IVIg and subcutaneous IgG (SCIg) samples were analyzed for anti-SARS-CoV-2 IgG by ELISA and chemiluminescent microparticle immunoassay (CMIA). Blood sera of 16 immune neuropathy patients (mean age 65±16 years, 25% female) were prospectively analyzed for anti-SARS-CoV-2 IgA, IgG, and IgM before and one week after IVIg infusion subsequent to consecutive COVID-19 mRNA vaccine doses and 12 weeks thereafter. Forty-two healthy subjects were recruited as a control group (mean age 42±13 years, 83% female).

Results: 52 percent of therapeutic immunoglobulin samples contained anti-SARS-CoV-2 IgG. All patients with immune neuropathies showed anti-SARS-CoV-2 IgG reactivity after COVID-19 vaccination. Anti-SARS-CoV-2 IgA titers significantly decreased 12–14 weeks after vaccination (p=0.02) whereas IgG titers remained stable (p=0.2). IVIg did not affect anti-SARS-CoV-2 IgA/IgG serum titers in immune neuropathies (p=0.69). IVIg-derived anti-SARS-CoV-2 IgG did not increase serum anti-SARS-CoV-2 IgG titers (p=0.67).

Conclusion: IVIg does not impair the antibody response to COVID-19 mRNA vaccine when administered a minimum of two weeks after each vaccine dose. The infusion of current IVIg preparations that contain anti-SARS-CoV-2 IgG does not enhance serum anti-SARS-CoV-2 IgG reactivity.

Disclosure: No study-related funding was obtained.

Epilepsy 1

EPO-044

Outcomes by Seizure Type From A Mirroring Clinical Practice Study of Perampanel in Adults and Adolescents (AMPA)

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Background and aims: AMPA (NCT04257604; Study 501) was a multicentre study that evaluated the effectiveness of adjunctive perampanel in patients with focal-onset seizures (FOS), with/without focal to bilateral tonic-clonic seizures (FBTCS), in a real-life clinical setting in Italy. We report a post hoc analysis of efficacy and safety by seizure type (FBTCS, FOS with/without FBTCS or all seizures).

Methods: Patients aged ≥12 years with insufficiently controlled seizures while receiving 1–3 anti-seizure medications were prescribed adjunctive perampanel per the approved indication. Seizure diaries and treatment-emergent adverse events (TEAEs) were verified at study visits (baseline and after 3/6/12 months of treatment). Primary endpoint: percentage change from baseline in seizure frequency/28 days at 6 months (secondary endpoint: 12 months); other secondary and safety endpoints: 50% and 75% responder, seizure-freedom and retention rates and TEAEs over 12 months.

Results: Of the 234 patients with FOS who received perampanel (Safety Analysis Set [SAS]; with FBTCS, n=90; without FBTCS, n=144), 135 completed the study (with FBTCS, n=55; without FBTCS, n=80). Overall, 202 patients had baseline/post-baseline seizure data and formed the Intent-to-Treat (ITT) Analysis Set (with FBTCS, n=80; without FBTCS, n=122). Median percent reductions in seizures and 50% and 75% responder and seizure-freedom rates were higher for FBTCS alone versus all seizures in patients with/without FBTCS (ITT; Figure 1). Retention rates and TEAE incidences were comparable between patients with/without FBTCS (SAS; Figure 2 and Table 1).
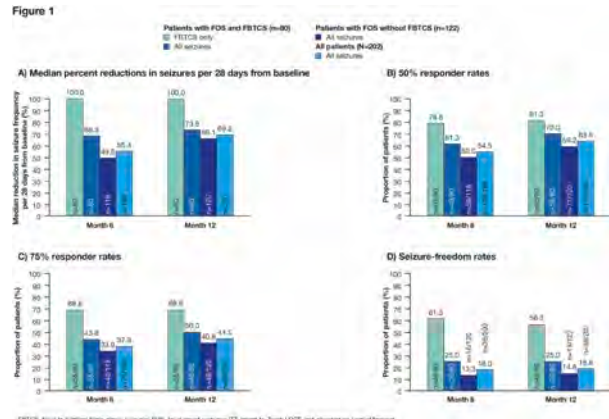
Figure 1. (A) Median percent reductions in seizure frequency per 28 days from baseline, (B) 50% responder rates, (C) 75% responder rates and (D) seizure-freedom rates by seizure type using LOCF analysis in the AMPA study (ITT Analysis Set)
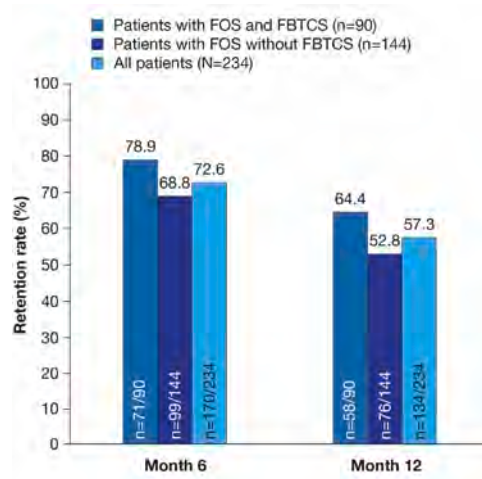
Figure 2. Retention rates by seizure type in the AMPA study (Safety Analysis Set)

	FOS with FBTCS (n=90)	FOS without FBTCS (n=144)	All patients (N=234)
TEAEs, n (%)	51 (56.7)	81 (56.3)	132 (56.4)
Treatment-related TEAEs, n (%)	43 (47.8)	68 (47.2)	111 (47.4)
Serious TEAEs, n (%)	5 (5.6)	9 (6.3)	14 (6.0)
Deaths	0 (0.0)	0 (0.0)	0 (0.0)
TEAEs leading to perampanel dose adjustment, n (%)	32 (35.6)	56 (38.9)	88 (37.6)
Withdrawal	13 (14.4)	32 (22.2)	45 (19.2)
Dose reduction	16 (17.8)	19 (13.2)	35 (15.0)
Pharmacologic therapy	6 (6.7)	12 (8.3)	18 (7.7)
Most frequently reported TEAEs (≥2% patients in overall study population), n (%)			
Dizziness/vertigo	22 (24.4)	29 (20.1)	51 (21.8)
Irritability	4 (4.4)	16 (11.1)	20 (8.5)
Somnolence	7 (7.8)	12 (8.3)	19 (8.1)
Balance disorder	2 (2.2)	7 (4.9)	9 (3.8)
Behaviour disorder	4 (4.4)	5 (3.5)	9 (3.8)
Asthenia	1 (1.1)	4 (2.8)	5 (2.1)

FBTCS, focal to bilateral tonic-clonic seizures; FOS, focal-onset seizures; TEAE, treatment-emergent adverse event

Table 1. Overview of TEAEs and the most frequently reported TEAEs by seizure type during the AMPA study (Safety Analysis Set)

Conclusion: Adjunctive perampanel in a real-world setting was efficacious and generally well tolerated in adult and adolescent patients with FOS, with/without FBTCS.

Disclosure: Funding: Eisai S.r.l. Umberto Aguglia has no real or apparent conflicts of interest to disclose in relation to this work.

EPO-045

Long-term seizure outcome in patients with acute symptomatic seizures secondary to Autoimmune Encephalitis

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Background and aims: Seizures are one of the hallmark manifestations during the acute phase of Autoimmune Encephalitis (AE), but the long-term outcome of seizures and the risk of developing epilepsy varies among different published series and is still a matter of study. We present the long-term seizure outcome data from AE patients followed up in our center.

Methods: From our center's cerebrospinal fluid biobank, we selected patients who met diagnostic criteria for definitive or probable AE and had experienced symptomatic seizures in the acute phase. We retrospectively assessed serological status; seizure outcome in the last follow-up, and use of antiseizure medication (ASM) in the long term.

Results: We identified 9 definite AE patients with seizures during the acute phase. Patients had antibodies against LGI1 (n=2), NMDAR (n=2), MOG (n=1) and onconeuronals (n=2). From the two seronegative patients, one of them had Immune Checkpoint Inhibitors related AE. After a median follow-up of 7.5 months (range 3–24), most patients (8/9) were on ASM in the last follow-up despite the 88.8% (8/9) achieved seizure freedom. The patient who continued to experience seizures was seronegative EA despite four antiepileptic drugs.
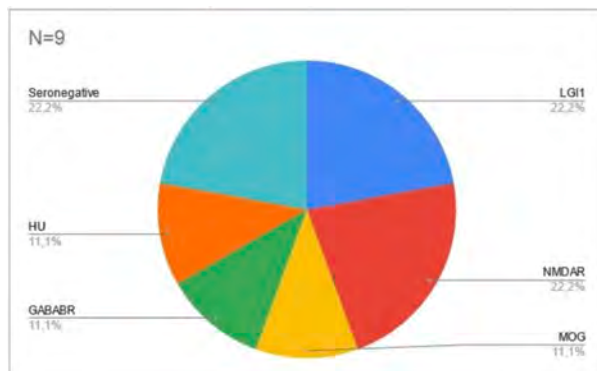
Identified antibodies
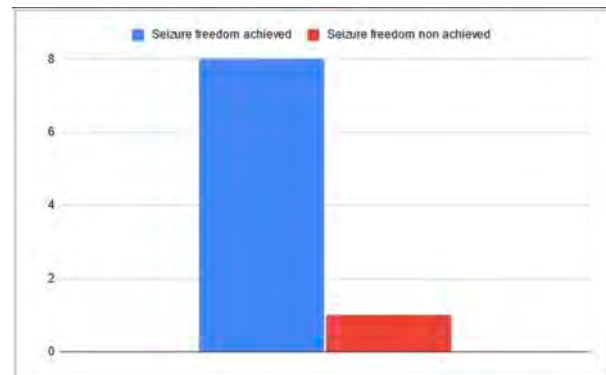
Percentage of seizure freedom

Conclusion: In our series of AE patients with seizures during the acute phase, most of them achieved seizure freedom in the long-term follow-up but the majority are still on ASM. The need for chronic ASM in seizure-free AE patients should be assessed. The absence of neural autoantibodies may be a risk factor for long-term epilepsy in AE patients.

Disclosure: Nothing to disclose.

EPO-046

Abstract withdrawn

EPO-047

SEEG-guided radiofrequency thermocoagulation in refractory focal epilepsy.

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Background and aims: Epilepsy surgery may be effective for patients with drug-resistant focal epilepsy. When intracranial EEG is required in the presurgical evaluation, depth electrodes can be used to destruct or disrupt epileptogenic zone using radiofrequency thermocoagulation (RFTC). RFTC is a minimally invasive ablative option for refractory focal epilepsy.

Methods: A retrospective chart review was conducted of all patients who underwent stereo EEG- guided RF-TC at our center. Total number of patients with follow-up more than 6 months were 49.

Results: The mean age of onset was 24.2 years and the mean age at SEEG was 35.2 years. MRI lesions were not identified in 65 % of the series. 56.5% of the patients were seizure free at 1 month. The mean duration of improvement was 4.8 months. 4 patients were seizure free for >12. 4 patients had functional deficits post-procedures, transient in 3 patients and prolonged in one of whom. 3/4 were anticipated following the results of cortical stimulation. Multivariate analysis found 2 independent criteria linked to RFTC efficiency one month after RFTC: frequency of the seizures before RFTC and number of contacts used.

MRI (axial T2) of RFTC in postcentral gyrus in 12 h. Destruction zone and edema zone.
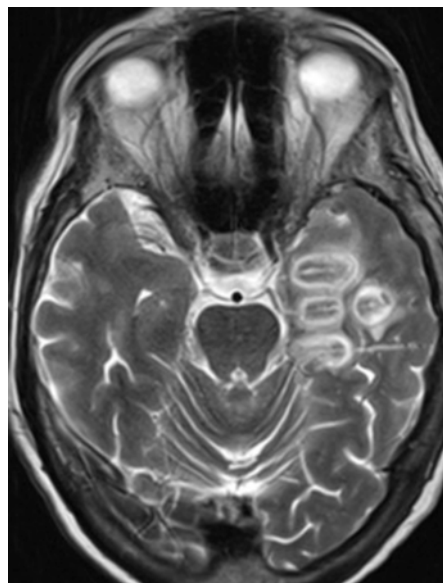
MRI (axial T2) of RFTC in medial structures of the left temporal lobe in 12 h. Destruction zone and edema zone.

MRI (axial T2) of RFTC in precentral gyrus in 12 h. Destruction zone and edema zone.

Conclusion: RFTC is a safe method providing important predictive information for surgical resection. An improvement in seizure frequency, often transient, is seen in 2/3 of our patients. RFTC could be useful as a palliative technique for patients with an epileptogenic zone overlapping with eloquent areas, with minimal risk of complications.

Disclosure: Nothing to disclose.

EPO-048

Health-related quality of life between epilepsy patients with sleep-related versus wake seizures

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Background and aims: Epilepsy is a chronic neurological disorder characterized by recurring seizures. Epileptic seizures may be occurring from sleep, from the awake state, or combined. Compared to the general population health-related quality of life (HRQOL) in patients with epilepsy (PWE) is lower. We aimed to reveal the role of sleep/wake distribution of seizures in formation of HRQOL in PWE.

Methods: We assessed PWE from tertiary epilepsy and sleep centers. They underwent clinical interview, and were asked about circadian occurrence of seizures. They were further divided into groups: patients with seizures in wake (WSG) and patients with sleep-related seizures (SSG). HRQOL in PWE was assessed by SF-36 questionnaire, consisting of 8 domains: D1 – Physical Functioning, D2 – Physical Role-Limitations, D3 – Role Limitations Due to Emotional Problems, D4 – Energy/Fatigue, D5 – Emotional Well-Being, D6 – Social Functioning, D7 – Pain, D8 – General Health.

Results: Our study involved 148 PWE (mean age – 35.6, SD – 13.6; female – 48.2%), WSG participants - 119 and SSG participants - 29. The SF-36 values for both groups are given in means for each domain representing the WSG/SSG ratio: D1 ? 66.0/80.7 ($p<0.05$), D2 ? 39.1/55.7 ($p>0.05$), D3 ? 40.9/49.9 ($p<0.05$), D4 ? 50.7/60.3 ($p>0.05$), D5 ? 51.4/61.8 ($p>0.05$), D6 ? 60.9/73.5 ($p<0.05$), D7 ? 63.4/72.8 ($p>0.05$), D8 ? 48.3/51.0 ($p>0.05$).

Conclusion: HRQOL was lower in patients with epilepsy who had seizures in wake, and was better in patients with sleep-related seizures in domains related to physical, emotional and social health.

Disclosure: Nothing to disclose.

EPO-049

Clinical characteristics of patients achieving seizure freedom in a phase 2 trial evaluating adjunctive cenobamate

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Background and aims: Cenobamate is an antiseizure medication (ASM) approved in Europe as adjunctive therapy for adults with inadequately controlled focal seizures. This post-hoc analysis examined baseline clinical characteristics of patients who became seizure free with cenobamate treatment during the open label extension (OLE) of Study C017.

Methods: Adults with focal seizures despite treatment with 1-3 concomitant ASMs completed the double-blind treatment period with ≥1 year of follow-up. Post-hoc analysis of patients who achieved seizure freedom (zero seizures for ≥1 year) examined duration of epilepsy, concomitant ASMs, number of previously failed ASMs, and seizure type reported in these patients.

Results: As of June 2020, 23.2% (65/280) of participants achieved seizure freedom for ≥1 year from the first day of the OLE study. Seizure free patients had a median duration of epilepsy of 24.2 years compared with a median duration of 24.4 years for patients who did not achieve seizure freedom. Analysis of concomitant ASM grouped by mechanism of action found that 25.5% of those taking concomitant GABAA modulators and 23.5% of those taking GABAA modulators with benzodiazepines or sodium channel blockers were seizure free for ≥1 year. Among patients who experienced secondarily generalized tonic-clonic seizures, focal onset unaware seizures, or focal onset aware seizures at baseline, 27.6%, 22.3%, and 17.5% achieved seizure freedom for ≥1 year, respectively.

Conclusion: Nearly a quarter of patients treated with cenobamate experienced total seizure freedom for at least 1 year in the long-term follow-up. This proportion was generally consistent across diverse types of patient characteristics at baseline.

Disclosure: Studies Study C021 (NCT02535091) sponsored by SK Life Science, Inc. (Paramus, NJ, USA) and these analyses were supported by Angelini S.p.a. (Rome, Italy).

EPO-050

Functional outcome in NORSE and FIRES patients treated with immunotherapy: a systematic review

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Background and aims: To determine the frequency of patients with NORSE and FIRES treated with immunotherapy (IT) that achieved a good functional outcome.

Methods: We performed a systematic review of the literature through MedLine and EMBASE. Studies with ≥5 patients with NORSE or FIRES; at least one patient treated with IT; and where a good functional outcome can be determined were included. Good functional outcome was defined as a modified Rankin score (mRS) ≤2 in the last available follow-up. Only patients with known functional outcome were included for analysis. The outcome in patients without IT was also obtained for comparison.

Results: 17 studies (6/17 FIRES studies) with a total of 161 patients were included. A total of 141/161 (87.5%) received IT. In patients who received IT a good functional outcome was achieved in 56/135 (41.4%) and 20/121 (16.5%) died; compared to 6/20 (30%) and 3/14 (21%) respectively in patients without IT. For each IT type, a good functional outcome was achieved in: 36/89 (40.4%) for glucocorticoids; 27/71 (38%) IVIg; 11/37 (29.7%) plasma exchange; 5/17 (29.4%) rituximab; and 2/13 (15.3%) cyclophosphamide.

Conclusion: IT in NORSE and FIRES is frequent despite the absence of randomized clinical trials. Patients with second-line therapy obtained a lower frequency of good prognosis, probably because they suffer a more severe and refractory illness. Despite the use of IT, the majority of patients with NORSE and FIRES remain in a situation of dependency and mortality is high.

Disclosure: Nothing to disclose.

EPO-051

Evolutionary neurodvelopment in children with epileptic and developmental encephalopathies

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Background and aims: According to the 2017 revision of the ILAE classification, the term "developmental and epileptic encephalopathy" (DEE) is part of the spectrum of severe epilepsies characterized by early-onset seizures and refractory seizures that occur in the context of impaired cognitive and behavioral development independent of onset of epilepsy.

Methods: Clinical and paraclinical outcomes of 17 children diagnosed with DEE were assessed. Evaluation period - 5 years. Examinations: Video EEG monitoring, brain MRI, psychological - Raven test, Beck scale.

Results: Of the 17 children, S–mul Lennox–Gastaut was confirmed in 4 (23.5%), 3 (17.64%) cases – S–mul West, 4 (23.5%) – epilepsy with continuous peak discharge – slow wave during sleep (CSWS), 2 (11.76%) – S-m Dravet, 2 (11.76%) – myoclonic–atonic epilepsy, 1 (5.88%) case – S–mul Ohtahara and 1 (5.88%) case – structural epilepsy as a result of tuberous sclerosis complex. 15 (88.23%) children remained resistant to antiepileptic therapy. 16 (94.11%) – were confirmed with varying degrees of impairment of cognitive and behavioral development. Children (31.25%) with up to 10 generalized seizures per week and antiepileptic treatment with 2 drugs, were diagnosed with a moderate degree of psycho–verbal retardation, and those with more than 10 generalized seizures per week (68.75%) and treatment with 3 or more antiepileptics – with severe psycho–verbal retardation. The cognitive decline tested in dynamics was characteristic in 94.11% of children.

Conclusion: Early identification of EDE could increase the chances of targeted antiepileptic treatment to improve cognitive impairment and the quality of life of affected children.

Disclosure: Developmental and epileptic encephalopathy, evolutionary neurodevelopment, Video EEG monitoring, brain MRI, psychological - Raven test, Beck scale.

EPO-052

Event-related potentials in the assessment of cognitive performance in patients with epilepsy of unknown etiology

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Background and aims: Event-related potentials (ERP) are used in the evaluation of cognitive performance in the course of central nervous system disorders. The aim of the study was an assessment of ERP parameters in the patients with epilepsy of unknown etiology, with regard to clinical and neuropsychological findings.

Methods: The study comprised 50 patients with epilepsy of unknown etiology (6 men, 44 women, aged 35.6) and 46 healthy, age- and sex-matched controls. Auditory ERP were performed in both groups and P300 component parameters were compared between them. In the group of patients with epilepsy, the relationships were analyzed between P300 parameters and clinical characteristics of epilepsy, electroencephalography (EEG) results and performance in neuropsychological tests (Tab. 1).

Results: In the study group, abnormal result of at least one neuropsychological test was found in 43 (86%) of patients and 33 (66%) failed in more than one test (most commonly those evaluating verbal memory, attention and executive functions (Tab. 1)). Median P300 latency was significantly prolonged in the study group compared to the controls Tab. 2). Significant relationships were observed between P300 parameters and duration of epilepsy, type and frequency of seizures and polytherapy. Median P300 amplitude was lower in the subjects with abnormal EEG. No differences in P300 parameters were found between the patients with or without cognitive impairment revealed in neuro-psychological tests (Tab. 3).

Table 2. Comparison of P300 parameters in the patients with epilepsy and the controls (25Q – 25 quartile; M – median; 75Q – 75 quartile)

	STUDY GROUP (n=44)			CONTROL GROUP (n=46)			
	25Q	M	75Q	25Q	M	75Q	
P300 latency							
Fz	316.8	356.8	370.0	305.0	321.0	335.0	p=0.00005
Cz	315.0	355.3	367.8	304.0	324.0	335.0	p=0.00019
Pz	322.5	354.0	369.0	305.0	322.5	339.0	p=0.00004
P300 amplitude							
Fz	3.68	5.40	8.35	4.00	6.73	10.00	p=0.218
Cz	5.18	6.93	9.83	4.95	7.35	10.00	p=0.449
Pz	6.55	8.20	11.25	5.80	8.15	11.60	p=0.882

Table 3. Significant relationships between P300 parameters and epilepsy-related variables (R – Spearman's Rank correlation coefficient; 25Q – 25 quartile, M – median, 75Q – 75 quartile; ms – millisecond; mV – millivolt; EEG – electroencephalogram)

	DURATION OF EPILEPSY						
P300 latency							
Fz		p=0.0116			R=0.38		
Cz		p=0.00627			R=0.41		
Pz		p=0.00708			R=0.40		
	TYPE OF SEIZURES						
	focal onset			generalized onset			
	25Q	M	75Q	25Q	M	75Q	
P300 latency (ms)							
Fz	322.5	362.3	391.5	306.5	349	360	p=0.0255
Cz	327	359.5	391.5	310.5	345.8	359.5	p=0.0272
Pz	337	358	389.5	313.5	347.8	357	p=0.00427

	FREQUENCY OF SEIZURES												
	>1/week			1/week- 1/month			1/month- 1/year			<1/year			
	25Q	M	75Q	25Q	M	75Q	25Q	M	75Q	25Q	M	75Q	
P300 amplitude (mV)													
Fz	2.1	3.65	5.2	5.05	7.8	9.4	5.5	7.2	11.4	5	5.3	10.1	p=0.0177
Cz	2.7	5.85	8.1	6.0	8.25	11.5	6.15	7.45	11.5	4.5	6.7	10.05	p=0.120
Pz	4.8	7.5	8.7	7.55	9.55	12.45	7.1	7.8	8.95	6.4	9.5	14.9	p=0.223

	TREATMENT						
	monotherapy			polytherapy			
	25Q	M	75Q	25Q	M	75Q	
P300 latency (ms)							
Fz	306.5	320.3	355	353	362.3	377	p=0.00997
Cz	310.5	319.5	349	355	360	373.5	p=0.00498
Pz	316	327	352	353	358	370.5	p=0.00796
	EEG						
	no abnormalities			epileptic discharges			
	25Q	M	75Q	25Q	M	75Q	
P300 amplitude (mV)							
Fz	4.45	7.20	8.70	3.53	5.25	8.25	p=0.393
Cz	6.93	9.33	11.50	4.83	5.78	6.75	p=0.00101
Pz	6.33	8.70	13.23	6.55	7.63	9.53	p=0.309

Conclusion: P300 component of ERP may be used as an electrophysiological marker of cognitive impairment in patients with epilepsy of unknown etiology, parallel to neuropsychological testing.

Disclosure: The authors have nothing to disclose.

EPO-053

Abstract withdrawn

Table 1. Impaired cognitive performance in the study group based on results of neuropsychological tests (AVLT – Rey Auditory Verbal Learning Test, ROCF – Rey-Osterrieth Complex Figure, TMT – Trail Making Test, WAIS-R – Wechsler Adult Intelligence Scale, VFT – Verbal Fluency Test)

TEST	No (%) of subjects with abnormal results
AVLT	31 (62%)
ROCF	17 (34%)
TMT	28 (56%)
WAIS-R Digit Span Test	7 (14%)
WAIS-R Similarities Test	1 (2%)
VFT	19 (38%)
≥ 1 abnormal result	43 (86%)
≥ 2 abnormal results	33 (66%)

EPO-054

Epilepsy and employment: classification of workplaces and optimized legislation in Austria – a qualitative study

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Background and aims: People with epilepsy face difficulties in obtaining or keeping employment. The question whether epilepsy must be disclosed during the application process is of central importance. In extreme cases, people with epilepsy can be dismissed under the term of violation of confidence.

Methods: 12 personnel managers and five occupational health practitioners underwent a telephone interview concerning the opportunities and limitations of job applications by people with epilepsy in Austria. The interviews were analyzed by the qualitative method of content analysis (Kuckartz). The legal situation was also analyzed.

Results: Employers are confident that co-workers with epilepsy can be managemed well in case a value system and first responders are in place. The Austrian law permits only retrospective juridical clarification. The authors developed a classification system for work places with "D-0" meaning no health or financial danger (e.g. office workers), "D-1" poses still no health hazard but includes regular work with cash (e.g. salespersons), and "D-2" with potential medical implications for the person with epilepsy or any other person at the workplace (e.g. industrial worker). With D2, occupational health practitioners evaluate the applicant`s medical fitness for the job without disclosing medical details. We designed a "compartment model of medical information in the application process" to guarantee that the occupational physician is the only person who learns about the applicant`s medical details.

Conclusion: A practical and simple classification of workplaces and concept for keeping medical information confident are presented. These measures may result in diminishing enacted and felt stigma in the working world.

Disclosure: No conflicts of interests concerning this publication. Markus Leitinger reports travel grants from UCB Pharma and speaker`s honoraria from Eisai, unrelated to the present work.

EPO-055

Hand Postures and Localization in Pediatric Patients at Video EEG Monitorization

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Background and aims: One third of pediatric patients with epilepsy are resistant. Epilepsy surgery can be applied to appropriate patients when antiepileptic therapy is insufficient in resistant epilepsy. Long-term video EEG monitoring is performed to evaluate suitability for epilepsy surgery.

Methods: The hand postures of patients with generalized or focal epilepsy who underwent video EEG monitoring in our department during ictal activity and the relationship of these postures with the epileptogenic zone. Hand postures of patients during ictal activity were classified into six subgroups; fist, politician fist, cup, pincer, extended hand and pointing. Epileptogenic foci of the patients were classified as generalized and focal.

Hand positions

Results: 523 patients who were monitored in the VEM unit were screened, and 55 patients were evaluated. Hand postures were evaluated by three different researchers at different times and independently of each other. The most common epileptic hand postures were "fist" and "politician fist". Extended hand, cup, pointing and pincer postures were seen with decreasing frequency. The epileptogenic zone of 18 patients out of 55 could not be differentiated and was found to be generalized. It was observed that 14 patients originated from the temporal, 9 patients from the frontocentral, 8 patients from the frontotemporal, 3 patients from the temporoparietal, 2 patients from the frontocentrotemporal and 1 patient from the central region.

Conclusion: Fist, politician's fist and extended hand posture were evaluated as contralateral lateralized sign, and pincer, pointing hand and cup postures were evaluated as ipsilateral lateralized signs.

Disclosure: The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

EPO-056

Predictors of Nonconvulsive Status Epilepticus in the Neurology Intensive Care Unit

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Background and aims: Nonconvulsive status epilepticus (NCSE) is a clinical condition with high morbidity and mortality. Early diagnosis and treatment positively affect prognosis. There is a need to determine parameters that can help identify patients who need urgent EEG. In this study, we aimed to determine clinical, laboratory, and radiological parameters that may predict NCSE.

Methods: Patients who underwent video-EEG monitoring (VEM) for possible NCSE in our center between 2009–2020, were identified from patient charts and EEG reports. We recorded demographic data, indication and duration of VEM, history of epilepsy, presence of convulsions before VEM, Glasgow coma scale (GCS) and Sequential Organ Failure Assessment (SOFA) scores, neurological examination findings, use of antiseizure medications (ASM) before VEM, brain MRI characteristics, routine EEG findings before VEM and blood parameters. These variables were compared statistically between patients with and without NCSE.

Results: We included 192 (32 NCSE and 160 non-NCSE) patients. History of epilepsy (p=0.05), convulsions before VEM (p=0.000), use of ASM, epileptiform/ictal discharge in routine EEG (p=0.001) and blood lactate levels (p=0.038) were higher in the NCSE group. History of epilepsy (p=0.01;OR=2.941), epileptiform/ictal discharge in routine EEG (p=0.003;0R=3.668), elevated serum lactate levels (p=0.003;0R=2.58), no eye opening with stimulus (p=0.032;0R=-1.963) and extensor plantar response (p=0.016;0R=2.406) predicted NCSE after logistic regression analysis.

	NCSE n=32 n (%)	Non-NCSE n=160 n (%)	P value
Age (year, median+std, IQR)	59.5 (± 15.7, 50.2-70.7)	63.3 (± 17.4, 56-66)	0.489
Sex			
Male	19 (59.4)	77 (48.1)	0.245
Female	13 (40.6)	83 (51.9)	
Indication of hospitalization			
Ischemic or hemorrhagic stroke	14 (43.8)	110 (68.8)	
Meningoencephalitis	5 (15.6)	10 (6.3)	
Intracranial mass	3 (9.4)	2 (1.3)	
Epilepsy	3 (9.4)	8 (5)	
Autoimmune encephalitis	3 (9.4)	5 (3.1)	
Dementia	0 (0)	5 (3.1)	
Other	4 (12.5)	20 (12.5)	
History of epilepsy	7 (21.9)	14 (8.8)	**0.050**
Convulsions before VEM	20 (62.5)	36 (22.5)	**0.000**
Epileptiform/ictal discharge on routine EEG before VEM	17 (80.9)	27 (38.5)	**0.001**
Antiepileptic usage before VEM	28 (87.5)	97 (60.6)	**0.004**
Indication of VEM			
Altered state of consciousness	13 (40.6)	79 (79.4)	
Abnormal motor movement	19 (59.4)	79 (79.4)	
Not available	0 (0)	2 (1.2)	
Duration of VEM (hour, mean+std, IQR)	89.6 (± 64.3, 41-127.5)	36.8 (±37.7, 17-44)	**0.000**
GCS at onset of VEM			
≤8	17 (53.1)	63 (39.4)	0.150
>8	15 (46.9)	97 (60.6)	
SOFA at onset of VEM			
0-6	21 (65.6)	115 (71.9)	
7-9	10 (31.2)	31 (19.4)	0.359
10-12	1 (3.1)	13 (8.1)	
13-14	0 (0)	1 (0.6)	
Neurologic examination			
Non-cooperated	20 (64.5)	84 (52.5)	0.219
Non-oriented	25 (78.1)	117 (73.1)	0.556
Aphasia-dysarthria	23 (74.1)	129 (81.6)	0.339
No eye-opening with stimulus	17 (53.1)	58 (36.3)	0.074
Abnormal motor response	10 (31.3)	38 (23.8)	0.645
Brisk reflexes	7 (21.9)	25 (15.6)	0.386
Extensor plantar response	13 (40.6)	42 (26.3)	0.101
Radiographic features (present)			
Cortical involvement	29 (90.6)	134 (84.2)	0.426
Unihemispheric-unilobar	2 (6.2)	14 (8.7)	
Unihemispheric-multilobar	9 (28.1)	64 (40)	
Bihemispheric	18 (56.2)	56 (35)	
Basal ganglia/ thalamus involvement	6 (18.8)	40 (25.1)	0.429
Brain stem/ cerebellum involvement	4 (12.5)	40 (25.1)	0.121
Fazekas score			
0-1	12 (37.5)	71 (44.3)	
2-3	19 (59.3)	76 (47.5)	0.331
n/a	1 (3.1)	13 (8.1)	

M: male, F: female; VEM: video-EEG monitoring; GCS: Glasgow coma scale; SOFA: Sequential Organ Failure Assessment; n/a: not available

Table 1: Demographic and clinical characteristics of the NCSE and non-NCSE groups

Variables	NCSE n=32 (%)	Non-NCSE n=160 (%)	P value
Laboratory Findings (abnormal)			
PH	10 (34.4)	36 (25.7)	0.334
Lactate	20 (62.5)	67 (47.8)	**0.038**
Glucose	10 (31.2)	47 (29.4)	0.832
Electrolyte	21 (65.6)	81 (50.6)	0.121
Leucocyte	16 (50)	67 (41.9)	0.397
Renal function tests	2 (6.3)	28 (17.5)	0.110
Liver function tests	10 (31.3)	39 (24.4)	0.415

Table 2: Laboratory findings of the NCSE and non-NCSE groups

Variables	B	SE	Wald	Sig.	EXP(B)	95% CI for EXP(B)	
History of Epilepsy	2.941	1.146	6.581	**0.01**	18.935	2.002	179.124
Epileptiform/ictal discharge on pre-VEM routine EEG	3.668	1.237	8.795	**0.003**	39.185	3.469	442.574
Eye-opening with stimulus	-1.963	0.914	4.617	**0.032**	0.14	0.023	0.842
Extensor plantar response	2.406	0.998	5.811	**0.016**	11.088	1.568	78.422
Elevated serum lactate	2.58	0.862	8.963	**0.003**	13.197	2.437	71.448

Table 3: Predictors of NCSE

Conclusion: These results imply that some clinical symptoms, neurological examination data, EEG findings, and blood values can be used to predict the presence of NCSE. Prospective studies with more patients are needed to validate our findings.

Disclosure: Dr. Sokmen has nothing to disclose. Dr. Ayvacioglu Cagan has nothing to disclose. Dr. Arsava has nothing to disclose. Dr. Topcuoglu has nothing to disclose. Dr. Dericioglu has nothing to disclose.

EPO-057

Risk of hospitalization and death for COVID-19 in persons with epilepsy: the EpiLink Bologna cohort, Italy

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Background and aims: People with epilepsy (PWE) show a paradigmatic pattern of frailty, due to seizures, antiseizure medications-related adverse events and, in the subgroup of people with epileptic encephalopathies (EE), intellectual disability. Data on COVID-19 outcomes in PWE are scarce. We aimed to study the risk of hospitalization and death for COVID-19 in a cohort of PWE from March 1, 2020 to October 30, 2021.

Methods: Historical cohort design (EpiLink Bologna), comparing PWE cohort (adults with at least one outpatient visit in 2018 and 2019 at our epilepsy center, distinguishing focal epilepsy (FE), idiopathic generalized epilepsy (IGE) and EE), with a control population cohort (ratio 1:10) matched for age, sex, comorbidity and residence, living in the Local Healthcare Trust of Bologna (about 800,000 residents). Clinical data were linked to health administrative data.

Results: In both cohorts (EpiLink n=1,576, 1,128 FE, 267 IGE, 148 EE, 32 other; controls n=15,326) 52% were females and mean age was 50 years (SD 18). Hospital admissions for COVID-19 in the whole period were 49 (3.1%) in PWE and 225 (1.5%) in controls. The adjusted hazard ratio in PWE was 2.0 (95% CI 1.4–2.7) (Fig. 1). FE (Fig. 2) and EE (Fig. 3) were the subgroups at higher risk. Two-month risk of death was 18% both in PWE and controls.

Figure 2. Risk of hospitalization in persons with focal epilepsy (PFE) and in the control cohort, period 01 March 2020 - 30 October 2021, Bologna, Italy.
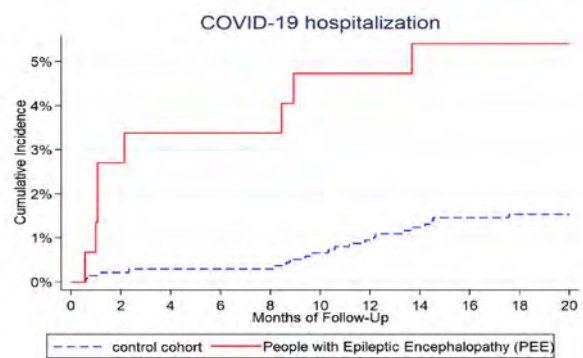
Figure 3. Risk of hospitalization in persons with epileptic encephalopathy (PEE) and in the control cohort, period 01 March 2020 – 30 October 2021, Bologna, Italy.

Conclusion: During the first two epidemic peaks in Bologna, PWE (namely FE and EE) had a doubled risk of COVID-19 hospital admission compared to a control population. Conversely, epilepsy did not represent a risk factor for COVID-19-related death.

Disclosure: Nothing to disclose.

Figure 1. Risk of hospitalization in persons with all kind of epilepsy (PWE) and in the control cohort, period 01 March 2020 - 30 October 2021, Bologna, Italy.

Headache 1

EPO-058

Quality of life in migraine patients in university students in Slovakia

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Background and aims: Migraine was ranked as the second most disabling disorder according to The Global Burden of Disease in 2016. The aim of our study was to determine the impact of migraine on disability in university students.

Methods: We screened 472 university students (356 women, age 22.00±2.40 years) of Comenius University in Bratislava via an online questionnaire for any type of headache. Subsequently, we searched for migraine using diagnostic criteria according to International Classification of Headache Disorders version 3. In positive patients, we used Migraine Disability Assessment questionnaire.

Results: 29.45% (n=139) fulfilled migraine criteria. These subjects missed 1.42±2.68 days at school (absenteeism) due to migraine in the last 3 months. They reported 6.47±8.56 days with reduced productivity by half or more (presenteeism). Inability to do, or reduced productivity of household works counted for 5.08±6.89, and 4.42±4.82 days, respectively. Inability to attend family, social and leisure activities was equal to 3.39±4.89 days. We identified 17.98% (n=25) subjects with no or little disability, 17.98% (n=25) with mild disability, 30.22% (n=42) with moderate disability, and 33.81% (n=47) subjects with severe disability.

Conclusion: We confirmed moderate or severe disability in more than half of students suffering from migraine, leading to significantly decreased productivity. Therefore, targeted screening of patients with migraine is crucial for early and accurate diagnosis and adequate treatment, which might lead to reduction of overall socioeconomic impact of migraine.

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EPO-059

Impact of Eptinezumab on Patient-Reported Outcomes in Patients With Prior Preventive Treatment Failures

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Background and aims: In DELIVER, eptinezumab, an anti-calcitonin gene-related peptide monoclonal antibody, reduced migraine frequency and was well tolerated in patients with migraine and prior preventive treatment failures. This analysis evaluated changes in patient-reported outcomes (PROs) over 24 weeks.

Methods: DELIVER (NCT04418765; phase 3b, multinational, parallel-group, double-blind study) randomized adults with migraine and 2–4 prior preventive treatment failures (within the past 10y) to intravenous eptinezumab or placebo every 12 weeks. The assessed PROs included EuroQol 5-Dimensions 5-Levels visual analogue scale (EQ-5D-5L VAS; higher scores better); 6-item Headache Impact Test (HIT-6; lower scores better), Patient Global Impression of Change (PGIC; lower scores better), most bothersome symptom (MBS; lower scores better), and Migraine-Specific Quality of Life Questionnaire (MSQ, v2.1; higher scores better).

Results: Patients received eptinezumab 100mg (n=299), 300mg (n=294), or placebo (n=298). Mean changes from baseline to Week 12 (Wk12) in EQ-5D-5L VAS scores were 2.0 (100mg, p=0.0007) and 4.4 (300mg, p<0.0001) versus -3.1 (placebo), and were maintained or further improved to Wk24 (2.0, 5.2, -2.8, respectively). Mean baseline HIT-6 total scores were ~66.4, with mean changes of -6.9 (100mg, p<0.0001) and -8.5 (300mg, p<0.0001) versus -3.1 (placebo) at Wk12 that were further improved through Wk24 (-8.9 and -9.9 vs -3.9). PGIC and MBS scores showed greater improvement for eptinezumab than placebo at Wk12 and Wk24, and changes in MSQ domain scores were greater with eptinezumab versus placebo.

Conclusion: In adults with migraine and prior preventive treatment failures, eptinezumab robustly improved health-related quality of life and migraine-related burden over 24 weeks versus placebo.

Disclosure: H. Lundbeck A/S, Copenhagen, Denmark.

EPO-060

Effects of Transcranial Direct Current Stimulation on CGRP and PACAP-38 Levels in Menstrual Migraine

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Background and aims: In this randomized controlled study, Transcranial Direct Current Stimulation (tDCS), was applied to patients with menstrual migraine (MM) whose attacks could be resistant to treatment. It was aimed to evaluate the efficacy of treatment and Calcitonin gene-related peptide (CGRP) and Pituitary adenylate cyclase-activating peptide 38 (PACAP-38) levels.

Methods: 56 female patients between the ages of 18–45 years, including 35 MM, 21 non-menstrual migraine (MM-), were included in this study. Three consecutive sessions of anodal tDCS were applied to the left dorsolateral prefrontal cortex with an intensity of 2mA for 20 minutes to 29 patients. Migraine attack frequency, severity, analgesic usage and CGRP and PACAP-38 levels of the patients were followed for a month after tDCS.

Results: After tDCS, in the active group compared to the 'sham' group, the frequency (p=0.031), severity (p=0.003) of attacks, the number of days with headache (p=0.004), the use of analgesics (p=0.024) were all decreased. In both MM and MM- groups, the frequency and severity of attacks and analgesic usage were decreased in those receiving active stimulation (p<0.001 for each). CGRP and PACAP-38 levels were similar in the active group and the sham group after tDCS (p:0.466) (p:0.707).

Conclusion: According to our results, tDCS which was shown to be effective in the migraine prophylaxis, can also be used as an alternative treatment option in MM. The absence of changes in serum CGRP and PACAP-38 levels may suggest that tDCS efficacy may point out to a different cerebral electrophysiological mechanism.

Disclosure: Nothing to disclose.

EPO-061

Long-term safety and tolerability of atogepant for preventive treatment of migraine: a phase 3, 40-week, extension trial

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Background and aims: A phase 3 trial, ADVANCE (NCT03777059), demonstrated that atogepant, an oral, CGRP receptor antagonist dosed once daily, results in a clinically meaningful reduction in mean monthly migraine days. This open-label extension for ADVANCE trial completers evaluated the long-term safety and tolerability of atogepant over 40 weeks.

Methods: Participants in this trial (NCT03939312) rolled over from the lead-in ADVANCE trial and were treated with atogepant 60 mg once daily for 40-weeks, with a 4-week safety follow-up period. Only safety data were collected.

Results: 685 participants took at least one dose of study drug, 74.6% completed the 40-week treatment period; mean age of 41.8 years, 88.2% female, 84.4% white, and mean BMI of 30.58 kg/m2. Mean (SD) treatment duration was 233.6 (89.32) days. Overall, 62.5% of participants experienced a treatment-emergent adverse event (TEAE), with 8.8% considered treatment-related by the investigator; serious adverse events (SAEs) occurred in 3.4% of participants, none were treatment-related. Table 1 reports the most frequent AEs leading to discontinuation; Table 2 reports the most frequent TEAEs observed. Table 3 reports hepatic-related laboratory parameter values of clinical interest. Participants with aminotransferase elevations ≥3 x ULN (4[0.6%]; defined in the protocol as Adverse Events of Special Interest) had no symptoms associated with liver disease and all 4 cases resolved without treatment. No deaths were observed.

Table 1. Overall Summary of Adverse Events – Safety Population

Category	Total (N=685) n / N (%)
Treatment-emergent adverse events (TEAE)	428 (62.5)
Deaths	0 (0.0)
Treatment-emergent serious adverse events (SAE)	23 (3.4)
Treatment-related TEAE	60 (8.8)
TEAE Leading to Study Intervention Discontinuation [1,2]	22 (3.2)
Nausea	3 (0.4)
Abdominal Pain	2 (0.3)
Vomiting	2 (0.3)
Weight Decreased	2 (0.3)
Dizziness	2 (0.3)
Migraine	2 (0.3)

Participants are counted only once within each category.
N = number of participants in the Safety Population.
n = number of participants within a specific category.
Percentages are calculated as 100 x (n/N).
[1] The inset AEs represent the most frequent AEs leading to discontinuation in the extension study.
[2] Three patients with AE onset date in the lead-in (ADVANCE) trial rolled over to the extension study and discontinued in the extension study.

Table 2. Comparison of P300 parameters in the patients with epilepsy and the controls (25Q – 25 quartile; M – median; 75Q – 75 quartile)

	STUDY GROUP (n=44)			CONTROL GROUP (n=46)			
	25Q	M	75Q	25Q	M	75Q	
P300 latency							
Fz	316.8	356.8	370.0	305.0	321.0	335.0	p=0.00005
Cz	315.0	355.3	367.8	304.0	324.0	335.0	p=0.00019
Pz	322.5	354.0	369.0	305.0	322.5	339.0	p=0.00004
P300 amplitude							
Fz	3.68	5.40	8.35	4.00	6.73	10.00	p=0.218
Cz	5.18	6.93	9.83	4.95	7.35	10.00	p=0.449
Pz	6.55	8.20	11.25	5.80	8.15	11.60	p=0.882

Table 3. Number (%) of Participants with Hepatic-Related Laboratory Parameter Values of Clinical Interest - Safety Population

Parameter Criteria	Atogepant 60 mg QD (N=685) n/N1 (%)[a]
ALT or AST [U/L]	
≥3 x ULN	4/683 (0.6)
Total Bilirubin (TBL) [umol/L]	
≥2 x ULN	0 (0)
Alkaline Phosphatase (ALP) [U/L]	
≥1 x ULN	84/683 (12.3)
≥1.5 x ULN	6/683 (0.9)
≥2 x ULN	0 (0)
Potential Hy's Law	
ALT or AST ≥3xULN; and TBL ≥2xULN; and ALP <2xULN	0 (0)

[a]Percentages are calculated as 100 * (n/N1)
N, number of participants in the Safety Population; N1, number of participants with at least one non-missing post-baseline value; n, number of participants in the specific category; U/L, Units per liter; umol/L, micromoles per liter; ULN, Upper limit of normal value

Conclusion: These safety results are consistent with the known safety profile of atogepant from previous trials and support the long-term safety and tolerability of once daily dosing of atogepant 60 mg.

Disclosure: Funded by AbbVie (previously Allergan). All authors had access to relevant data, participated in drafting, review, and approval. Matt DiStasi, PhD, MS of AbbVie Inc., provided medical writing assistance for development of this publication.

EPO-062

Effect of KATP channel blocker glibenclamide on PACAP38-induced headache and hemodynamic

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Background and aims: Pituitary adenylate cyclase-activating polypeptide-38 (PACAP38) dilates cranial arteries and triggers headache. The PACAP38 signaling pathway is partly dependent on activation of ATP-sensitive potassium (KATP) channels. Here, we investigated the effect of the KATP channel blocker glibenclamide on PACAP38-induced headache and vascular changes in healthy volunteers.

Methods: In a double-blind, randomized, placebo controlled and crossover design, 22 healthy volunteers were assigned to receive an intravenous infusion of 10 picomole/kg/min PACAP38 over 20 minutes followed by oral administration of 10 mg glibenclamide or placebo. The primary endpoint was the difference in incidence of headache (0–12 hours) between glibenclamide and placebo. The secondary endpoints were a difference in AUC for headache intensity scores, middle cerebral artery velocity (VmeanMCA), superficial temporal artery diameter (STA), radial artery (RA) diameter, heart rate (HR), mean arterial blood pressure (MABP) and facial skin blood flow between the two study days.

Results: 20 participants completed the study. We found no difference in the incidence of PACAP38-induced headache after glibenclamide (19/20, 95%) compared to placebo (18/20, 90%) (p=0.6985). The AUC for headache intensity, VmeanMCA, STA, RA, facial skin blood flow, HR and MABP did not differ between PACAP38-glibenclamide day compared to PACAP38-placebo day (p>0.05).

Conclusion: Posttreatment with KATP channel inhibitor glibenclamide did not attenuate PACAP38-induced headache and hemodynamic changes in healthy volunteers. We suggest that PACAP38-triggered signaling pathway could be mediated by specific isoforms of sulfonylurea receptor subunits of KATP channels.

Disclosure: Nothing to disclose.

EPO-063

The Relation between blood hypercoagulability and migraine

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Background and aims: A relation between migraine and stroke has been proposed for many years, although conclusive evidence has not been reported. Several theories about hypercoagulability have advocated the association of ischemic stroke and migraine especially migraine with aura. This study aimed to assess blood coagulability in patients with migraine.

Methods: This is a case-control study conducted on 70 subjects (35 migraine patients and 35 healthy individuals). Patients were recruited from the headache clinic during the period from August 2020 to December 2020. The study proposal was approved by the ethical committee of the Neurology Department, Faculty of Medicine, Cairo University. The aim and nature of the study was explained for each participant before inclusion. An informed written consent was obtained from all candidates prior to participation. Policy of data confidentiality was strictly applied.

Results: Mean serum levels of both protein S and anti-thrombin III were significantly lower in migraine patients in comparison to control subjects. Migraine patients had abnormal MRI findings in the form of white matter hyperintensities and ischemic foci compared to healthy controls. The study detected significant negative correlation was between serum protein C level and intensity of migraine headache. Finally, Serum protein C deficiency was considered an independent predictor for migraine intensity grade.

Conclusion: There is an association between migraine and hypercoagulability, which may indicate increased risk of cerebral ischemia in migraine patients and suggest adding prophylactic therapy to the management strategies of such patients.

Disclosure: The authors declare that they have no competing interests.

EPO-064

Acute Confusional Migraine in CADASIL: Clinical and Neuropsychological Assessment

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Background and aims: Acute confusion in migraine (ACM) is a cause of transient alteration in consciousness, characterized by defects in sensorium, impaired awareness of environment, agitation and amnesia, mainly seen in children [1–2]. Around 30–60% of cerebral autosomal dominant arteriopathy with subcortical infarcts and leukoencephalopathy (CADASIL) patients get affected by migraine attacks, often with aura. Acute confusional state during migraine has been rarely described in CADASIL [3].

Methods: A 54-year-old female presented bimonthly episodes of migraine associated with visual aura since the age of 30. She had an ischemic stroke with left brachio-crural hemiparesis at the age of 43. Nine years later, she was admitted to another hospital because of severe migraine attack with aura characterized by visual impairment, speech disturbance, mild psychomotor agitation and delirium. At 53 years-old, she was evaluated in our Emergency Room for a similar episode.

Results: Brain MRI was negative for new ischemic lesions but showed typical CADASIL neuroimaging; EEG revealed bilateral sharp slow delta waves (Figure A-B-C). A complete neuropsychological assessment during the acute phase showed complex visual hallucinations, severe cognitive global alteration with attention and executive impairment (Table 1). The psychomotor agitation and confusional status suddenly disappeared and EEG recording returned normal (Figure E) seven days later. After excluding other possible causes, a diagnosis of ACM was made.
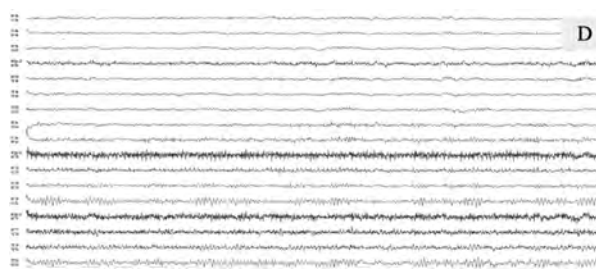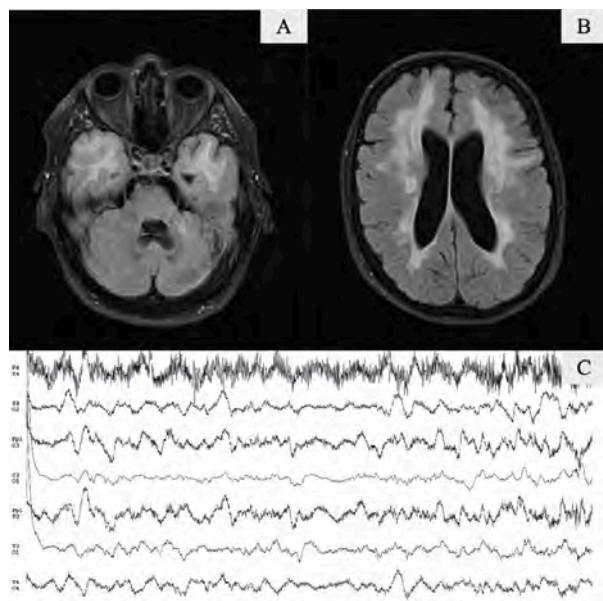
Figure D. Normal EEG recorded two days after the end of confusional migraine attack.

Conclusion: We presented clinical and neuropsychological features depicting an unusual case of ACM in an adult with CADASIL. Our case highlighted the lack of adequate knowledge about this entity and prompting further larger studies to explore its incidence and characteristics.

Disclosure: I hereby certify that, to the best of my knowledge, no aspect of my current personal or professional circumstance places me in the position of having a conflict of interest with this presentation.

Brain MRI (FLAIR sequences) showed: (A) temporal white matter hyperintensity (B); hemispheric white matter bilateral hyperintensity, prevalent in the frontal lobes. (C) EEG during acute confusional migraine showed slow bilateral activity

Neuropsychological tests	Patient scores (raw)	Patient scores (corrected/PE)
Mini-mental state examination:	15	13,31*
Short Story Recall		
Free and Cued Selective reminding test	7,6	1
RI:		
Free Recall >=19,60	14	0*
Total >=35	32	
Sensitivity index >=0,9	0,81	
Intrusions < 0	7	0*
RD:		
Free Recall >=6,32	10	
Total >=11	10	
Intrusions < 0	2	
Digit Span Forward	5	2
Digit Span Backward	<3	0*
Attentional Matrices	15	0*
Trail Making A	n.e.	*
Trail Making B	n.e.	*
Frontal assessment battery	7	0*
Stroop Color and Word Test		
Interference Scores (Time)	0	4
Interference Scores (Errors)	21,5	0*
Raven's progressive matrices (PM 47)	11	0*

Table 1. Each asterisk signals patient pathological scores. Scores equivalent (extracted from calibrated tests performed on samples of Italian population): 0=pathological; 4>50°percentage)

EPO-065

A systematic review on the preventive treatment of refractory chronic cluster headache

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Background and aims: The best preventive treatment strategy for Refractory Chronic Cluster Headache (rCCH) is still unknown.

Methods: The review was performed following PRISMA guidelines. The protocol was registered in PROSPERO (ID CRD42021290983). The search was performed on September 2021 on databases Pubmed, Embase and Cochrane. Studies of preventive strategies for rCCH defined by the European Headache Federation criteria were selected. For risk of bias assessment, the Cochrane Handbook Risk Of Bias tool was used for randomized clinical trials (RCT) and ROBINS-E was used for observational studies (OS).

Results: 43 articles met the inclusion criteria. The largest number of articles studied occipital nerve stimulation (ONS) accounting for 1 ECA and 11 OS for a total of 436 patients, followed by deep brain stimulation (DBS): 1 RCT and 8 OS; 118 patients. All ONS studies reported a significant reduction in attack frequency and the 50% responder rate ranged from 29.4% to 80.0%. DBS studies reported a 50% responder rate of 50–100%. Reported adverse events (AE) were more serious in DBS studies. The remaining 24 articles (anti-CGRP pathway drugs, ketamine-magnesium infusions, serial occipital nerve blocks, clomiphene, onabotulinum toxin A, ketogenic diet, sphenopalatine ganglion radiofrequency or stimulation, vagus nerve stimulation, percutaneous bioelectric current stimulation, upper cervical cord stimulation and vidian neurectomy) present weaker results or have poorer quality of evidence.

Conclusion: Considering the quality of the published studies, their results and the profile of AE, ONS could be the first therapeutic strategy for patients with rCCH based on the current evidence.

Disclosure: The authors declare no conflicts of interest.

EPO-066

Could symptom severity predict the response to anti-CGRP monoclonal antibodies in migraine?

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Background and aims: Little is known about predictors of response to monoclonal antibodies against CGRP and its receptor (anti-CGRP/r) in migraine patients. This study aims to find a clinical responsiveness predictor.

Methods: Prospective cohort study of migraine patients treated with anti-CGRP galcanezumab or anti-CGRPr erenumab with 6 months of follow-up at a Headache Clinic of a third level hospital. Symptoms severity was assessed using the Migraine Severity Symptom Score (MSSS). MIDAS and HIT-6 were used for disability assessment. The primary endpoint was the responder rate (RR, defined as ≥50% monthly headache days decrease after 6 months). Exploratory stepwise multiple logistic regression analysis was used for independent predictors of response identification.

Results: 126 patients were recruited. Diagnosis was chronic migraine in 75.4% (95/126) and high frequency episodic migraine in 24.6% (31/126). Baseline monthly headache days, MIDAS and HIT-6 had a mean (SD) of 20.2 (7.2), 75.0 (63.0) and 65.8 (8.5) respectively. After 6 months, the RR was 61.1% (77/126) and monthly headache days, MIDAS and HIT-6 showed a decrease of 9.4 (10.2), 40.1 (61.3) and 9.1 (13.4) respectively. Only one clinical variable, the severity of the worsening of pain with routine activities on MSSS at baseline, was associated with responsiveness (OR 0.54, 95%CI: 0.34–0.87; p=0.012). Mild adverse events (AE) appeared in 55.6% (70/126), none of them lead to treatment discontinuation.

Conclusion: Among the clinical features, worsening with activities severity could be a predictor of response to anti-CGRP/r monoclonal antibodies. These therapies are effective showing frequent but mild AE in real clinical practice.

Disclosure: The authors have no conflicts of interest to declare.

EPO-067

Effect of Galcanezumab in migraine and concomitant medication overuse headache without prior drug withdrawal

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Background and aims: Medication overuse headache (MOH) is a disabling and usual comorbidity in migraine patients. We aim to evaluate the effect of Galcanezumab (anti-CGRP monoclonal antibody) in migraine patients with concomitant MOH without prior drug withdrawal.

Methods: Prospective cohort study of migraine patient with comorbid MOH treated with galcanezumab in the Headache Clinic of a third level hospital. Results were evaluated at 3 and 6 months. The primary endpoint was the change in headache frequency. Change in drug intake and MIDAS and HIT-6 scores were also evaluated.

Results: 46 patients were recruited. The median (P25–P75) of headache days per month were 20 (15–30), with a median monthly intake of 15 (0–30) NSAIDs and 13 (0–20) triptans. Baseline MIDAS and HIT-6 scored 50 (21.3–127.5) and 67 (62.5–71.0), respectively. After 3 months of galcanezumab treatment, headache frequency decreased to 8 (4–13) days per month, with a monthly intake of 4 (0–10) NSAIDs and 4 (0–8) triptans; MIDAS scored 12.5 (3.0–40.8) and HIT-6, 55 (48.3–62.0). At month 6, headache frequency further decreased to 7.5 (4–15) days per month, with a monthly intake of 3.5 (0–9.8) NSAIDs and 5.5 (2.8–10.0) triptans; MIDAS scored 14.5 (4.0–51.3) and HIT-6, 59.5 (50.8–63.3). All differences from baseline show statistical signification (p<0.001). MOH resolved in 37% (17/46) of patients at month 3 and 65.2% (30/46) at month 6.

Conclusion: Galcanezumab is a valid therapeutic option in migraine patients with comorbid MOH, being able to decrease headache burden, drug intake and disability without prior drug withdrawal.

Disclosure: The authors declare no conflicts of interest.

EPO-068

HEADWORK as innovative tool for monitoring MABs effect on migraine-related disability

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Background and aims: Monoclonal antibodies (MABs) are a game changer for migraine treatment since their approval; in addition to the well-known metrics for assessing treatment efficacy, HEADWORK has been recently developed specifically to assess the impact on work-related migraine disability.

Methods: 30 patients from our Headache Center at IRCCS C.Besta, diagnosis of migraine without aura, eligible for MABs treatment, were enrolled and followed up to 3 and 6 months (3M and 6M). Data were collected on monthly headache frequency, medications intake/month, MIDAS. Employed patients were also asked to complete the HEADWORK questionnaire, consisting of two sections: "Work-related difficulties" (HW1), and "Factors contributing to work-related difficulties" (HW2). The effect size (ES: mean difference divided by baseline SD) was calculated.

HeadWork part 1

HeadWork part 2

Results: Seven males and 23 females were enrolled: mean age (50±8), mean disease duration (34y±13). Monthly headache frequency decreased from 12.5±4.2 to 5.8±3.7 (3M) and 5±4.1 (6M – ES 1.8); medications/month from 14±5.3 at baseline to 5±3.7 (3M) and 5±3.1 (6M – ES 1.7); MIDAS from 42±54 at baseline to 5.5±13.4 (3M) and 1±11 (6M – ES 0.7); HW1 from 23±8.9 at baseline to 11±9.6 (3M) and 1±7 (6M – ES 2.5); HW2 from 11±6.1 at baseline to 7±4.4 (3M) and 1±4.8 (6M – ES 1.7).
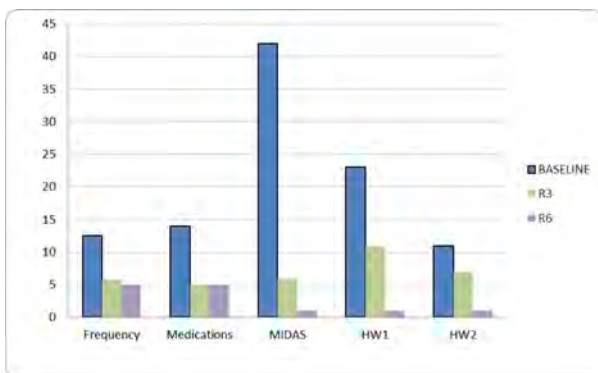
Results (Frequency and Medication per month - HW1 - HW2)

Conclusion: The effect of MABs on monthly headache frequency and medications intake is impressive, but even larger the effect on migraineurs' work-related disability, as evidenced by the ES in both HW1 and HW2.
Disclosure: Nothing to disclose.

EPO-069

Homewithdrawal plus behavioural approach (Be-Home) in Chronic Migraine and Medication Overuse during COVID-19

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Background and aims: Chronic Migraine (CM) is a disabling condition affecting 2% of the general population, in particular if combined with Medication Overuse (MO). The detoxification program is an essential step in the treatment strategy (4, 5). Aim of this pilot study was to assess the feasibility and the long-term effectiveness of a specific protocol, designed during the COVID-19 pandemic emergency, consisting of a home withdrawal plus behavioral treatment (mindfulness) delivered by web.

Methods: Twenty patients with diagnosis of CM-MO (according to IHS criteria) were enrolled into the study; they performed the withdrawal program at home, (oral administration of steroids and benzodiazepine) for 5 days, including education to manage pain, combined with six weekly 1-hour-video mindfulness sessions. Home-practice was encouraged by 12-minutes mindfulness sessions on smartphone; follow-up visits scheduled at 3-6-12 months after withdrawal. Percentage of patients with absence of MO at 6 months from withdrawal (assessed by Daily Diary Card), and percentages of patients obtaining a decrease of at least 50% in the number of migraine days/month and medications/month were considered.

Results: Twenty patients enrolled: 16 females and 4 males, (mean age 44±12; mean duration of disease 19,5±12,7). Results showed a significant decrease in medications/month (18±8,3 at baseline vs 6±3.8 at 6 months), and migraine days/month (15±6,4 at baseline vs 8±4,1 at 6 months). None of the patients recorded a MO condition at 6 months follow-up.

	age	sex	onset	duration	R0		R3		R6	
					frequence	medication	frequence	medication	frequence	medication
mean (d.s.)	44(±12)	17 f - 3 m	20(±9,7)	19(±12)	15(±6,4)	18(±8,3)	6,5(±7,4)	4,5(±7,2)	8(±4)	6(±3.8)

Results

Conclusion: Clinical results are significant. The "BeHome" program seems to be effective, and sustainable in particular during the COVID-19 pandemic emergency, also at a medium-term follow-up.

Frequency per month
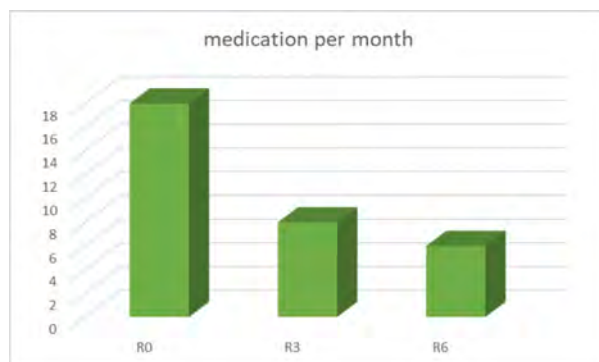
Medications per month

Disclosure: Nothing to disclose.

EPO-070

The Burden of Coronavirus Disease (COVID-19) Pandemic on Headaches in Adolescents: Other Side of the Coin

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Background and aims: In early months of the lockdown, limited reports concluded an improvement on headache in children associated with reduction in school-related stress during coronavirus disease 2019 (COVID-19) pandemic. However, the long term impact of pandemic on headache in adolescents is not known yet.

Methods: 10 to 18 years old attendees were included to the multicenter study.Questions explored the presence and features of headache, academic performance, exposure to COVID-19, exposure to electronics.The scales of Patient Health Questionnaire, Generalized Anxiety Disorders Scale and Coronavirus Anxiety Scale were used.

Results: A total of 851 (531 female) participants were recruited to study with a headache frequency of 89% (756/851).Among 756 subjects, 10% reported new onset headache, 27% worsened, 3% improved and 61% stable. Even 62% of the adolescents was dissatisfied with online education as similar across all groups, reduction in school effort and decrease in student achievement were reported more common in worsened and new onset groups.Those respondents have also declared an exacerbation of headache due to prolonged computer screen exposure, more frequently.The depression and general anxiety scores were significantly higher in worsened and new onset groups compared to stable and improved.Coronavirus anxiety scores were significantly higher in worsened group compared to stable group.Headache frequency and severity showed significant correlations with age, depression and anxiety.

Conclusion: The psychosocial consequences in long term of pandemic are likely to exacerbate headache among adolescents in our study.Identifying any headache triggering factors related to the pandemic is important to implement lifestyle modifications to reduce the future burden of the diseases.

Disclosure: The study was supported by Global Migraine and Pain Society.

EPO-071

Plasma levels of CGRP are elevated but not related to migraine attacks after 2-hour infusion of VIP

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Background and aims: The activation of perivascular fibers and the consequent release of vasoactive peptides, including the vasoactive intestinal polypeptide (VIP), play a role in migraine pathogenesis. A 2-hour infusion of VIP provoked migraine, but the mechanisms remain unknown. We investigated whether 2-hour infusion of VIP caused alterations in plasma levels of the calcitonin gene-related peptide (CGRP) and whether any changes might be related to the induced migraine attacks.

Methods: We enrolled individuals with migraine and healthy participants to randomly receive a 2-hour infusion of either VIP (8 pmol/kg/min) or placebo (sterile saline). We collected clinical data and measured plasma levels of VIP and CGRP at fixed time points: at baseline (T0) and every 30 min, until 180 min (T180) after the start of the infusion.

Results: Blood samples were collected from episodic migraine patients without aura (n=19) and healthy individuals (n=12). Mixed effects analysis revealed a significant increase of plasma CGRP (p=0.027) during VIP infusion, specifically at T30 (vs. T180, adjusted p value= 0.039) and T60 (vs. T180, adjusted p value=0.027) in migraine patients. We found no increase in plasma CGRP during VIP-induced migraine attacks (p=0.219). In healthy individuals, there was no increase of plasma CGRP during VIP (p=0.205) or placebo (p=0.428) days.
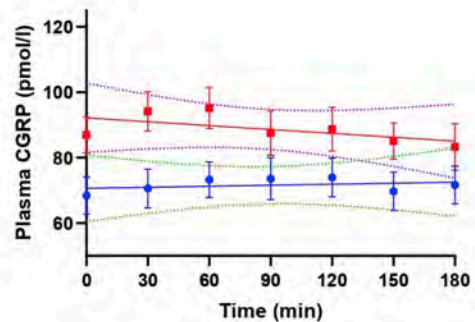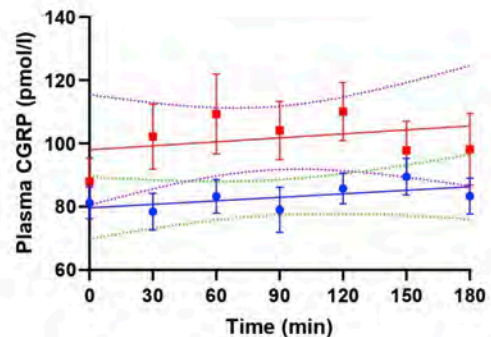
Linear regression lines of plasma CGRP during VIP (red) and placebo days (blue) in patients with migraine (A) and healthy individuals (B).
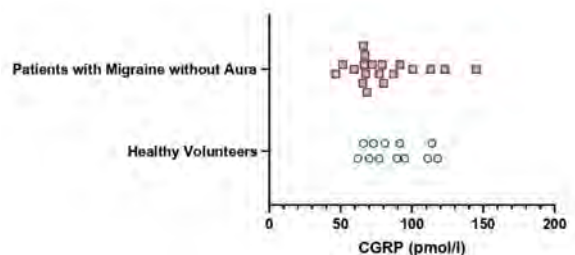
Mean plasma concentration of CGRP at the baseline in healthy individuals and patients with migraine.

Conclusion: Plasma CGRP was elevated in patients with migraine during a prolonged infusion of VIP, but these alterations were not associated with VIP-induced migraine attacks.

Disclosure: This work was performed as part of a research collaboration with Novartis Pharma AG.

Headache 2

EPO-072

Efficacy and Safety of Eptinezumab for Migraine Prevention in Patients With 2–4 Prior Preventive Treatment Failures

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Background and aims: DELIVER evaluated the efficacy and safety of eptinezumab for migraine prevention in patients with migraine and prior preventive treatment failures.

Methods: DELIVER (NCT04418765) is a phase 3b, multicenter, parallel-group, double-blind, randomized clinical trial evaluating eptinezumab 100mg and 300mg vs placebo (administered intravenously every 12 weeks) for migraine prevention. Eligible patients included adults (18-75y) with episodic or chronic migraine and documented evidence of 2–4 previous preventive treatment failures within the past 10y. The study consists of a 28–30-day screening period, 24-week placebo-controlled period, and 48-week dose-blinded extension period. The primary endpoint is change from baseline in monthly migraine days (MMDs) over Weeks (Wks) 1–12. These data focus on the placebo-controlled study period.

Results: 96.3% (100mg, 288/299), 96.6% (300mg, 284/294), and 98.3% (placebo, 293/298) of patients completed the placebo-controlled period. Eptinezumab met the primary endpoint, achieving statistically significant reductions in MMDs versus placebo over Wks1-12 (100mg, -4.8; 300mg, -5.3; placebo, -2.1; p<0.0001), which was maintained over Wks13-24. Over Wks1-12, more eptinezumab-treated than placebo treated patients achieved ≥50% (100mg, 42.1%; 300mg, 49.5%; placebo, 13.1%; P<0.0001) and ≥75% MMD reduction (15.7%, 18.8%, 2.0%; p<0.0001). Changes from baseline in Headache Impact Test (HIT-6) at Wk12 were -6.9 (100mg) and -8.5 (300mg) versus -3.1 (placebo; p<0.0001). Incidence of treatment-emergent adverse events was 42.5% (100mg), 40.8% (300mg), and 39.9% (placebo).

Conclusion: In adults with migraine and prior preventive treatment failures, eptinezumab robustly decreased MMDs across Wks1–12 and Wks13–24 compared to placebo, with a safety and tolerability profile comparable to that observed previously.

Disclosure: H. Lundbeck A/S, Copenhagen, Denmark.

EPO-073

Long-term reductions in disease impact in patients with chronic migraine following preventive treatment with eptinezumab

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Background and aims: This analysis evaluated item-level changes in the Migraine Disability Assessment (MIDAS) questionnaire in patients with chronic migraine (CM) after eptinezumab treatment over 2 years.

Methods: PREVAIL (NCT02985398) was an open-label, phase 3 study in which 128 adults received intravenous eptinezumab 300mg every 12 weeks for up to 8 doses. MIDAS, which entails a 3-month recall period for all questions, was administered at baseline, week (wk) 12, and every 12 weeks thereafter. MIDAS total score comprises 5 items, each measuring the number of days with migraine-related disability. Two supplementary items (not in total score) assess number of headache days and average headache pain severity (from 0 [none] to 10 [worst]).

Results: Mean MIDAS headache days were reduced from 47.4 at baseline to 17.1 at wk12 and to 16.3 at wk104. Mean average headache pain severity was reduced from 7.3 (baseline) to 5.5 (wk12) to 4.5 (wk104). The greatest baseline disability was noted in days of reduced productivity in household work (mean 16.4) and missed household work (mean 15.6), which was reduced to 5.5 and 4.7 days, respectively, at the first post-baseline assessment (wk12). Mean days of missed work/school, reduced work/school productivity, and missed family/social/leisure activities were reduced from 5.4, 12.0, and 8.0 at baseline to 2.2, 4.8, and 2.8 at wk12, respectively. Reductions at wk12 were generally sustained through wk104.

Conclusion: Long-term treatment with eptinezumab suggested early and sustained reductions in migraine-related disability in patients with CM, in part related to reductions in MIDAS headache day frequency and pain severity.

Disclosure: H. Lundbeck A/S, Copenhagen, Denmark.

EPO-074

The effect of anatomical predictors of trigeminal Neuralgia on the severity of pain syndrome in the postoperative period

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Background and aims: Trigeminal neuralgia is one of the most persistent pain syndromes in clinical neurology. According to numerous studies, it has been revealed that the pathogenesis of trigeminal neuralgia may be based on various anatomical predictors.

Methods: A clinical study of 32 patients with trigeminal neuralgia was conducted. The studied patients were aged from 21 to 74 years. All patients underwent microvascular decompression using retrosigmoid access. The following anatomical predictors were considered: vasoneural conflict, volume and cross-sectional area of the cerebellum, volume, length, cross-sectional area of the trigeminal nerve and intertriheminal angle. To assess the severity of the pain syndrome, VAS and the McGill pain intensity questionnaire were used. The pain syndrome was assessed before the operation, as well as in the postoperative period (3-6 months after treatment).

Results: Vascular compression was identified in all the studied patients as the main anatomical predictor of trigeminal neuralgia. It was revealed that in patients with a more acute intertriheminal angle of 38.4° (26.4/50.2)°, smaller cross-sectional area of the cerebellar cistern 180.2 mm^2 (102.1/284.4) mm2, higher values were noted on the VAS scale before (8±2) and after surgery (6±3), on the sensory and evolutive scales of the McGill pain intensity scale (p<0.05).

Conclusion: Trigeminal neuralgia has a multifactorial nature. The combination of vasoneural conflict with an acute intertriheminal angle and a smaller cross-sectional area of the cerebellar cistern are significantly significant predictors of a more pronounced pain syndrome in the postoperative period.

Disclosure: Nothing to dislcose.

EPO-075

Real-world Reductions in Migraine and Headache Days for Patients With Migraine Initiating Fremanezumab in Germany

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Background and aims: Fremanezumab, a humanised monoclonal antibody selectively targeting calcitonin gene-related peptide, is reimbursed in Germany for adults with episodic/chronic migraine (EM/CM) with ≥4 monthly migraine days (MMD) who were unsuitable for or did not respond to or tolerate ≥4 prior preventive treatments. The current study assessed real-world fremanezumab effectiveness after 3 months of treatment for reducing MMD and monthly headache days (MHD).

Methods: This German panel-based online physician chart review used electronic case report forms. Patient inclusion criteria were: physician diagnosis of CM/EM; first fremanezumab treatment initiation (index date) at ≥18 years from June 2019−July 2021; ≥3 months of continuous treatment after initiation; MMD assessments 1 month before (pre-index) and 3 months (±15 days) after (post-index) initiation; and ≥3 months of information about migraine treatments prior to fremanezumab. p<0.05 was considered statistically significant.

Results: Data from 63 clinicians and 207 patients were included (CM, 100[48%]; EM, 107[52%]; high frequency EM [HFEM, 8-14 MHD], 61[57%]; low frequency EM [LFEM, 0-7 MHD], 44[41%]). Overall, mean (SD) age was 40.3(9.6) years; 153(74%) patients were female; 84(41%) initiated quarterly fremanezumab dosing and 123(59%) monthly dosing. Mean (SD) baseline MMD and MHD, respectively, were 10.3(4.4) and 12.1(5.4); mean (SD) reductions at month 3 post-index were -6.1(3.5) and -6.5(4.0) (both p<0.001). Statistically significant reductions in MMD and MHD were observed across evaluated subgroups (Table).

Table. MMD and MHD at Baseline and Month 3 Post-index Overall and by Migraine Frequency and Fremanezumab Dosing Regimen at Initiation[a]

Outcome	Overall	CM	EM	HFEM[b]	LFEM[b]	Quarterly fremanezumab	Monthly fremanezumab
MMD	(n=207)	(n=100)	(n=107)	(n=61)	(n=44)	(n=84)	(n=123)
Baseline, mean (SD)	10.3 (4.4)	11.3 (5.0)	9.3 (3.5)	10.9 (3.3)	7.3 (2.7)	10.2 (5.0)	10.4 (3.9)
Month 3 post-index, mean (SD)	4.2 (3.3)	4.8 (3.8)	3.7 (2.5)	4.3 (2.6)	2.8 (2.1)	4.4 (3.7)	4.1 (3.0)
Change from baseline to month 3 post-index, mean (SD), %[c]	-6.1 (3.5),[d] 60.2%	-6.6 (3.9),[d] 59.0%	-5.7 (3.0),[d] 61.3%	-6.5 (3.4),[d] 59.4%	-4.5 (1.8),[d] 64.2%	-5.9 (3.7),[d] 59.5%	-6.3 (3.3),[d] 60.6%
MHD	(n=116)	(n=56)	(n=60)	(n=36)	(n=23)	(n=48)	(n=68)
Baseline, mean (SD)	12.1 (5.4)	13.8 (5.9)	10.4 (4.4)	12.4 (4.4)	7.5 (2.1)	12.3 (6.2)	11.9 (4.8)
Month 3 post-index, mean (SD)	5.5 (4.1)	6.6 (4.8)	4.5 (3.0)	5.4 (3.2)	2.9 (1.7)	5.9 (4.6)	5.3 (3.7)
Change from baseline to month 3 post-index, mean (SD), %[c]	-6.5 (4.0),[e] 55.1%	-7.1 (4.3),[e] 52.6%	-6.0 (3.7),[e] 57.4%	-6.9 (4.2),[e] 55.4%	-4.6 (2.0),[e] 61.0%	-6.4 (4.7),[e] 52.7%	-6.6 (3.5),[e] 56.8%

MMD, monthly migraine days; MHD, monthly headache days; CM, chronic migraine; EM, episodic migraine; HFEM, high frequency episodic migraine; LFEM, low frequency episodic migraine.

[a]For each outcome, results are reported for patients with data for the given outcome available at both baseline and month 3 post-index.

[b]HFEM, 8-14 MHD; LFEM, 0-7 MHD; both include ≥4 MMD.

[c]Mean percent reduction from baseline to month 3 post-index.

[d]P<0.001 for baseline versus month 3 post-index; evaluated using clustered Wilcoxon signed-rank tests that accounted for correlation structure of the data (ie, patient- and physician-level correlation from repeated observations and multiple patients per physician).

[e]P<0.004 for baseline versus month 3 post-index; evaluated using clustered Wilcoxon signed-rank tests that accounted for the correlation structure of the data.

Conclusion: Fremanezumab treatment was associated with clinically meaningful reductions in MMD and MHD for migraine patients 3 months after initiating fremanezumab treatment in a German real-world setting.

Disclosure: Funded by Teva Pharmaceuticals.

EPO-076

Real-world Reductions in Migraine-related Healthcare Resource Utilization for German Patients Initiating Fremanezumab

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Background and aims: Fremanezumab, a humanised monoclonal antibody selectively targeting calcitonin gene-related peptide, is reimbursed in Germany for adults with episodic/chronic migraine (EM/CM) with ≥4 monthly migraine days (MMD) who were unsuitable for or did not respond to or tolerate ≥4 prior preventive treatments. This retrospective chart review assessed real-world changes in migraine-related healthcare resource utilisation (HCRU) with fremanezumab treatment in adult patients in Germany over 6 months.

Methods: This German panel-based online physician chart review used electronic case report forms. Patient inclusion criteria included a physician diagnosis of CM/EM; first fremanezumab treatment initiation (index date) at >=18 years from June 2019−July 2021; ≥3 months of continuous treatment after fremanezumab initiation; MMD assessments within 1 month before (pre-index) and at 3 months(±15 days) after (post-index) fremanezumab initiation; and ≥3 months of information about migraine treatments prior to fremanezumab. Migraine-related HCRU, including outpatient office visits, urgent care/emergency room (ER) visits, inpatient admissions, and telehealth consultations, were compared for 6 months pre-index and 6 months post-index. p<0.05 was considered statistically significant.

Results: Data were included from 63 clinicians and 207 patients (CM, 100[48%]; EM, 107[52%]). Outpatient office visits, urgent care/ER visits, and inpatient admissions decreased significantly from 6 months pre-index to 6 months post-index after first fremanezumab initiation in the overall patient population and CM/EM subgroups (all p<0.05); telehealth consultations decreased non-significantly (Table).

Table. Migraine-related HCRU at 6 Months Pre- and Post-Index After Initiating Fremanezumab Overall and by Migraine Diagnosis Type[a]

Outcome	Overall	CM	EM
Outpatient office-based visits	(n=91)	(n=45)	(n=46)
6 months pre-index, mean (SD)	6.9 (5.3)	5.7 (4.4)	8.0 (5.9)
6 months post-index, mean (SD)	3.8 (2.5)	4.0 (2.4)	3.7 (2.5)
P value[b]	<0.001	0.003	0.005
Urgent care or ER visits	(n=70)	(n=31)	(n=39)
6 months pre-index, mean (SD)	2.9 (3.4)	1.8 (2.3)	3.7 (4.0)
6 months post-index, mean (SD)	0.7 (1.3)	0.5 (1.2)	0.8 (1.5)
P value[b]	<0.001	0.002	0.003
Inpatient admissions	(n=71)	(n=33)	(n=38)
6 months pre-index, mean (SD)	1.1 (1.9)	0.6 (1.2)	1.5 (2.2)
6 months post-index, mean (SD)	0.3 (0.7)	0.2 (0.4)	0.4 (0.9)
P value[b]	0.005	0.008	0.046
Telehealth consultations	(n=61)	(n=25)	(n=36)
6 months pre-index, mean (SD)	4.4 (7.1)	2.3 (3.7)	5.8 (8.5)
6 months post-index, mean (SD)	2.8 (4.4)	2.1 (3.4)	3.4 (4.9)
P value[b]	0.205	0.376	0.201

HCRU, health care resource utilization; CM, chronic migraine; EM, episodic migraine; ER, emergency room.

[a]Results are reported for the subset of patients with HCRU data available for both 6 months pre-index and 6 months post-index.

[b]P values comparing HCRU for 6 months pre-index versus 6 months post-index were calculated using clustered Wilcoxon signed-rank tests that accounted for the correlation structure of the data (ie, patient- and physician-level correlation from repeated observations and multiple patients per physician).

Conclusion: Fremanezumab treatment was associated with significant reductions in migraine-related HCRU for migraine patients over 6 months after initiating fremanezumab treatment in a German real-world setting.

Disclosure: Funded by Teva Pharmaceuticals.

EPO-077

Anti-CGRP antibodies efficacy in Chronic Migraine: an italian tertiary center experience

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Background and aims: Monoclonal antibodies targeting the calcitonin gene-related peptide pathway (anti-CGRP mAbs) are promising therapies for Chronic Migraine: (CM) prevention and randomised clinical trials (RCTs) assessed their safety and efficacy. As a real-life study, we investigated anti-CGRP mAbs efficacy in CM patients from our center.

Methods: We selected patients diagnosed with CM (IHS 2018 criteria) who were candidate to erenumab, fremanezumab or galcanezumab based on AIFA guidelines. We collected patients information, the Monthly Headache Days (MHDs) and the Migraine-related Disability Assessment (MIDAS) questionnaire at baseline and after 6 months. Clinically meaningful response was defined as ≥50% decrease in MHDs.

Results: We included 55 patients (49 females), whose median migraine onset age and chronicization age were respectively 17 and 40 years. At baseline, the median MIDAS was 70 (IQR 50–95), the median MHDs was 20 days (IQR 13–25) and 42 patients (76%) were overusing medications. After 6 months, we observed a sharp decrease both in MIDAS (median reduction 84%, IQR 75–94%) and MHDs (median reduction 85%, IQR 67–92%) and only five patients (9%) were overusing medications. No significant difference in efficacy was found among the three mAbs (pMIDAS=0.90, pMHDs=0.34). In total, 49 patients (89%) were responders, three patients experienced a MIDAS and MHDs decrease without reaching a clinically meaningful response, two patients were non-responders and suspended treatment. No severe adverse effect was reported.

Conclusion: Anti-CGRP mAbs showed optimal efficacy and safety in most patients. The three studied mAbs did not show significant differences in clinical response.

Disclosure: Nothing to disclose.

EPO-078

Patterns of use of monoclonal antibodies for the preventive treatment of migraine: Results from the OVERCOME (EU) study

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Background and aims: The aim of this analysis was to investigate the reasons for starting, stopping or switching treatment with calcitonin gene-related peptide (CGRP) monoclonal antibodies (mAbs) for migraine prevention in the European ObserVational survey of the Epidemiology, tReatment and Care of MigrainE (OVERCOME [EU]) study.

Methods: Data were obtained from a cross-sectional web-based survey (2020–2021). Adult respondents fulfilled International Classification of Headache Disorders (ICHD)-3 criteria for migraine or had a self-reported physician diagnosis. Respondents who ever used mAbs (erenumab, fremanezumab, galcanezumab) were considered in this analysis. Reasons to start, stop, or switch treatment were collected and summarised using descriptive statistics.

Results: Of 20,756 respondents, 2,167 (10.4%) had used one or more mAbs. Among users of mAbs, the mean (standard deviation [SD]) age was 32.9 (10.4) years, 38.8% were female, and mean (SD) headache days per month was 3.4 (4.4). A total of 333 (15.4%) had switched and 1,189 (54.9%) had stopped. No dominant reasons for starting mAbs could be identified (all reported as 15–20%). The 3 most common reasons for switching were recommendation from the doctor (27.0%) or a friend/family member (26.7%), and preference for the injector/needle used (26.7%). Reasons for stopping included improvement in headaches, recommendations from others, dosage, or tolerability. Only 11.5% stopped their medication because it was not working.

Conclusion: Reasons for starting mAbs were multiple, including physician recommendation and patient efficacy expectations. The finding that recommendation from others was the most frequent reason for switching highlights the importance of the patient-physician relationship and family support in the management of migraine.

Disclosure: JP: advisory boards for Allergan-Abbvie, Amgen-Novartis, Eli Lilly, and Teva. SE: consultation/speaker for Allergan-Abbvie, Eli Lilly, Lundbeck, Novartis, Perfood and Teva. TP, GDA and DN: full-time employees and stock-holders of Eli Lilly.

EPO-079

Traditional preventive medication and treatment satisfaction in migraine: Results from the OVERCOME (EU) study

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Background and aims: This analysis describes the current use of traditional preventive medications (antidepressants, antihypertensives, antiseizures, onabotulinum toxin A) and treatment satisfaction in people with migraine eligible for prevention in the European ObserVational survey of the Epidemiology, tReatment and Care of MigrainE (OVERCOME [EU]) study.

Methods: Data were obtained from a cross-sectional web-based survey (2020–2021). Adult respondents fulfilled International Classification of Headache Disorders (ICHD)-3 criteria for migraine or had a self-reported physician diagnosis. This analysis focused on medically diagnosed patients, with a mean ≥4 migraine headache days/month (HD/m) over the last 90 days and ≥11 Migraine Disability Assessment Score (MIDAS), excluding calcitonin gene-related peptide (CGRP)-monoclonal antibody users.

Results: Of 20,756 respondents, 2,749 (13.2%) were considered in this analysis. Mean age was 40.7 years and 70.4% were female (Table 1). Overall, 26.1% of them currently used traditional preventive medications, with a slightly higher percentage (32.3%) in those with ≥15 HD/m. Of eligible patients who took a preventive in the last 3 months, 12.7% took one and 13.4% took ≥2, with generally higher percentages in those with more frequent HD/month. Nearly two-thirds of patients (61.8%) who were candidates for preventive medications and stopped the most recent medication did so within 6 months (Table 2). Only 33% of traditional preventive users reported "a lot" or "complete" satisfaction with current medication (Table 3).

Number of eligible patients	Overall N=2749	4-7 HD/m n=1458	8-14 HD/m n=792	>=15 HD/m n=499
Age (years, mean)	40.7	40.3	40.8	41.4
Sex (% female)	70.4	69.7	68.9	74.7
Time to diagnosis (years, mean)	2.8	2.8	3.0	2.5
HD/m (mean)	9.4	5.2	10.2	20.5
Number of comorbidities (mean)	4.3	3.9	4.3	5.2
Employment rate (%)	69.3	72.9	69.8	58.1

HD/m, headache days per month.

Table 1. Demographic and clinical characteristics

	Overall N=2749	4-7 HD/m n=1458	8-14 HD/m n=792	>=15 HD/m n=499
Currently used preventives (N; %)	717; 26.1	350; 24.0	206; 26.0	161; 32.3
1 preventive	349; 12.7	173; 11.9	97; 12.2	79; 15.8
2 preventives	164; 6.0	73; 5.0	50; 6.3	41; 8.2
>= 3 preventives	204; 7.4	104; 7.1	59; 7.4	41; 8.2
Preventive medication category (N; %, not mutually exclusive)				
Antiseizure	341; 12.4	170; 11.7	99; 12.5	72; 14.4
Antidepressant	415; 15.1	201; 13.8	115; 14.5	99; 19.8
Antihypertensive	403; 14.7	202; 13.9	121; 15.3	80; 16.0
Onabotulinum toxin A	67; 2.4	37; 2.5	18; 2.3	12; 2.4
Length of most recent preventive treatment before stopping (N; %)				
	N=272**	N=125**	N=83**	N=64**
<3 months	102; 37.5	49; 39.2	33; 39.8	20; 31.3
4-6 months	66; 24.3	30; 24.0	20; 24.1	16; 25.0
7 or more months	104; 38.2	46; 36.8	30; 36.1	28; 43.8

HD/m, headache days per month.
*Patients with >=4 HD/m on average over the last 90 days and >=11 Migraine Disability Assessment Score (MIDAS).
Users of CGRP-monoclonal antibodies were excluded.
**Patients who stopped preventive medication.

Table 2. Traditional preventive treatment patterns in the eligible* population

	Overall	4-7 HD/m	8-14 HD/m	>=15 HD/m
Number of respondents	806	401	223	182
Satisfaction categories (%)				
Completely	9.3	11.7	9.0	4.4
A lot	23.9	24.9	24.2	21.4
Somewhat	39.0	37.7	40.8	39.6
A little	18.6	17.7	17.5	22.0
Not at all	5.2	2.5	6.3	9.9
Don't remember	4.0	5.5	2.2	2.7

HD/m, headache days per month
*Patients with >=4 HD/m on average over the last 90 days and >=11 Migraine Disability Assessment Score (MIDAS).
Users of CGRP-monoclonal antibodies are excluded.

Table 3. Patient satisfaction with current treatment in the eligible* population

Conclusion: The findings confirm unmet needs regarding preventive migraine medications. Most patients reported not using preventive medication despite being eligible and at least moderately disabled, and many indicated low treatment satisfaction and early termination of treatment.

Disclosure: JP: advisory boards for Allergan-Abbvie, Amgen-Novartis, Eli Lilly, and Teva. SE: consultation/speaker for Allergan-Abbvie, Eli Lilly, Lundbeck, Novartis, Perfood and Teva. TP, GDA and DN: full-time employees and stock-holders of Eli Lilly.

EPO-080

The Vienna Idiopathic Intracranial Hypertension (VIIH) database – an Austrian real-world cohort

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Background and aims: Idiopathic intracranial hypertension (IIH) is an increasingly prevalent disease bearing the risk of visual impairment and affecting quality of life. Clinical presentation and outcome are heterogeneous. Large, well-characterized cohorts are scarce. The aimed to describe the Vienna-Idiopathic-Intracranial-Hypertension (VIIH) database aiming to characterize the clinical spectrum, diagnostic findings, therapeutic management and outcome of IIH.

Methods: Applying the modified Dandy criteria we identified 113 IIH-patients treated at our center between 2014 and 2021.

Results: Of 113 patients, 89% were female (mean age 32.3 years). Median body mass index (BMI) was 31.8, with 85% overweight (BMI>25). Papilledema was found in 95% with 5% classified as IIH without papilledema. Headache was present in 84% and showed migrainous features in 36%. Median opening pressure in lumbar puncture was 31cm H_2O. Pharmacotherapy (predominantly acetazolamide) was established in 99%, 56% required at least one therapeutic lumbar puncture and 13% surgical intervention. After a median follow-up of 3.7 years, 43% had not achieved significant weight loss, papilledema was present in 49% and headache in 76% (58% improved). Comparing initial presentation to follow-up, perimetry was abnormal in 67% vs. 50% (8% worsened, 24% improved) and transorbital sonography in 87% vs 65% with a median optic-nerve-sheath-diameter of 5.4mm vs. 4.9mm. Median peripapillary-retinal-nerve-fiber-layer thickness had decreased from 199µm to 94µm and ganglion-cell-layer thickness from 40µm to 36µm.

Conclusion: The VIIH database constitutes a large representative and well-characterized cohort and emphasizes substantial long-term sequelae of IIH. Future analyses will aim to refine phenotyping and identify factors predicting outcome.

Disclosure: No disclosures relevant to this study.

EPO-081

Characterization and long-term follow-up of headache after posterior reversible encephalopathy syndrome

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Background and aims: Posterior reversible encephalopathy syndrome (PRES) is a neurological disorder consisting in cerebrovascular dysregulation with reversible subcortical vasogenic brain edema characterized by acute neurological symptoms, including headache. However, little is known on headache as a sequela of PRES. We aimed to explore its prevalence, characteristics, and impact.

Methods: We retrospectively recruited consecutive patients with PRES diagnosis presented at our center from April 2018 to December 2021. We described baseline demographics, previous headache history, neuroimaging and clinical characteristics of the hospitalization episode. We evaluated presence of headache, its characteristics and impact during and after the initial episode.

Results: We included 25 patients with a median follow-up time after symptom onset of 18 months and mortality rate of 44% (11 patients). Fourteen patients could be contacted and 9 responded (response rate 64.3%). Of them, 3 patients (33%) had history of episodic migraine. Five patients (55.6%) reported headache during PRES hospitalization episode. After PRES resolution, 8 patients (88.9%) had headache with migraine-like features, no other clinically relevant sequelae were reported. Headache was episodic (<15 days/month) in all patients except one with concomitant reversible cerebral vasoconstriction syndrome, developing chronic headache (>15 days/month) of moderate-severe intensity with medication overuse. No one received specific headache treatment.

Conclusion: Our data suggest that almost every patient has headache as a main sequela of PRES. Migraine-like features point to the existence of shared pathophysiological mechanisms with migraine, that may mainly involve vascular and endothelial functions, however more studies are warranted.

Disclosure: The authors declare that they have no relevant or material financial interests that relate to the research described in this study.

EPO-082

Internal Carotid Artery Dissection presenting as a new-onset episodic cluster-like headache

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Background and aims: Symptomatic cluster headache (CH) has been described in association with structural lesions, mainly vascular, tumoral and inflammatory pathologies located in the middle fossa. Some cases of CH secondary to internal carotid artery dissection were reported.

Methods: We describe a patient with symptomatic cluster-like headache associated with an internal carotid artery dissection.

Results: A 55-year-old man, with no history of headaches, started with 15-day history of recurrent episodes of sudden and stabbing left periorbital pain, accompanied by ipsilateral ptosis, conjunctival injection, lacrimation and cutaneous allodynia. Attacks occurred once a week, predominantly at night and lasting about 2 hours. The patient remained with milder fronto-parietal pain of pressing quality between attacks. Non-steroidal anti-inflammatory drugs were ineffective and zolmitriptan provided a fast relieve of pain attack. Neurological examination revealed ptosis and miosis in the left eye in absence of pain. An ecoDoppler of extracranial vessels was negative. A brain MRI showed an intramural hematoma in distal cervical and petrous segments of left internal carotid artery, leading to the diagnosis of a spontaneous left internal carotid artery dissection. The patient was treated with antiaggregants (acetylsalicylic acid 150 mg) and analgesics. During the subsequent days he did not present further attacks.
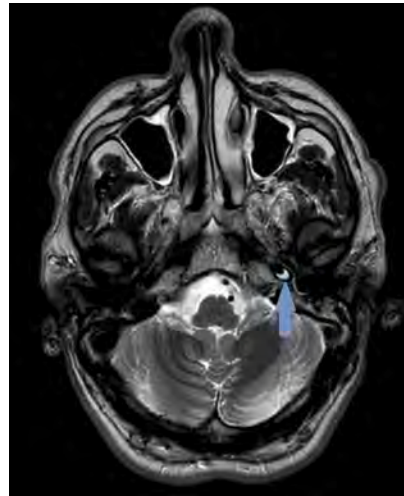
Intracranial left carotid internal artery dissection - Axial Brain MRI T2-sequence

Conclusion: Our patient presented typical CH attacks with a favourable response to triptans, although persistence of miosis and slighter pain in-between attacks raised the suspicion of a secondary cause. Brain MRI imaging showed a rare carotid artery dissection location involving both extracranial and intracranial portions. This case stresses the need to investigate secondary CH.

Disclosure: None of the authors has any conflict of interest to disclose.
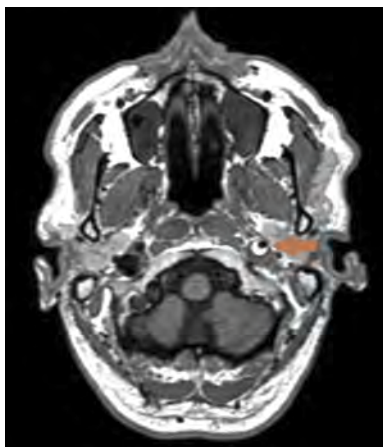
Extracranial left carotid internal artery dissection - Axial Brain MRI T1-sequence

EPO-083

Optimization study for treatment of occipital neuralgia by occipital infiltration

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Background and aims: The treatment of choice for ON (occipital neuralgia) is AB (anesthetic block), however, there are no studies comparing the result of infiltration of A (anesthetic alone), AC (anesthetic with corticosteroid) or BT (botulinum toxin type A) in the treatment of NO. A study is proposed to evaluate RR (rate of responders), CR (complete response) and DE (duration of treatment effect) by infiltration of A, AC or BT.

Methods: Prospective, longitudinal, open, uncontrolled and randomized study. Patients with a diagnosis of ON were selected in the Headache Unit of our hospital in the period from June 1, 2017 to June 30, 2020.

Results: 33 patients were recruited. 12 patients received treatment with A, 10 with AC and 11 with BT. The RR was 60% A, 70% AC and 65% BT, without statistically significant differences between them; CR of 40%, 30% and 40% respectively; prolonged DE (more than 3 months) was obtained in 30%, 85% and 55%, obtaining statistically significant differences in favor of AC.

Conclusion: The clinical and sociodemographic characteristics of the patients diagnosed with ON in our study were superimposable with those of previous series. The three therapeutic alternatives compared showed similar RR and CR. However, a higher DE was obtained when AC was administered, although with a higher rate of adverse effects than with the other alternatives, so its use should be limited to patients with a partial response or a short duration of effect.

Disclosure: Nothing to disclose.

EPO-084

Difference of episodic and chronic migraine in trpv1 gene 1911A>G polymorphism: a possible biomarker of chronification?

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Background and aims: TRPV1 receptors expressed in trigeminal neurons are implicated in migraine pain. Recent genetic studies suggested that the single nucleotide polymorphism (SNP) 1911A>G affects functional activity of the receptors and is involved in different pain conditions. However, this SNP has not been tested in migraine. Here was evaluated the frequency distribution of AA, AG and GG variants of 1911A>G in the TRPV1 gene in healthy individuals and patients with episodic (EM) and chronic migraine (CM) to test the influence of the SNP on susceptibility to these forms of migraine.

Methods: The study included 106 patients with migraine (32 EM and 24 CM) and 50 healthy controls. DNA from peripheral blood was used to test TRPV1 SNP using allele-specific PCR.

Results: The genotype frequency distribution in EM was comparable with that in controls (AA-38%, AG-53%, GG-9% and AA-34%, AG-46%, GG-20%, respectively, p=0.467) but a tendency of GG variant frequency reduction is noticeable. In CM the distribution differed significantly from control and EM (p=0.012 and p=0.049): the AA genotype doubly increased, whereas the GG variant was completely absent, AA-67%, AG-33%, GG-0% (Fig.1).
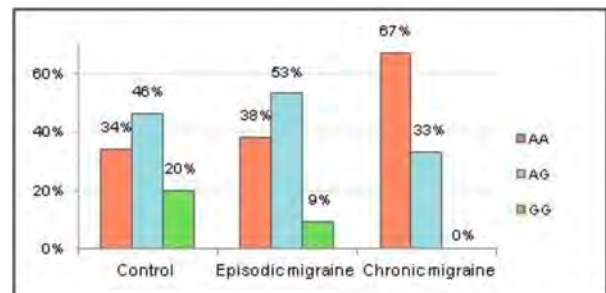
Fig. 1 TRPV1 1911A>G SNP distribution in the control group, episodic and chronic migraine patients

Conclusion: This is first indications of distinctive involvement of TRPV1 1911A>G genotypes in EM and CM. Our data reveal a different predisposition to chronic pain in migraine and give a new look at the nature of its chronification, proposing that the absence of GG genotype may be considered as potential biomarker of migraine chronification risk.

Disclosure: This work was supported by the Program of Competitive Growth of Kazan Federal University.

Infectious diseases 1

EPO-085

Neuro-HIV: A Single Center Experience

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Background and aims: Neurological complications of human immunodeficiency virus (HIV) infection continue to be observed despite antiretroviral therapies (ARTs). In this study, the parameters that can predict the development of neuro-HIV and the change of disease presentation over the years were evaluated.

Methods: Individuals living with HIV followed in our center between January 2011-October 2021 were evaluated.

Results: Among 978 HIV-positive patients, 27 patients with confirmed neuro-HIV diagnoses were included. Female to male ratio was 1:5.75, and the median follow-up was 26 months. While 51.9% of the patients had neurological involvement at the time of diagnosis, 13 patients developed neurological involvement during follow-up (median 48 months). CD4/CD8 and serum leukocyte count at the time of neuro-HIV diagnosis were found to be significantly lower than the values at the time of HIV diagnosis (p<0.05). When neuro-HIV patients and age and sex-matched HIV positive control subjects were compared, it was found that the initial leukocyte and lymphocyte counts were significantly lower in the neuro-HIV group (p<0.01), and HIV viral load at the time of the first diagnosis tended to be higher (p=0.94). Moreover, it was observed that neurological involvement and presentation of the patients changed over the years; while opportunistic infections and lymphomas were more frequent between 2011-2015, immune-reconstruction syndromes, peripheral and cognitive involvement, and transient demyelination became more frequent after 2015.

Conclusion: Neuro-HIV can be predicted by routine parameters such as initial leukocyte and lymphocyte. Increasing awareness among physicians and ARTs has led to a change in the neurological presentation of the disease over time.

Disclosure: The authors have nothing to disclose.

EPO-086

Epstein-Barr virus detected in cerebrospinal fluid causative agent or just an observer?

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Background and aims: Neurological complications secondary to Epstein Barr virus (EBV) infection are uncommon. Optimal therapeutic strategies remain unclear, and except in immunocompromised patients, the pathogenic role and clinical significance of EBV is debatable.

Methods: Retrospective study including patients admitted to our hospital between January 2011 and April 2021 with neurological manifestations and positive EVB PCR in cerebrospinal fluid (CSF).

Results: A total of 28 patients were included (71.4% women; mean age of 51.60 years), of which 39.30% had an immunosuppressive condition. In 21 cases, neurological symptoms were explained by other causes. Systemic infections were the most frequent (7), followed by autoimmune diseases (5). In this group, EBV detection in CSF was regarded as nonpathogenic, and in those cases secondary to immune pathologies, EBV infection was considered a feasible precipitating factor. As a hemorrhagic CSF was obtained after a traumatic lumbar puncture in 52.40% of the cases, an amplification of the virus on serum leucocytes could not be ruled out. Of the seven patients with clinical diagnosis of EBV encephalitis, three were immunocompromised. Encephalitis cursed with fever (85.70%), headache (71.40%), focal neurological deficits (71.40%) and confusional state (57.10%). In all cases, a pathologic CSF was obtained, revealing pleocytosis and elevated proteins. Three patients showed nonspecific MRI lesions (14.30% focal, 28.60% diffuse). All seven patients received empiric therapy with acyclovir with a median duration of 13.28 days, and none kept disabling neurological sequelae at discharge.

Conclusion: EBV detection on CSF should be cautiously interpreted, and be considered as pathogenic once more frequent etiologies have been ruled out.

Disclosure: The authors declare no conflict of interests.

EPO-087

Bilateral papillitis: neurosyphilis, a diagnosis to consider

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Background and aims: Syphilis is a sexually transmitted disease caused by Treponema pallidum. It has an extensive range of clinical presentations, which can mimic many conditions. The natural history of the disease is complex, with chronological overlap between the different phases. Neurosyphilis can present at any stage. Ocular symptoms as a first clinical manifestation of syphilis are uncommon, especially in immunocompetent individuals. Optic nerve involvement is particularly rare. All patients with this presentation must be submitted to a lumbar puncture to confirm neurological involvement.

Methods: Here we describe 2 cases of neurosyphilis, presented as bilateral papillitis.

Results: Two men, 57 and 65 years old, with no relevant medical background, came to the ER due to progressive painless vision loss. They denied headache, vomit, nausea, fever or any other systemic symptoms. Fundoscopic examination revealed bilateral papilledema. Visual fields evaluation disclosed a central scotoma. Tests were worse in the right eye for both patients. The remaining neurological examination was normal. They had positive serum serology for Treponema pallidum and a brain MRI with no signs of intracranial hypertension. CSF analysis revealed lymphocytic pleocytosis and positive TPHA tests. HIV tests were negative. The diagnosis of syphilitic papillitis was assumed. Treatment with penicillin 4 UM, 4/4 hours, for 14 days, was decided. Both patients significantly improved after treatment.

Conclusion: The diagnosis of ocular syphilis may be challenging, since it lacks characteristic pathognomonic findings. Papillitis is an uncommon, yet possible, ocular manifestation of neurosyphilis, which is potentially treatable. Therefore, syphilis infection should be ruled out in patients presenting with papillitis.

Disclosure: The authors declare that there is no conflict of interest.

EPO-088

CSF neurofilament light chain concentrations predict unfavourable outcome in community-acquired bacterial meningitis

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Background and aims: Unfavorable outcome after meningitis is mainly caused by an excessive inflammation reaction of the host's immune system in reaction to the bacterial infection, leading to injury to the central nervous system. Neurofilament light chain (NfL) is a biomarker for neuro-axonal damage, that has been found to be elevated proportionally to the degree of neuronal damage in neurological diseases.

Methods: We measured NfL concentration in CSF samples from a prospective cohort study of adults with community-acquired bacterial meningitis and determined associations between NfL CSF concentrations and outcome in multivariate analyses. We identified independent predictors of an unfavorable outcome (Glasgow Outcome Scale score 1-4) by logistic regression.

Results: CSF NfL concentrations were evaluated in 429 episodes. Median age was 62 years (IQR 50–69). 290 of 422 (68%) episodes presented with an altered mental status (GCS<14). The overall case fatality rate was 15% and unfavorable outcome occurred in 37%. Median CSF NfL concentration was 600 pg/mL (IQR 348–1047). NfL concentrations were higher in patients presenting with focal cerebral deficits, in patients with an unfavorable outcome, and in patients that died. High CSF NfL concentration (OR 1.5, CI95% 1.07–2.00) showed to be an independent predictor of unfavorable outcome, together with older age (OR 1.03, CI 95% 1.01–1.05), cranial nerve palsy (OR 4, CI 95% 1.6–10.3) and high serum CRP (OR 1.3, CI 95% 1.01–1.05).

Conclusion: CSF NfL concentration is independently associated with unfavorable outcome in adults with community-acquired bacterial meningitis, suggesting that CSF NfL concentration may be a useful biomarker in bacterial meningitis.

Disclosure: Nothing to disclose.

EPO-089

Intracerebral hemorrhage in bacterial meningitis

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Background and aims: To determine the incidence, clinical course, and clinical outcome of intracerebral hemorrhage (ICH) complicating community-acquired bacterial meningitis.

Methods: The clinical characteristics and outcome of patients with intracerebral hemorrhage as a complication in bacterial meningitis were studied in a prospectively nationwide cohort in the Netherlands performed from 2006 to 2018.

Results: ICH was identified in 44 of 2306 episodes of bacterial meningitis (1.9%). Nine of these patients (20%) were diagnosed with ICH on admission and 35 (80%) during admission after a median of 5 days (1-9). ICH was diagnosed after a new decrease of consciousness level in 30 of 44 (68%), persistent decrease in the level of consciousness in 1 (2%), new focal neurological deficits in 9 of 44 (20%), systemic complications such as severe sepsis with multiorgan failure in 4 of 44 (9%), and seizures in 1 (2%) patient. ICH occurred in 4 patients with endocarditis (9%), 9 patients on anticoagulation (vitamin K antagonists and heparin; 20%), and 10 patients with cerebral infarctions (23%). ICH in bacterial meningitis was associated with high rates of death (24 of 44 [55%] vs. 346 of 2200 [16%]; P<0.001) and unfavorable outcome compared to non-ICH patients (39 of 44 [89%] vs. 798 of 2200 [36%]; P<0.001). Neurological sequelae on discharge occurred frequently in ICH survivors compared to non-ICH patients (15 of 20 [75%] vs. 190 of 797 [24%]; P<0.001).

Conclusion: ICH is a rare but severe complication in patients with bacterial meningitis associated with endocarditis, cerebral infarction, anticoagulant use, high rates of death, and unfavorable outcome.

Disclosure: Nothing to disclose.

EPO-090

Serum and cerebrospinal fluid values of collectins and ficolins in patients with Angiostrongylus cantonensis

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Background and aims: The lectin pathway constitutes an effector mechanism of the innate immune response against different danger signals detected in the host. However, as it is still under study, its role in parasitic infections such as eosinophilic meningoencephalitis by Angiostrongylus cantonensis is yet unknown. The aim of this work was to evaluate the behavior of serum and cerebrospinal fluid values of MBL, ficolins, MASP2 and CLK1 in adult patients from Cuba and Ecuador with meningoencephalitis due to A. cantonensis.

Methods: An observational analytical study of cases and controls was conducted in 60 adult Ecuadorian and Cuban subjects. Serum and cerebrospinal fluid levels of MBL proteins, H and M ficolins, MASP2 and CLK1 were quantified by commercial ELISA packages.

Results: In serum and CSF of the patients, there was a significantly higher increase in the mean values of these proteins in relation to the controls. The increase in protein levels in CSF of the patients corresponded with the increase in serum. Ecuadorian patients showed significantly higher mean levels of these proteins than Cuban patients.
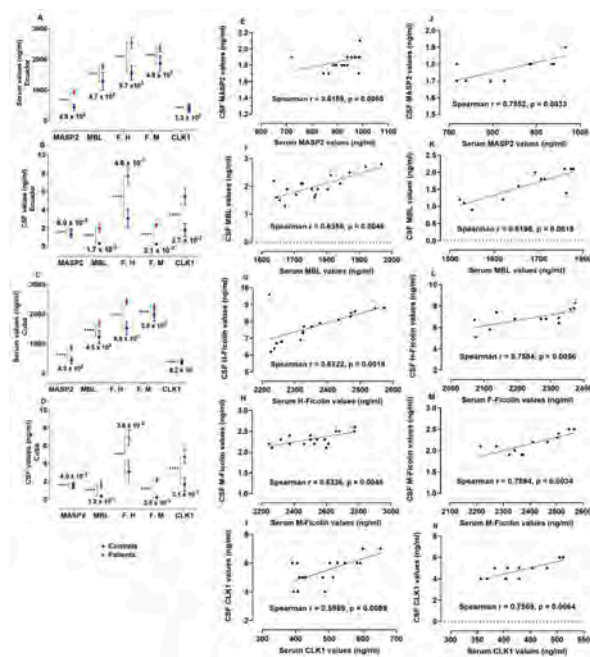
Figure

Variables	Cases		
	Ecuador (n = 18)	Cuba (n = 12)	p-value
Sex (total. %)	F: 8 (44.4%)	F: 7 (58.3%)	0.710[a]
	M: 10 (55.6%)	M: 5 (41.7%)	
Age (years; mean ± DE)	29.9 ± 8.0	33.6 ± 9.9	0.269[b]
MASP2 serum	924.3 ± 68.3	855.1 ± 93.6	0.025[c]
MASP2 LCR	1.9 ± 0.1	1.8 ± 0.1	0.046[c]
MBL serum	1761.7 ± 94.2	1671.3 ± 95.3	0.042[c]
MBL LCR	2.0 ± 0.4	1.6 ± 0.4	0.043[c]
ficolin H serum	2533.0 ± 168.8	2407.8 ± 111.3	0.042[c]
ficolin H LCR	7.7 ± 1.0	6.9 ± 0.9	0.042[c]
ficolin M serum	2357.8 ± 112.9	2241.8 ± 116.8	0.049[c]
ficolin M LCR	2.3 ± 0.2	2.2. ± 0.2	0.044[c]
CLK1 serum	486.7 ± 82.2	427.4 ± 51.0	0.042[c]
CLK1 LCR	5.3 ± 0.8	4.7 ± 0.6	0.046[c]
Variables	Controls		
	Ecuador (n = 18)	Cuba (n = 12)	p-value
Sex (total. %)	F: 9 (50%)	F: 4 (33.3%)	0.465[a]
	M: 9 (50%)	M: 8 (66.7%)	
Age (years; mean ± DE)	30.2 ± 10.0	34.7 ± 8.0	0.202[b]
MASP2 serum	431.6 ± 101.5	425.3 ± 117.9	0.594[c]

Table 1

Conclusion: In adult subjects with A. cantonensis meningoencephalitis there is a marked response of the activating proteins of the lectin pathway, especially ficolin H and CLK1 in CSF and ficolin H in serum compared to controls. The sick subjects from Ecuador had mean values of these proteins higher than the ones of Cuban sick subjects.
Disclosure: Yes.

EPO-091

HIV and Treponemal Serology in an Interesting Case of Subacute Inflammatory Demyelinating Polyradiculoneuropathy

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Background and aims: Both HIV and Syphilis are associated with early and late peripheral neurological presentations and share significant overlap in risk factors for acquisition. Here we present an interesting case of concomitant positive HIV and treponemal serology in a patient presenting with SIDP, and discuss considerations in their acute and chronic management.
Methods: Patient case report and review of literature.
Results: A 33-year-old patient presented with a 6-week history of progressive distal four limb weakness and paraesthesia with gait unsteadiness. They were globally areflexic at presentation, with mute plantars and glove and stocking paraesthesia. Cerebrospinal fluid, CSF, was lymphocytic with a raised protein of 0.88g/L. HIV antibody and p24 antigen were positive, and CD4 count was 350cells/ml. Treponemal tests were positive and rapid plasma reagin, RPR, was 1:4. CSF virology and treponemal testing was negative. Treatment with intravenous immunoglobins for HIV seroconversion-associated SIDP was instituted to good effect, with marked improvement in motor symptoms at two weeks. Commencement of antiretrovirals was deferred until clinical improvement and repeat treponemal serology planned for 2 months post-discharge.
Conclusion: Inflammatory demyelinating polyradiculo-neuropathies associated with both HIV and Syphilis have been described, and the two may co-present. Intravenous immunoglobin is an effective treatment in this setting, and penicillin treatment is unlikely to be required in the absence of positive CSF treponemal serology with RPR values of less the 1:8.
Disclosure: The authors declare no conflicts of interest.

EPO-092

Ischaemic stroke and infectious endocarditis by Gemella Morbillorum: usefulness of mechanical thrombectomy for diagnosis

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Background and aims: Stroke is a frequent complication of infectious endocarditis (IE), but the presence of this complication rarely aids the diagnosis of IE. Our objective is to present a case of IE caused by an infrequent opportunistic pathogen (Gemella morbillorum) that debuted as a stroke.

Methods: Description of a clinical case.

Results: A 73-year-old hypertensive woman with no history of dental procedures developed sudden aphasia, right hemiparesis, and fever. Examination showed a mitral systolic murmur and a NIHSS of 25. ECG was in sinus rhythm, initial CT showed ASPECTS of 9 and a left M1 distal segment occlusion. Treatment involved thrombolysis with Tenecteplase, and mechanical thrombectomy with TICI 3; the thrombus was frozen for study. The patient improved clinically (NIHSS 4). On the third day post-stroke, blood cultures were positive por Gemella morbillorum. A transesophageal echocardiogram revealed severe degenerative mitral regurgitation without vegetations. Cranial MRI showed infarcts in all arterial territories (figure 1). A PET-CT showed a septic embolus in the spleen (figure 2). Finally, the thrombus was sent for culture, and was positive for the same pathogen. The diagnosis of IE was confirmed by fulfilling a major criterion (new regurgitation) and 3 minor criteria (fever, vascular phenomena, and microbiological evidence). Treatment with Ceftriaxone 2g every 24h resulted in an excellent clinical evolution, with an mRS of 1 after 3 months.
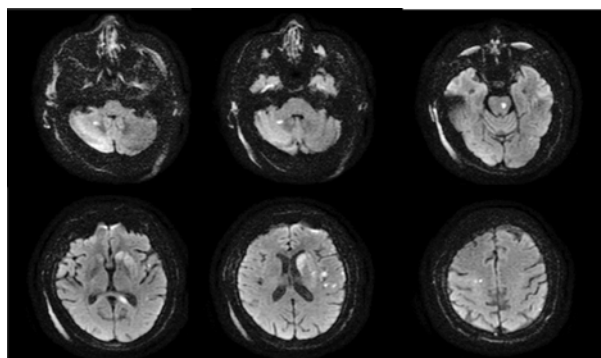
Figure 1: Cranial MRI, diffusion sequences show multiple supratentorial and posterior fossa ischaemic foci.
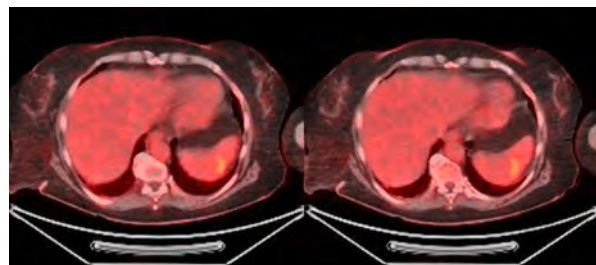
Figure 2. PET-CT. Focal increase in metabolism in the spleen parenchyma of approximately 2 cm, hypodense on CT, which in the context suggests an embolus

Conclusion: Histological study of thrombi can help identify the etiological mechanism of cryptogenic ischemic strokes, but the microbiological study of this material can also be key for diagnosis.

Disclosure: Authors have no clonficts of interest to disclose.

EPO-093

Seizures in adults with suspected central nervous system infection

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Background and aims: Seizures can be part of the clinical presentation of a central nervous system (CNS) infection. We describe patients suspected of a neurological infection who present with a seizure and study diagnostic accuracy of clinical and laboratory features predictive of CNS infection in this population.

Methods: We analysed all patients suspected of a CNS infection presenting with a seizure who underwent cerebrospinal fluid (CSF) examination that were included in two prospective cohort studies in the Netherlands.

Results: Of 900 episodes of suspected CNS infection, 124 (14%) presented with a seizure. The median age was 60 years (IQR 45–71) and 53% of patients were female. CSF examination showed a leukocyte count > 4/mm^3 in 41% of episodes. A CNS infection was diagnosed in 27 of 124 episodes (22%), a CNS inflammatory disorder in 8 (6%) episodes, a non-neurological infection in 10 (8%), a non-infectious non-inflammatory neurological disease in 77 (62%) and in 2 (2%) episodes a non-neurological, non-infectious disorder was diagnosed. There were no distinctive differences between diagnostic groups with regard to clinical presentation, blood examination and radiological features. Sensitivity and specificity of these characteristics for diagnosing CNS infection were low. CSF leukocyte count was the best predictor for CNS infection in patients with suspected CNS infection presenting with a seizure (area under the curve 0.94).

Conclusion: Clinical and laboratory features fail to distinguish CNS infections from other causes of seizures in patients with a suspected neurological infection. CSF leukocyte count is the best predictor for the diagnosis of CNS infection in this population.

Disclosure: Nothing to disclose.

EPO-094

Primary progresive multiple sclerosis (ppms): chamaleon what is hiding behind?

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Background and aims: Human immunodeficiency virus (HIV) is responsible for multiple neurological complications, affecting both the peripheral and central nervous system (CNS). Even though it is barely described in scientific literature, HIV's CNS infection may clinically simulate a PPMS.

Methods: Clinical case admitted to the department of Neurology of Hospital Clínico San Carlos of Madrid.

Results: A 44-year-old male without prior medical history complained of five months progressive gait difficulties and urinary incontinence. The neurological examination revealed pyramidal quadriparesis (inferior limbs severely affected), global hyperreflexia and bilateral Babinski's sign associated with spastic-ataxic gait. In addition, he presented impaired attention and abnormal response latency. The initial topographic diagnosis was a myelopathy due to possible PPMS. Therefore a brain and spine magnetic resonance imaging (MRI) was performed, revealing extensive and confluent subcortical leukopathy that affected both cerebral hemispheres (Figure 1 and 2) and, surprisingly, spared spinal cord. No mass effect, contrast enhancement, restricted diffusion or juxtacortical involvement was found. Cerebrospinal fluid analysis revealed mild protein (77mg/dl) and leukocytes elevation (10/uL, being 100% mononuclear) and a positive result for HIV's RNA with polymerase chain reaction test. The CD4-cell-count was 75/mm3 and the viral load was more than 70.000 copies/ml. Antiretroviral treatment was initiated and the patient experienced rapid clinical and immunological improvement. The diagnosis of atypical HIV encephalopathy was made.
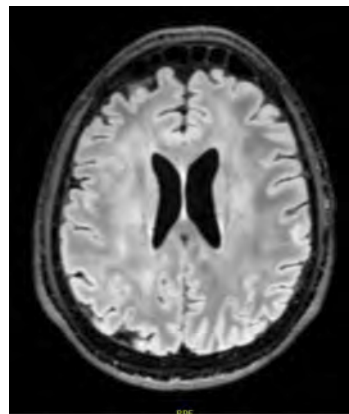
Figure 1. Axial fluid-attenuated inversion recovery brain MRI (FLAIR) showing confluent subcortical leukopathy that affected both cerebral hemispheres
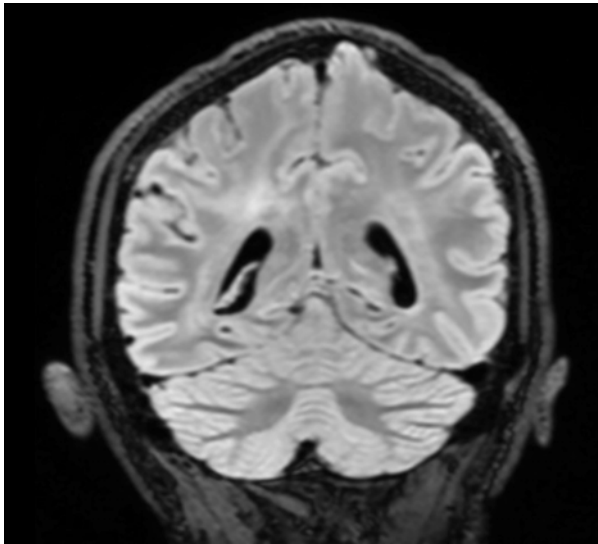
Figure 2. Coronal fluid-attenuated inversion recovery brain MRI (FLAIR) showing confluent subcortical leukopathy that affected both cerebral hemispheres

Conclusion: VIH CNS's infection is a thousand faces disease. Due to its potential treatability, with this clinical vignette we underline the importance of considering it as an alternative diagnosis to MS.

Disclosure: Nothing to disclose.

EPO-095

Diagnostic value of C-reactive protein level in cerebrospinal fluid in HIV/AIDS patients with cerebral toxoplasmosis

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Perm State Medical University named after academician E.A. Vagner, Perm, Russian Federation

Background and aims: The main purpose of the study is to evaluate correlation between C-reactive protein (CRP) level in cerebrospinal fluid and clinical severity of cerebral toxoplasmosis (CT) neurological manifestations in patients with HIV/AIDS.

Methods: In this cohort study 26 patients with determined CT were included. For evaluation of CT severity we modified NIH-stroke scale based on the same clinical manifestation (e.g. meningeal signs, cerebral dislocation symptoms and seizures were included). Identification of CRP concentration in CSF realized by ELISA test.

Results: The outcomes of CT in investigated group were positive in 22 cases (full or partial neurological functions recovery) and lethal in 4 cases. Average value of CT-severity scale was 10.5 [9;14] points (max -50 points). Average concentration of CRP in CSF was 0.1375 M/e [0.0375;0.70] and positive correlation between CRP level and CT-severity scale value was divided (R=0.584043, p<0.05).

Conclusion: CRP is an inflammatory blood-circulation biomarker and blood-brain barrier (BBB) isn't permeable for it in a healthy condition. High level of CRP in CSF indicates pathological BBB-permeability in HIV/AIDS patients with CT and may be alternative diagnostic criteria of CT-severity and prognostic biomarker of CT-outcomes.

Disclosure: The authors confirm that there is no conflict of interests.

EPO-096

Mortality and Characteristic of Cryptococcal Meningitis between HIV and non-HIV infected Patients: A Comparative Study

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Background and aims: Cryptococcal meningitis (CM) considered as the devastating infectious diseases in both HIV and non-HIV patients. We aimed to compare clinical features, laboratory and imaging finding and in-hospital mortality of CM patients between HIV and non-HIV patients.

Methods: We conducted an analysis of the data derived from Chiang Mai University Hospital registry between 2017 and 2021. We included consecutive CM patients who were 18 or older. Study outcomes were incidence and characteristic patients, risk factors, laboratory and imaging profile and in-hospital mortality.

Results: Of 46 cryptococcal meningitis patients, twenty-seven were HIV infected while 19 were non-HIV infected. HIV with CM infrequent occurred in age more than 50 (25.9% vs 63.2%, p=0.012). HIV group had higher Charlson Comorbidity index (6 (Interquartile range (IQR) 6,7) vs 2 (IQR 1,4), p<0.001). Leukopenia was likely found in CM with HIV (51.9% vs 5.3%, p=0.001). CM in HIV patients infrequently had white cells in cerebrospinal fluid more than 50 cells/mm3 (44.4% vs 55.6%, p=0.012). CM in HIV had less hydrocephalus from brain imaging comparing with non-HIV group (22.2% vs 63.2%, p=0.005). The mortality rate of CM in HIV and non-HIV was not statistically difference (7.4% vs 5.3%, p=0.772). The independent risk factor for in-hospital mortality of CM were albumin level (Odds ratio 0.02, 95% confident interval 0.01–0.66).

Conclusion: The clinical features, laboratory, imaging of Cryptococcal meningitis in HIV and non-HIV patients were different. Hypoalbuminemia was the independent risk factor for in-hospital mortality. However, mortality was not different between HIV and non-HIV patients.

Disclosure: Nothing to disclose.

EPO-097

Not always necrophorum: A rare case of adult Lemierre syndrome with paradoxical septic emboli by K. pneumoniae

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Background and aims: We present a patient with Lemierre syndrome (LS) from Klebsiella pneumoniae following an untreated otitis media, with septic emboli in the central nervous system, lungs, and abdomen.

Methods: A malnourished 48-year-old man with a history of untreated diabetes, and heavy alcohol and tobacco use, presented with purulent right-sided otorrhea of 15 days and involuntary eye movements. Clinical examination revealed nuchal rigidity, peripheral right-sided facial palsy, and concurrent horizontal gaze-evoked, and upbeat nystagmus.
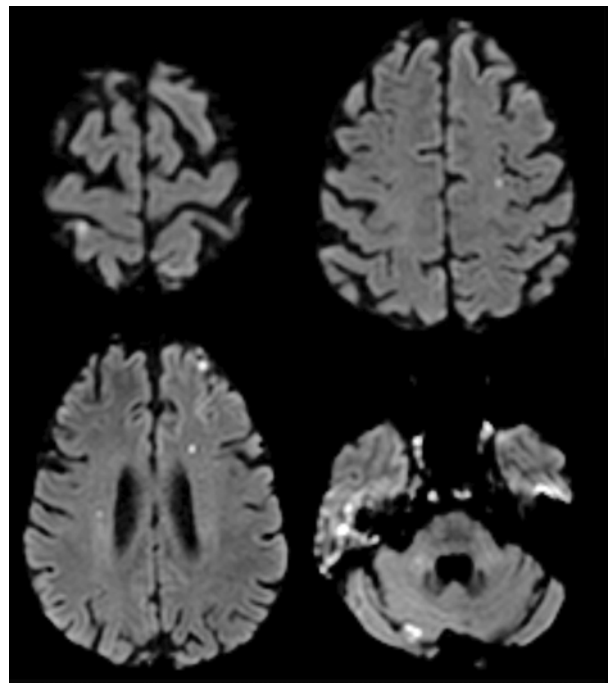
DWI MRI indicating small bilateral arterial infarcts.
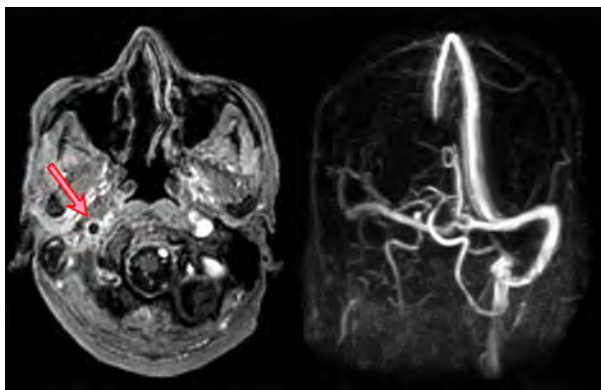
LEFT: T1 MRI with contrast (left) indicating thrombosis of the right internal jugular vein (red arrow). RIGHT: MRV indicating flow disturbance in the right transverse, sigmoid sinuses and the right internal jugular vein.
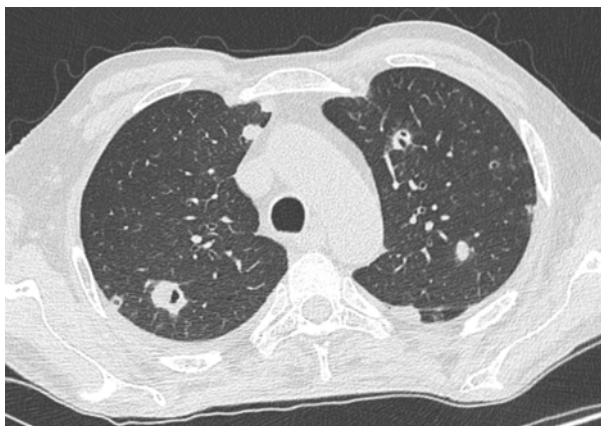
Chest CT showing bilateral septic emboli in the lung parenchyma.

Results: Brain imaging revealed right-sided mastoiditis, erosion into the posterior cranial fossa, multiple small arterial cerebral and cerebellar infarcts, and thrombosis in the right transverse and sigmoid sinuses extending to the internal jugular vein. Lumbar puncture findings indicated bacterial meningitis. Klebsiella pneumoniae was cultivated from otic discharge and cerebrospinal fluid. Computed tomography revealed multiple lung septic emboli and a lesion in the head of the pancreas. Transesophageal echo was negative for endocarditis but revealed a patent foramen ovale (PFO). Following clinical improvement and remission of the lesions after targeted antibiotic therapy, the patient was transferred to undergo mastoidectomy.

Conclusion: We believe this to be a rare case of LS caused by Klebsiella pneumoniae in an adult. LS is a dangerous complication of ear, nose, and throat infections that can rarely present in adult patients, and can very rarely be caused by organisms other than Fusobacteriae. When considering LS clinicians should always rule out endocarditis, and in the presence of septic emboli in both circulations, a PFO should be suspected.

Disclosure: Nothing to disclose.

EPO-098

Risk score for identifying adults at low risk of bacterial meningitis and other urgent treatable causes

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Background and aims: Distinguishing between bacterial meningitis and non-urgent causes of cerebrospinal fluid (CSF) leukocytosis in patients suspected of a CNS infection is difficult when the CSF Gram stain is negative. We studied diagnostic accuracy of an updated risk score to identify patients with bacterial meningitis or another urgent treatable cause (UTC) of CSF leukocytosis and a negative Gram stain.

Methods: We validated an updated risk score based on the composite variables altered immune status, abnormal physical examination and abnormal laboratory findings (1 point each) in three cohorts of adult patients showing >10 CSF leukocytes/mm3 and a negative Gram stain. Sensitivity and specificity of a high-risk score (≥1 point) for bacterial meningitis and a UTC were calculated.

Results: We included 109 bacterial and 196 viral meningitis/encephalitis cases in the United States (2014–2019) and 438 patients suspected of a CNS infection in the Netherlands (2006–2020): 216 with bacterial, 68 with viral meningitis and 154 with another diagnosis. The sensitivity for bacterial meningitis was 100% (95% CI 99–100) in the US cohort and 100% (95% CI 98–100) in the Dutch cohorts. The specificities were 34% (95% CI 28–41) and 31% (95% CI 20–43), respectively. The sensitivity for a UTC was 100% (95% CI 97–100) and the specificity 23% (95% CI 16–31).

Conclusion: The risk score had 100% sensitivity to identify patients with bacterial meningitis or any UTC of CSF leukocytosis and a negative Gram stain. It has the potential to reduce empiric treatment and hospitalization by identifying patients at low risk of a UTC.

Disclosure: Nothing to disclose.

EPO-099

Efficacy and safety of corticosteroids in viral encephalitis: a systematic literature review and meta-analysis

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Background and aims: Specific antiviral treatment is only available for a small subset of viral encephalitis (VE). Little evidence for the use of glucocorticoids as (adjunct) treatment exists. We present a systematic review and metaanalysis on the efficacy and safety of steroids in VE.

Methods: We conducted a systematic literature review (CRD42021233965) and report it according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) standards. Two observational studies from unpublished or partially published data were added (Linz/Houston cohort). For the metaanalysis, we employed the metaphor package for R.

Results: For the report selection process see Figure 1. 155 patients were added from the Houston and Linz cohorts. Further details and GRADE (Grading of Recommendations Assessment, Development and Evaluation) ratings see Table 1. Patient outcomes were heterogeneous. Only three of the trials report an advantage of steroid therapy. Steroid-induced side effects were scarce. Individual data were available for 281 persons (excluding single case reports), 120 of whom received steroids. For causative pathogens see figure 2. Ten cohorts were included into the metaanalysis. For the pooled data, the null hypothesis could not be rejected (p=0.245) using a random effects model, i.e. a benefit of steroid treatment on survival in VE could not be shown.

Viral pathogens diagnosed in those patients with available individual data. CMV-cytomegalovirus, EBV-Epstein-Barr-virus, TBEV-tick-borne encephalitis virus, VZV-varicella zoster virus, WNV-West Nile virus

Selection of included reports. Flow-chart depicting the selection process of reports included in this review according to PRISMA guidelines.

GRADE assessment of the included trials and observational studies.

Conclusion: Steroids as potent anti-inflammatory agents may act through a reduction of secondary inflammation-mediated damage. Our data do not support the use of steroids in VE. However, multiple shortcomings apply. Standardized controlled trials are needed and should also investigate optimal dosing and timing of glucocorticoid administration.

Disclosure: Nothing to disclose.

Movement disorders 1

EPO-100

Simultaneous recording in Parkinson's disease with STAT-ONTM and subthalamic local field potentials (PerceptTM)

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Background and aims: An increasing number of novel technologies are becoming available to monitor motor complications of Parkinson's disease (PD). Our aim is to describe in clinical practice simultaneous recording of local field potentials (LFPs) and inertial sensors with STAT-ONTM in a patient with PD undergoing deep brain stimulation (DBS).

Methods: A 40-year-old male with advanced early-onset PD (PARK2) underwent bilateral DBS of the subthalamic nucleus (STN) with the PerceptTM neurostimulator (Medtronic). After verifying the correct anatomical location of the electrodes, motor activity was recorded for one week with the STAT-ONTM device and LFPs with PerceptTM, before applying continuous stimulation. The patient recorded different events: best "on", worst "off", generalized (i.e., "peak dose") and leg (i.e., "biphasic") dyskinesias, and medication intake.

Results: It was observed that the events recorded by our patient were synchronous with the typology of recordings in STAT-ONTM and PerceptTM (Figures 1 and 2). Specifically, "off" periods coincided with "off" state recordings in STAT-ONTM and with beta bands; "peak-dose" dyskinesias were synchronous with those identified by STAT-ONTM, with gamma band and without beta band; "biphasic" dyskinesias coincided with a beta band; and STAT-ONTM detected episodes of gait freezing, most of them "off" and with beta bands. After activating DBS, a decrease in the daily beta band recordings was observed.

Figure 1 - Correlation graph between "off" and "on" events recorded by the patient and local field potentials (LFPs) frequency recording. a) "off" events clearly correlate with the recording of beta bands (10-30 Hz); b) "on" events show absence of beta bands and some gamma bands (31-200 Hz).

Figure 1

Figure 2 - Correlation between daily records of beta bands and motor status according to PerceptTM and STAT-ONTM, respectively. Beta bands coincided with "off" (red), "intermediate" (yellow) or "not applicable" (gray = no motion detected) motor status periods. The "on" periods (green) detected by STAT-ONTM coincide with beta band free periods. The majority of freezing of gait (FoG) episodes detected by STAT-ONTM coincided with non-"on" periods.

Figure 2

Conclusion: In our patient with PD treated with DBS of the STN, we observed consistent results in the indirect recording of motor complications using novel technologies. PerceptTM and STAT-ONTM may be two useful tools in therapeutic optimization.

Disclosure: I declare that this work has not been funded, totally or partially, by any company with economic interests in the products or equipment related to the content of this work.

EPO-101

Facial emotion expressivity in Parkinson's and Alzheimer's diseases

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Background and aims: One of the features in Parkinson's disease (PD) is reduced facial expressivity (hypomimia). Although parkinsonian signs are relatively common in Alzheimer's disease (AD), no study has specifically assessed the possible occurrence of reduced facial expressivity in these patients. We here aimed to investigate facial emotion expressivity in PD and AD patients compared to healthy controls (HCs).

Methods: 24 PD patients (17 M, mean age ± SD: 73.83±4.2years), 24 AD patients (9 M, 77.79±7.8years), and 24 HCs (13 M, 72.96±7.1years) were video-recorded while posing facial expressions of six primary emotions (anger, disgust, fear, happiness, sadness, surprise) and neutral expressions. Ten neurologists were screened for the ability to recognize facial expressions during an Emotion Recognition Task (ERT) and then asked to identify the emotion of the participants' pictures in a seven-forced-choice response format (Emotion Expressivity Task-EET). Accuracy of responses, reaction times, and confidence levels in the response were considered.
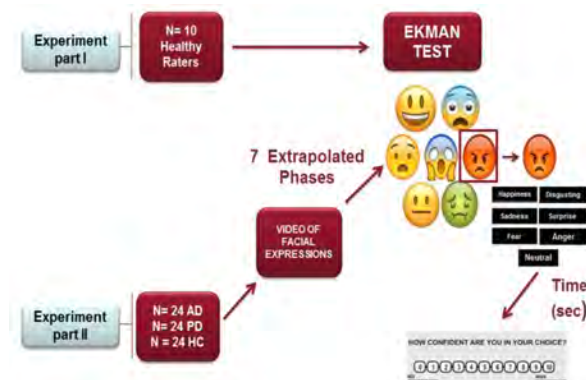
Experimental design for the evaluation of facial expressiveness

Results: The overall ERT score was higher than 80% (range:72–93%). In the EET, raters identified a lower number of correct responses in PD and in AD than in HCs (37%, 36%, and 52% respectively, p<0.01) with no differences between PD and AD (p=0.61). We also found longer reaction times for the evaluation of patients compared to HCs' pictures (p<0.05). The pattern of reduced facial emotion expressivity between PD and AD was similar.
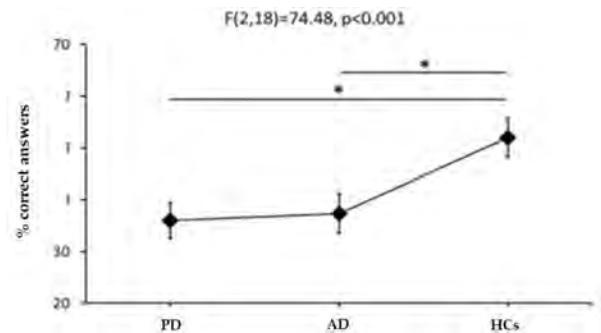
$F_{(2,18)}=74.48, p<0.001$

ANOVA showed a significant effect for the "GROUP" factor. Post-hoc analysis showed that raters were able to detect more correct responses in HCs than in patients with AD or PD (p<0.001 in both cases). No significant differences between AD and PD (p=0.61)
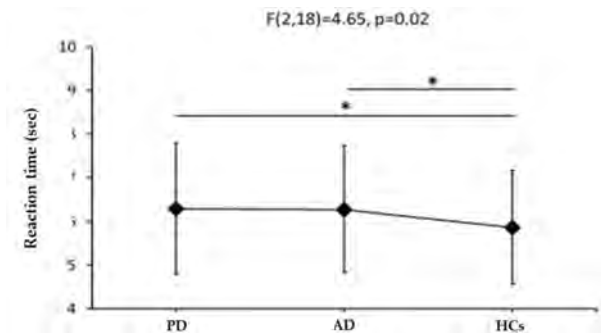
$F_{(2,18)}=4.65, p=0.02$

ANOVA showed a significant effect for the "GROUP" factor. Post-hoc analysis showed that raters spent less time responding when evaluating HCs than AD or PD (p<0.05 in both cases). No significant differences emerged between AD and PD (p=0.99).

Conclusion: As in PD, the study provides evidence of a reduced facial expressivity in AD. The facial expressivity deficit in PD and AD may result from common pathophysiology or a manifestation of distinct mechanisms. Further studies should better delineate the clinical relevance of reduced facial expressivity in AD.

Disclosure: Nothing to disclose. The authors report no conflicts of interest in this work.

EPO-102

Systematic Review and Network Meta-Analysis of COMT and MAO-B Inhibitors in Parkinson's Patients with Motor Fluctuations

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Background and aims: Levodopa (L-dopa) is the gold standard treatment for Parkinson's disease (PD). As its long-term use is associated with motor fluctuations (MF), adjuvant treatments such as monoamine oxidase B (MAO B) and catechol-O-methyl transferase (COMT) inhibitors are administered. This study compared the effects of COMT and MAO-B inhibitors on mean change from baseline to end-of-study in OFF-time for PD patients with MF using available literature.

Methods: A systematic review and random effects network meta-analysis model were conducted. Trials assessing the treatment of adults with idiopathic PD experiencing MF and/or wearing off with >25% OFF-time were included. Eligible trials included patients who could not be stabilised on L-dopa combinations and received one of the following add-on medications for ≥4 weeks: opicapone, entacapone, tolcapone, rasagiline, safinamide or placebo.

Results: Overall, 20 trials (n=5,659 patients) were included (Table). The estimated mean difference in change from baseline in OFF-time versus placebo in hours (95% confidence interval) were: -1.655 (-2.173;-1.137) for tolcapone-200mg; -1.591 (-2.183;-0.999) for tolcapone-100mg; -0.949 (-1.371;-0.527) for opicapone-50mg; -0.829 (-1.131;-0.527) for safinamide-100mg; -0.786 (-1.008;-0.564) for rasagiline-1mg; -0.704 (-1.072;-0.336) for safinamide-50mg; -0.606 (-0.812;-0.400) for entacapone-200mg; -0.415 (-0.827;-0.003) for rasagiline-0.5mg. The mean difference in change from baseline OFF-time versus placebo was -1.154 (-1.668;-0.640) for all COMT inhibitors combined and -0.734 (-0.884;-0.584) for all MAO-B inhibitors combined (Figure).

Table. Summary of studies included in the meta-analysis

Figure. The estimated difference in absolute change from baseline in OFF-time compared with placebo (hours) for COMT inhibitors and MAOB inhibitors. CI, confidence interval; COMT, catechol-O-methyl transferase; MAO-B, monoamine oxidase-B; RE, random effect

Conclusion: All treatments were more effective than placebo in reducing mean change from baseline OFF-time in PD patients with MF, with COMT inhibitors showing more efficacious trends than MAO-B inhibitors. Tolcapone and opicapone appeared to be the best performing drugs.

Disclosure: Supported by Bial.
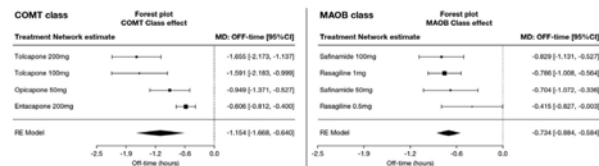
EPO-103

ELEGANCE – Prospective study of levodopa–entacapone–carbidopa intestinal gel (LECIG) in advanced Parkinson's disease

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Background and aims: Levodopa–entacapone–carbidopa intestinal gel (LECIG) was introduced in 2021 for treatment of patients with advanced Parkinson's disease (PD) and has received marketing authorisation in several European countries. The ELEGANCE study will collect real-world data on efficacy and safety of LECIG in routine clinical practice.

Methods: ELEGANCE is an international, non-interventional, observational study to be undertaken in ~16 countries after LECIG marketing authorisation is received. Study centres will offer participation to all adult advanced PD patients with severe motor fluctuations and hyperkinesia or dyskinesia despite optimised PD therapy and who have been prescribed LECIG in routine clinical practice. Subjects can be de novo patients or those who switch from another therapy. The planned total number of patients is ~300 across all countries.

Results: Primary objectives: To evaluate long-term efficacy and safety of LECIG over 24 months. Efficacy evaluations include effect on motor symptoms (MDS-UPDRS II and IV scores), required levodopa dose, other PD medication usage, Clinical and Patient Global Impression, and satisfaction with treatment. Adverse events will be monitored for evaluation of safety. Secondary objectives: Non-motor symptoms (change from baseline in Non-Motor Symptom Scale score, Parkinson's disease sleep scale-2, and MDS-UPDRS lb scores), quality of life (change from baseline in Parkinson's Disease Questionnaire total score [PDQ-8 or PDQ-39]) and healthcare resource utilisation. An interim analysis is planned.

Conclusion: ELEGANCE will provide real-world information on efficacy and safety of LECIG, as well as patient perspectives of this treatment and its impact on healthcare utilisation, to help inform clinical decisions.

Disclosure: The ELEGANCE study is sponsored by Britannia Pharmaceuticals Ltd and all authors are paid by Britannia as members of the study steering committee.

EPO-104

Subjective Cognitive Complaints in PD Patients. Frequency, Associated Factors and Comparison with a Control Group.

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Background and aims: Objective cognitive decline is more frequent among patients with Parkinson's Disease (PD) reporting subjective cognitive complaints (SCCs). Our aim was to analyze the frequency of SCCs in a PD cohort, to compare with a control group, and to determine associated factors and the relationship between their SCCs and cognitive performance.

Methods: PD patients and controls recruited from the Spanish COPPADIS cohort from January/2016, to November/2017, were followed-up during 2 years1,2. Cognitive status was assessed with the Parkinson´s Disease Cognitive Rating Scale (PD-CRS) at baseline (V0) and after 2-year follow-up (V2). Subjects with a score $\geq$ 1 on Domain-5 of the Non-Motor Symptoms Scale at V0 were considered as "with SCCs".

Results: SCCs were more frequent in PD patients (59.1% males; 62.39±8.66 years old) than in controls (48% males;

62.4±7.48 years old): 65.5% (327/499) vs 52.8% (65/123); p=0.006. PD patients with SCCs were significantly worse than those without SCCs in terms of motor and non-motor symptoms, disability, and quality of life (Table 1). At V0 and V2, cognitive function was worse (Figure 1A) and cognitive impairment (Figure 2A) was more frequent in patients classified as with SCCs compared to those without SCCs. A trend of significance (p=0.059) was observed for higher frequency of cognitive impairment at V2 in patients with SCCs compared to those without SCCs (17.3% vs 11%) in the subgroup with normal cognitive function (PD-CRS<80; n=383) at baseline (Figure 2B).

	All sample (N=499)	With SCCs (N=327)	Without SCCs (N=162)	P
Age	62.3 ± 8.6	62.8 ± 8.3	61.5 ± 9.1	0.187
Males (%)				
Disease duration (years)	5.5 ± 4.2	5.7 ± 4.3	5.1 ± 3.9	0.106
L-dopa eq. daily dose (mg)	579.7 ± 419.2	598.8 ± 417.8	543.9 ± 420.6	0.117
Motor phenotype (%)				0.608
- Tremoric dominant	47.1	45.9	49.4	
- PIGD	37.3	38.8	34.4	
- Indeterminate	15.6	15.3	16.2	
Hoehn & Yahr	2 [2, 2]	2 [2, 2]	2 [1.5, 2]	0.030
- Stage from 3 to 5(%)	9.4	11.3	6	0.053
UPDRS-III	22 ± 10.5	23.3 ± 10.8	19.7 ± 9.6	0.001
UPDRS-IV	2 ± 2.4	2.3 ± 2.5	1.4 ± 2	<0.0001
- Motor fluctuations (%)	33.3	37	26.2	0.009
- Dyskinesia (%)	18.9	20.4	16	0.147
FOG-Q	3.7 ± 4.7	4.2 ± 4.8	2.8 ± 4.2	<0.0001
- Patients with FOG (%)	34.1	39.4	24	<0.0001
- Patients with falls (%)	12.4	16.5	4.7	<0.0001
PD-CRS	92 ± 15.6	90.1 ± 15.7	95.5 ± 14.9	<0.0001
- Cognitive impairment (PD-CRS < 81) (%)	23.2	27.5	15.1	0.001
NMSS	45.1 ± 37.7	55.3 ± 40.2	25.8 ± 22.2	<0.0001
- Severe and/or very NMS burden (NMSS > 40) (%)	42.3	55	18	<0.0001
BDI-II	8.2 ± 6.9	9.9 ± 7.4	5 ± 4.5	<0.0001
- Major depression (%)	14.8	20.5	4.1	<0.0001
NPI	5.8 ± 7.9	6.7 ± 8.6	3.8 ± 6	<0.0001
QUIP-RS	4.3 ± 8.1	4.5 ± 8	3.4 ± 7.1	0.002
PDSS	117 ± 24.4	112.3 ± 26.2	126 ± 17.4	<0.0001
VAS-PAIN	2.5 ± 2.9	2.7 ± 2.9	2.1 ± 2.8	0.010
- Patients with pain (%)	56.7	61.5	47.7	0.002
VASF – physical	2.8 ± 2.7	3.3 ± 2.7	1.9 ± 2.4	<0.0001
VASF – mental	2.1 ± 2.5	2.5 ± 2.6	1.2 ± 2.1	<0.0001
ADLS	88.5 ± 10.2	86.9 ± 11	91.4 ± 7.8	<0.0001
- Patients with functional dependency (%)	9	12.2	2.9	<0.0001
PDQ-39SI	16.5 ± 12.9	19.9 ± 13.5	10.2 ± 8.8	<0.0001
EUROHIS-QOL8	3.7 ± 0.5	3.6 ± 0.5	3.9 ± 0.4	<0.0001

The results represent percentages, mean ± SD or median [p25, p75]. Chi-squared and Mann-Whitney-Wilcoxon test were applied for comparisons between patients with and without SCCs at baseline. Data about H&Y and UPDRS-III are during the OFF state (first hour in the morning without taking medication in the previous 12 hours).

ADLS, Schwab and England Activities of daily living Scale; BDI, Beck Depression Inventory-II; NMSS, Non-Motor Symptoms Scale; NPI, Neuropsychiatric Inventory; PD, Parkinson's disease; PD-CRS, Parkinson's Disease Cognitive Rating Scale; PDSS, Parkinson's Disease Sleep Scale; PIGD, Postural Instability Gait Difficulty; QUIP-RS, Questionnaire for Impulsive-Compulsive Disorders in Parkinson's Disease-Rating Scale; UPDRS, Unified Parkinson's Disease Rating Scale; VAFS, Visual Analog Fatigue Scale; VAS-Pain, Visual Analog Scale-Pain.

Table 1. Disease related characteristics, motor and non-motor symptoms, autonomy for activities of daily living and quality of life in PD patients with and without SCCs at baseline (n=499).
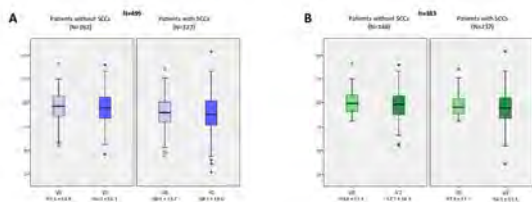
Figure 1. PD-CRS total score at V0 and at V2 in patients with SCCs (SCCs+) and without SCCs (SCCs-). A. Analysis considering all cohort (N=499). SCCs+ vs SCCs- at V0, p<0.0001; SCCs+ vs SCCs- at V2, p<0.0001; change from V0 to V2 in SCCs+, p=0.001; change.
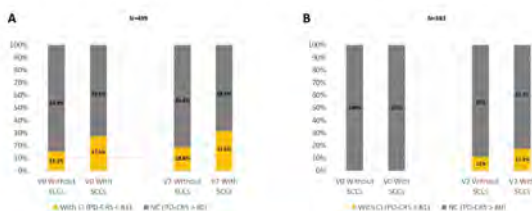
Figure 2. Frequency of cognitive impairment (PD-CRS < 81) in patients with SCCs (SCCs+) and without SCCs (SCCs-). A. Analysis considering all cohort (N=499). SCCs+ vs SCCs- at V0, p=0.001; SCCs+ vs SCCs- at V2, p=0.001; change from V0 to V2 in SCCs+, p=0.

Conclusion: SCCs are frequent in PD and are associated with cognitive impairment and a worse global PD status.
Disclosure: No financial disclosures.

EPO-105

Levodopa Pharmacokinetics in Different Levodopa Treatment Regimens plus Opicapone in Parkinson's Disease

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Background and aims: Levodopa (LD) therapy in Parkinson's disease (PD) is associated with the development of motor fluctuations (MF). Strategies to optimise LD regimen include increasing the total daily dose and/or increasing the number of intakes. The catechol-O-methyltransferase inhibitor opicapone (OPC) proved efficacious for treating end-of-dose MF in two Phase 3 trials. This study evaluated the effect of OPC on LD pharmacokinetics (PK) in different LD/carbidopa (LD/CD) dosage regimens in patients with PD and MF.

Methods: This Phase 2 study enrolled 24 patients with PD receiving baseline total daily LD/CD dose of 500/125 mg (Figure 1). During 14±2 days, patients received an LD/CD reference treatment of 100/25 mg five times a day. At baseline, patients were equally randomised to: • Total daily LD/CD dose of 400/100 mg 4 intakes a day every 4 hours (Q4H) plus OPC 50 mg • Total daily LD/CD dose of 400/100 mg 5 intakes a day every 3 hours (Q3H) plus OPC 50 mg Patients maintained their regimens for up to 14±2 days. PK were assessed at Visits 3 (baseline) and 4 (day 14±2).
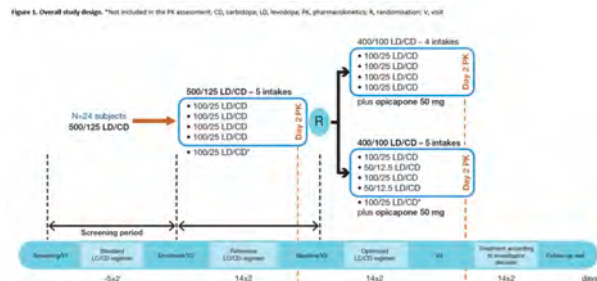
Results: Compared with the LD/CD 500/125 mg regimen, both OPC-containing regimens showed a ~30% increase in LD exposure. The Q3H plus OPC regimen was also associated with an increase in LD Cmin with no significant impact on LD Cmax, leading to a ~60–90% decrease in the

LD fluctuation (variation between Cmax and Cmin) (Figure 2).

Figure 2. LD pharmacokinetics in Q3H LD/CD 400/100 mg plus OPC 50 mg vs Q3H LD/CD 500/125 mg (a) and in Q4H LD/CD 400/100 mg plus OPC 50 mg vs Q3H LD/CD 500g/125 mg (b). CD, carbidopa; LD, levodopa; OPC50, opicapone 50 mg; Q3H, every 3 hours; Q4H, every 4 hours.
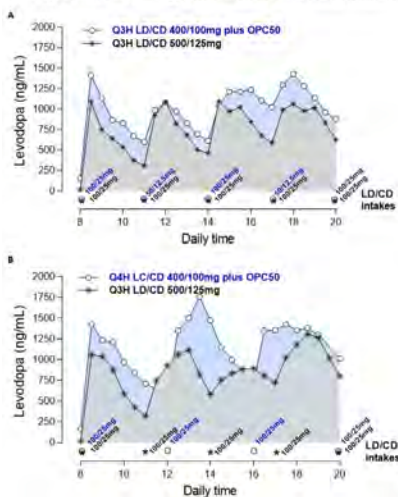
Conclusion: These preliminary data show that OPC 50 mg surpasses at least 100 mg LD in terms of LD exposure.
Disclosure: Supported by Bial.

EPO-106

Association of olfactory dysfunction and motor and non-motor function among motor subtypes of Parkinson's disease

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Background and aims: Numerous studies have evaluated the association between motor and non-motor symptoms and olfactory dysfunction in Parkinson's disease (PD). In this study, we investigated the relationship between olfactory dysfunction, which is measured using the UPSIT test, with other motor and non-motor symptoms separately in three motor subtypes of PD, including tremor dominant (TD), postural instability, and gait difficulty (PIGD), indeterminate and healthy subjects.

Methods: We recruited 487 early-stage PD patients [43 PIGD, 406 TD, and 38 Indeterminate] and healthy controls (HCs) (n=197) from the Parkinson Progression Markers Initiative (PPMI). All participants completed motor and non-motor tests at baseline visit and after four years of follow-up. Subjects underwent common PD scaling tests.

Results: Olfactory dysfunction was significantly correlated with declined motor and neurobehavioral functions in the TD subtype. Also, a mild connection was noticed between olfactory dysfunction and visuospatial skills in the intermediate subtype as well. Finally, no significant or meaningful association was observed in the PIGD subtype.

Anosmia and hyposmia subjects in TD group had worse motor and non-motor scores compared to normosmia subjects after four years.

Variable	HCs (n= 197)	PD (n= 487)	P-value
Age, mean (SD), years	61.4 (11.0)	61.7 (9.7)	0.700
Female/Male, No	66/131	152/335	0.692
Left-handed/Right0handed, No	29/168	55/432	0.112
Education, mean (SD), years	16.0 (2.8)	15.5 (3.1)	0.046
Disease duration, mean (SD), years	–	1.7 (1.0)	–
Hoehn and Yahr stage, mean (SD)	–	1.5 (0.4)	–
MDS-UPDRS part I score, mean (SD)	0.5 (1.1)	1.3 (1.7)	<0.001
MDS-UPDRS part II score, mean (SD)	0.3 (0.7)	3.9 (3.4)	<0.001
MDS-UPDRS part III score, mean (SD)	0.7 (1.5)	13.2 (7.7)	<0.001
Tremor score, mean (SD)	0.3 (0.9)	5.4 (3.5)	<0.001
PIGD score, mean (SD)	0.1 (0.4)	1.0 (1.1)	<0.001
UPSIT score, mean (SD)	34.0 (4.8)	23.3 (8.5)	<0.001
Modified Schwab & England ADL, mean (SD)	–	93.3 (5.9)	–
MoCA score, mean (SD)	28.2 (1.1)	27.1 (2.3)	<0.001

Table1. Demographic data and comparison of clinical information between HCs and PD

Results of partial correlation between UPSIT and other demographical and clinical data in HCs and different subtypes of PD

Conclusion: Olfactory dysfunction was significantly correlated with declined motor and neurobehavioral functions in the TD subtype. This is indicating that olfactory dysfunction may be an early motor and non-motor biomarker only in the TD subtype. However, it is possible that the involvement of olfactory function in other subtypes is not strong enough to make it a useful marker of diseases progression.

Disclosure: Conflict of interest The authors declare no conflict of interest regarding the publication of this paper.

EPO-107

The role of monoaminergic tones and brain metabolism in cognition in de novo Parkinson's Disease

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Background and aims: Cognitive impairment is frequent in Parkinson's Disease (PD) and several neurotransmitter changes have been reported since the time of diagnosis, although seldom investigated altogether in the same patient cohort. Our aim was to evaluate the association between neurotransmitter impairment, brain metabolism and cognition in a cohort of de novo, drug-naïve PD patients.

Methods: We retrospectively selected 95 consecutive drug-naïve PD patients (demographic and clinical characteristics in Table 1) undergoing at the time of diagnosis a brain 18F-FDG-PET as a marker of brain glucose metabolism and proxy measure of neurodegeneration, 123I-FP-CIT-SPECT as a marker and dopaminergic deafferentation in the striatum and frontal cortex, as well as a marker of serotoninergic deafferentation in the thalamus, and quantitative electroencephalography (qEEG) as an indirect measure of cholinergic deafferentation. Patients also underwent a complete neuropsychological test battery.

Table 1. Demographic, clinical and imaging characteristics of Parkinson's Disease group. Values are shown as mean ± standard deviation (SD).

	Parkinson's Disease (n=95; mean ± SD)
Age (yr)	71.89 ± 7.53
Education (yr)	10.92 ± 4.06
Gender (M:F)	60:35
MMSE score	28.09 ± 2.13
MDS-UPDRS-III score	20.72 ± 8.79
MCI (Y:N)	46:49
Striatal and thalamic [123I]FP-CIT SBR values	
Caudate [123I]FP-CIT SBR values	2.23 ± 0.81
Putamen [123I]FP-CIT SBR values	1.41 ± 0.87
Thalamus [123I]FP-CIT SBR values	1.24 ± 0.18
Cortical [123I]FP-CIT values	
Prefrontal [123I]FP-CIT SBR values	0.88 ± 0.11
qEEG Alpha/Theta ratio	
Posterior leads	2.17 ± 2.90

Legend: M = male, F = female, MMSE = Mini Mental State Examination, MDS-UPDRS-III = Movement Disorders Unified Parkinson's Disease Rating Scale, motor section, MCI = Mild Cognitive Impairment, SBR = specific to non-displaceable binding ratio

Table 1: Demographic, clinical and imaging characteristics of Parkinson's Disease group. Values are shown as mean ± standard deviation (SD).

Results: Positive correlations were observed between (i) executive functions and left cerebellar cortex metabolism (Figure 1), (ii) frontal dopaminergic tone and working memory, (iii) cholinergic tone and both memory and visuo-spatial functions. Detailed results are shown in Table 2.

	r values	p values (unc.)	FDR
Executive Functions			
Striatal and thalamic [123I]FP-CIT SBR values			
Caudate [123I]FP-CIT SBR values	-0.174	0.094	0.28
Putamen [123I]FP-CIT SBR values	-0.083	0.432	0.54
Thalamus [123I]FP-CIT SBR values	-0.030	0.779	0.77
Cortical [123I]FP-CIT SBR values			
Prefrontal [123I]FP-CIT SBR values	-0.139	0.186	0.31
qEEG Alpha/Theta ratio			
Posterior leads	0.112	0.112	0.28
Attention and Working Memory			
Striatal and thalamic [123I]FP-CIT SBR values			
Caudate [123I]FP-CIT SBR values	0.194	0.064	0.16
Putamen [123I]FP-CIT SBR values	0.103	0.331	0.55
Thalamus [123I]FP-CIT SBR values	0.070	0.505	0.63
Cortical [123I]FP-CIT SBR values			
Prefrontal [123I]FP-CIT SBR values	**0.304**	**0.003**	**0.015**
qEEG Alpha/Theta ratio			
Posterior leads	-0.005	0.960	0.96
Memory			
Striatal and thalamic [123I]FP-CIT SBR values			
Caudate [123I]FP-CIT SBR values	0.027	0.802	0.92
Putamen [123I]FP-CIT SBR values	0.021	0.843	0.92
Thalamus [123I]FP-CIT SBR values	-0.039	0.711	0.92
Cortical [123I]FP-CIT SBR values			
Prefrontal [123I]FP-CIT SBR values	0.010	0.924	0.92
qEEG Alpha/Theta ratio			
Posterior leads	**0.299**	**0.004**	**0.024**
Language			
Striatal and thalamic [123I]FP-CIT SBR values			
Caudate [123I]FP-CIT SBR values	0.203	0.052	0.08
Putamen [123I]FP-CIT SBR values	0.112	0.288	0.28
Thalamus [123I]FP-CIT SBR values	0.206	0.049	0.08
Cortical [123I]FP-CIT SBR values			
Prefrontal [123I]FP-CIT SBR values	0.176	0.092	0.11
qEEG Alpha/Theta ratio			
Posterior leads	0.226	0.030	0.08
Visuo-spatial			
Striatal and thalamic [123I]FP-CIT SBR values			
Caudate [123I]FP-CIT SBR values	0.159	0.131	0.21
Putamen [123I]FP-CIT SBR values	0.065	0.535	0.66
Thalamus [123I]FP-CIT SBR values	0.043	0.682	0.68
Cortical [123I]FP-CIT SBR values			
Prefrontal [123I]FP-CIT SBR values	0.202	0.054	0.13
qEEG Alpha/Theta ratio			
Posterior leads	**0.357**	**< 0.001**	**< 0.001**

Table 2: Correlation between neuropsychological domain composite scores, striatal and thalamic [123I]FP-CIT SBR values, frontal [123I]FP-CIT SBR values and qEEG Alpha/Theta ratio. Analyses were corrected for age and MDS-UPDRS-III score.
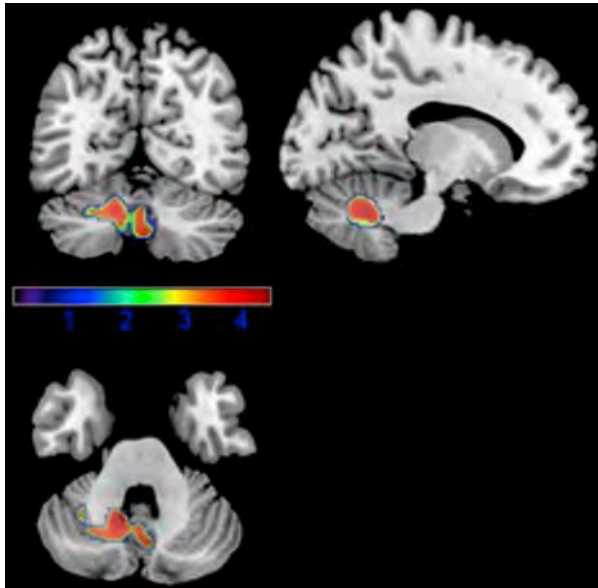
Figure 1: Results of the voxel-wise positive correlation analysis between executive functions and brain metabolism; nuisances: age and MDS-UPDRS-III score.

Conclusion: In subjects with de novo PD, the impact of regional brain glucose metabolism and diffuse projection systems degeneration differs across cognitive domains. These findings suggest possible tailored approaches to the treatment of cognitive deficits in PD.

Disclosure: MP: fees from Novartis, Merck and Biogen. DA: fees from Fidia, Bioprojet and Jazz. SM: speaker Honoraria from G.E. Healthcare. FN: fees from Roche, Bial, Biogen and G.E. Healthcare. All other authors report no conflicts of interest.

EPO-108

Use of MANAGE-PD to Identify Patients with Advanced PD with Inadequately Controlled Symptoms on Oral PD Medications

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Background and aims: MANAGE-PD is a validated, approved online/paper tool (registered as medical device; Conformité Européenne/CE mark). It is designed to support informed decisions for healthcare professionals in the timely management of Parkinson´s Disease (PD). MANAGE-PD has two sections with a total of 15 questions evaluating frequency/severity of PD clinical/treatment-related features. It is designed to classify PD patients into one of three categories: 1) controlled with current treatment regimen (as identified in section 1) or inadequately controlled and either 2) able to benefit from current treatment optimisation or 3) able to benefit from device-aided therapy (as identified in section 2). Here we report the real-world online use of MANAGE-PD.

Methods: MANAGE-PD use via managepd.eu was evaluated from October 2020–October 2021. Here we report the number of times users started the questionnaire, completed each section, and downloaded surveys.

Results: MANAGE-PD was launched in October 2020 in 14 countries (Australia, Austria, Belgium, Denmark, France, Germany, Italy, Japan, Norway, Saudi Arabia, Spain, Sweden, Turkey, United Arab Emirates) and in 11 languages (Danish, Dutch, English, French, German, Italian, Japanese, Norwegian, Spanish, Swedish, Turkish). The questionnaire was started 1434 times and sections 1 and 2 were completed 78% (n=1,119) and 73% (n=1,053) of the time. A total of 701 surveys were downloaded (Figure).
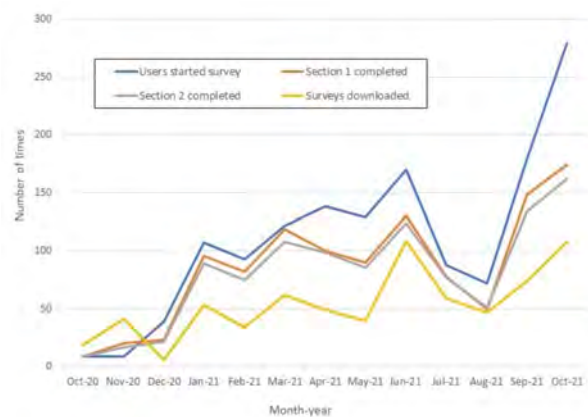
MANAGE-PD (managepd.eu) Online Use Over Time

Conclusion: MANAGE-PD online use has continued to increase since launch, with more countries and languages to be added. Continued efforts will establish MANAGE-PD as a screening tool that facilitates timely identification of PD patients who may benefit from treatment optimisation or device-aided therapy consideration.

Disclosure: This study was funded by AbbVie Inc. AbbVie Inc. participated in the study design; study research; collection, analysis, and interpretation of data; and writing, reviewing, and approving this abstract for submission.

EPO-109

Subcutaneous Foslevodopa/Foscarbidopa in Parkinson's Disease: Results by Age, Disease Duration, and Baseline "Off" Time

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Background and aims: Six-month interim results from a phase 3 trial of foslevodopa/foscarbidopa, a soluble formulation of levodopa and carbidopa prodrugs delivered as continuous subcutaneous infusion for Parkinson's disease (PD), demonstrated significant improvements in "Off" time, "On" time, motor experiences of daily living (m-EDL), sleep, and quality of life (QoL). Interim data by baseline age, PD duration, and "Off" time are reported.

Methods: This is an ongoing, open-label, single-arm study assessing the safety and tolerability of long-term exposure to foslevodopa/foscarbidopa (NCT03781167). Patients with PD whose motor symptoms were inadequately controlled by their current treatment are receiving a 24-hour/daily optimized dose of foslevodopa/foscarbidopa for up to 52 weeks.

Results: Patients with the greatest age, PD duration, or "Off" time had worse baseline QoL (PDQ-39 Summary Index Total Score; Table 1). Age and disease duration had no significant effect on change to month 6 in "Off" time, "On" time, m-EDL (MDS-UPDRS part II), and QoL (Figure 1). However, higher baseline "Off" time was associated with significantly greater improvements in absolute reduction of "Off" time (P<.01) and greater improvements in QoL (P<.05) at 6 months (Figure 1). Safety and tolerability were generally consistent among subgroups, though patients aged >70 years reported higher frequencies of serious and severe events (Table 2).

Age	<60 years (n=62)	60–70 years (n=105)	>70 years (n=56)
Age, years	51.9 (5.4)	64.9 (3.0)	74.8 (3.6)
Male, n (%)	47 (75.8)	60 (57.1)	27 (48.2)
PD duration, years	10.3 (5.3)	12.9 (4.9)	13.2 (5.2)
"Off" time, hours	5.8 (2.6)	6.4 (2.5)	5.7 (2.2)
MDS-UPDRS II	13.8 (5.6)	15.0 (7.5)	19.5 (8.1)
PDQ-39 Summary Index	32.0 (15.4)	33.9 (15.0)	37.6 (13.8)
PD duration	**<10 years (n=89)**	**10–14 years (n=64)**	**>14 years (n=70)**
Age, years	61.2 (10.5)	63.4 (8.3)	67.3 (7.4)
Male, n (%)	51 (57.3)	43 (67.2)	40 (57.1)
PD duration, years	7.5 (1.8)	12.1 (1.3)	18.4 (3.5)
"Off" time, hours	6.2 (2.6)	6.1 (2.4)	5.8 (2.5)
MDS-UPDRS II	14.6 (7.6)	15.4 (7.9)	17.6 (6.8)
PDQ-39 Summary Index	33.1 (14.1)	33.4 (15.3)	36.5 (15.4)
"Off" time[a]	**<5 hours/day (n=66)**	**5–7 hours/day (n=76)**	**>7 hours/day (n=73)**
Age, years	62.9 (9.9)	64.3 (8.7)	63.3 (8.7)
Male, n (%)	40 (60.6)	50 (65.8)	39 (53.4)
PD duration, years	12.3 (5.3)	12.2 (4.9)	12.2 (5.6)
"Off" time, hours	3.2 (1.3)	6.0 (0.7)	8.7 (1.3)
MDS-UPDRS II	15.3 (8.4)	16.1 (6.7)	15.8 (7.6)
PDQ-39 Summary Index	33.2 (16.7)	33.9 (14.1)	35.8 (14.2)

Data are mean (SD) unless otherwise specified.
[a]N=215.
MDS-UPDRS II, Movement Disorder Society Unified Parkinson's Disease Rating Scale part II; PD, Parkinson's disease; PDQ-39, 39-item Parkinson's Disease Questionnaire.

Table 1. Baseline Demographics and Characteristics

Figure 1. Change From Baseline to 6 Months in Efficacy Outcomes

Age	<60 years (n=62)	60–70 years (n=105)	>70 years (n=56)
Any TEAE	60 (96.8)	96 (91.4)	50 (89.3)
Any severe TEAE	13 (21.0)	24 (22.9)	19 (33.9)
Any serious TEAE	10 (16.1)	23 (21.9)	20 (35.7)
Any TEAE that are considered associated with study drug[a]	59 (95.2)	95 (90.5)	47 (83.9)
Any TEAE leading to premature discontinuation of study drug	12 (19.4)	26 (24.8)	16 (28.6)
Any TEAE leading to death	0	2 (1.9)	1 (1.8)
PD duration	**<10 years (n=89)**	**10–14 years (n=64)**	**>14 years (n=70)**
Any TEAE	83 (93.3)	59 (92.2)	64 (91.4)
Any severe TEAE	21 (23.6)	17 (26.6)	18 (25.7)
Any serious TEAE	18 (20.2)	12 (18.8)	23 (32.9)
Any TEAE that are considered associated with study drug[a]	82 (92.1)	58 (90.6)	61 (87.1)
Any TEAE leading to premature discontinuation of study drug	24 (27.0)	15 (23.4)	15 (21.4)
Any TEAE leading to death	1 (1.1)	1 (1.6)	1 (1.4)
"Off" time[b]	**<5 hours/day (n=66)**	**5–7 hours/day (n=76)**	**>7 hours/day (n=73)**
Any TEAE	60 (90.9)	70 (92.1)	68 (93.2)
Any severe TEAE	15 (22.7)	18 (23.7)	21 (28.8)
Any serious TEAE	18 (27.3)	14 (18.4)	19 (26.0)
Any TEAE that are considered associated with study drug[a]	57 (86.4)	68 (89.5)	68 (93.2)
Any TEAE leading to premature discontinuation of study drug	17 (25.8)	16 (21.1)	19 (26.0)
Any TEAE leading to death	1 (1.5)	1 (1.3)	1 (1.4)

Data are n (%).
[a]As assessed by the investigator.
[b]N=215.
PD, Parkinson's disease; TEAE, treatment-emergent adverse event.

Table 2. Safety Overview

Conclusion: This 6-month interim analysis demonstrated that the foslevodopa/foscarbidopa benefit/risk profile in PD is generally not affected by age or disease duration, including durations >14 years. Patients with more baseline "Off" time showed the greatest absolute reduction in "Off" time and improvement in QoL.

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EPO-110

Risk of Cognitive Impairment in PD Patients with Visual Hallucinations and Subjective Cognitive Complaints.

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Background and aims: Visual hallucinations (VH) and subjective cognitive complaints (SCCs) are associated with cognitive impairment (CI) in Parkinson´s disease (PD). Our aim was to analyze the association between VH and SCCs and the risk of CI development in a cohort of PD patients with normal cognition (PD-NC).

Methods: PD-NC (Parkinson´s Disease Cognitive Rating Scale [PD-CRS] total score >80) patients recruited from the Spanish COPPADIS cohort from January/2016, to November/2017, were followed-up during 2 years. Subjects at baseline (V0) with a score ≥1 on Domain-5 and Item-13 of the Non-Motor Symptoms Scale were considered as "with SCCs" and "with VH", respectively. CI at 2-year follow-up (V2) was defined as a PD-CRS total score <81.

Results: At V0 (n=376; 58.2% males, 61.1±8.7 years old), the frequency of VH and SCCs was 13.6% and 62.2%, respectively. VH were more frequent in patients with SSCs than in those without SCCs: 18.8% (44/234) vs 4.9% (7/142); p<0.0001. At V2, 15.2% (57/376) of the patients developed CI. To have VH at V0 was associated with a higher risk of CI at V2 (OR=3.755; 95% CI 1.623–8.684; p=0.002) after controlling the effect of age, disease duration, education, Hoehn & Yahr, LEDD (levodopa equivalent daily dose), and PC-CRS total score at V0. Although SCCs were not associated with CI at V2, to have at V0 both, VH + SCCs, increased more the probability of having CI at V2 (OR=5.085; 95% CI 2.077–12.45; p<0.0001).

Conclusion: VH are associated with SCCs and CI development after 2-year follow-up in PD-NC patients.

Disclosure: The authors have no conflicts of interest.

EPO-111

Do Patients' Experiences With Side Effects Affect Their Preferences for Adjunctive Parkinson's Disease Treatments?

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Background and aims: To quantify the preferences of patients with Parkinson's disease (PD) for features of adjunctive medications stratified by previous treatment experiences.

Methods: United States adults with self-reported PD treated with levodopa/carbidopa who experience OFF-episodes were recruited through the Michael J. Fox Foundation for Parkinson's Research for an online discrete-choice experiment. Respondents selected among experimentally designed profiles for hypothetical adjunctive PD treatments that varied in efficacy (minutes of additional ON-time), potential side effects (minutes of additional troublesome dyskinesia [TD], risk of diarrhea, risk of a change in urine/sweat/saliva color), and dosing frequency or "No additional medicine." Data were analyzed with random-parameters logit models and tested for differences based on three subgroups: hours of OFF-time daily, experience with bodily fluid discoloration, or TD. The survey included a fixed question based on attribute profiles similar to opicapone and entacapone.

Results: 480 adults completed the survey (average age 67 years, 69% diagnosed for 5+ years). Figures 1-3 show the relative importance of the medication features for each of three patient subgroups. Prior history of TD or fluid discoloration resulted in reduced importance for the respective attribute risk. In the fixed question presenting medication profiles like opicapone or entacapone, 65% to 85% selected an additional medicine over no medicine across all subgroups, and of these, 78% to 91% selected a profile similar to opicapone.

Conclusion: The risk of side effects affected patients' willingness to use an adjunctive PD medication. This analysis underscores the need for effective PD treatment options with acceptable side effect profiles.

EPO-112

Early Morning Dystonia in Parkinson's Patients Receiving Opicapone versus Entacapone: a Post-Hoc Analysis of BIPARK-I

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Background and aims: Opicapone (OPC) proved effective for end-of-dose motor fluctuations in patients with Parkinson's disease (PD) in BIPARK-I and II trials. BIPARK-I evaluated the effect of OPC-50mg versus placebo (having entacapone [ENT] as an active-control) in motor symptoms, including early morning dystonia (EMD) (item 35 part IV Unified Parkinson's Disease Rating Scale [UPDRS]).

Methods: This post-hoc analysis analysed UPDRS IV.35 data from BIPARK-I for the OPC-50mg and ENT arms at baseline and at the end of the double-blind period. The proportion of patients with and without EMD at baseline was evaluated and the odds ratio (OR) of amelioration (for those with EMD) and relative risk (RR) of deterioration (for those without EMD) were analysed using the Fisher's exact test.

Results: Overall, 237 patients (OPC, n=115; ENT, n=122) were included. At baseline, ~24% of patients in the OPC group versus 31% in the ENT group presented with EMD. At the end of the double-blind period, 63% and 17% of patients reported an amelioration following OPC and ENT treatment, respectively, with a significant OR of 8.5 favouring OPC (95% CI 2.75−25.19, p=0.0002). Similarly, at baseline, ~77% of OPC-treated and 69% of ENT-treated patients did not experience EMD. At the end of the double-blind period, 91% of OPC-treated and 95% of ENT-treated patients remained EMD-free with a non-significant 0.9 RR of deterioration between treatment arms (95% CI 0.86−1.04, p=0.3706).

Conclusion: OPC-50mg once-daily was associated with a significant improvement in EMD, with patients on OPC presenting a probability of 8.5-fold to become EMD-free compared with those on entacapone.

Movement disorders 2

EPO-113

Longitudinal study of clinical and neurophysiological features of essential tremor

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Background and aims: Essential Tremor (ET) is a common and heterogeneous movement disorder characterized by action tremor of upper limbs and other body parts, and non-motor symptoms. However, only a few studies have attempted to estimate symptoms progression in ET.

Methods: We enrolled 34 patients with ET. Each patient underwent the same evaluation at baseline and during a follow-up assessment (mean interval: 39 months). We assessed tremor by means of clinical rating scales and kinematic recordings; patients also underwent cognitive and psychiatric assessments. Subgroup and correlation analyses were also performed in order to investigate any factors that can influence the clinical worsening.

Results: At follow-up, we observed higher Fahn-Tolosa-Marin Tremor Rating Scale scores than baseline (20.04 ± 10.71 vs 28.89±12.88; p<0.01), with the involvement of more than one body segment (tremor spread) (baseline: 41.18% vs follow up: 82.35%; p<0.01). Kinematic analyses, however, did not reveal changes in head or upper limbs tremor parameters (all ps<0.05). At follow up we also observed an increase in the number of patients with rest tremor (25.53% vs 67.65%; p<0.01) and slower performance with reduced amplitude in repetitive movements tasks at kinematic analysis. The cognitive assessment showed a trend towards worsening of performance, while psychiatric evaluation showed no substantial differences. Subgroup and correlation analyses did not individuate clinical and demographic factors influencing the worsening of ET manifestations.

	T1	T2	p
Demographic data			
Sex	14F/20M	14F/20M	1
Age (years)	66.53 ± 11.51	69.79 ± 11.29	0.24
Age of onset (years)	50.87 ± 18,73	50.87 ± 18,73	1
Tremor duration (years)	15.66 ± 15.55	18.9 ± 15.65	0.4
Family history	21Y/13N (61.76%)	21Y/13N (61.76%)	1
Clinical data			
FTMTRS Total	20.04 ± 10.71	28.89 ± 12.88	**<0.01**
FTMTRS Section A	7.03 ± 3.51	10.03 ± 5.14	**0.01**
FTMTRS Section B	8.47 ± 5.29	12.49 ± 6.09	**0.01**
FTMTRS Section C	4.55 ± 3.44	6.36 ± 4.33	0.06
Head tremor (n. of patients)	9Y/25N (26.47%)	17Y/17N (50%)	0.08
Voice tremor (n. of patients)	7Y/27N (20.59%)	25Y/9N (73.53%)	**<0.01**
Tongue/face tremor (n. of patients)	3Y/31N (8.82%)	16Y/18N (47.06%)	**<0.01**
Lower limbs tremor (n. of patients)	2Y/32N (5.88%)	10Y/24N (29.41%)	**0.02**
Multiple body segments involvement	14Y/20N (41.18%)	28Y/6N (82.35%)	**<0.01**
Rest tremor (n. of patients)	8Y/26N (23.53%)	23Y/11N (67.65%)	**<0.01**
UPDRS III Total	6.1 ± 3.82	12.26 ± 8.25	**<0.01**

Demographic and tremor clinical data of patients at baseline (T1) and follow-up (T2) assessments. Significant p-values in bold.
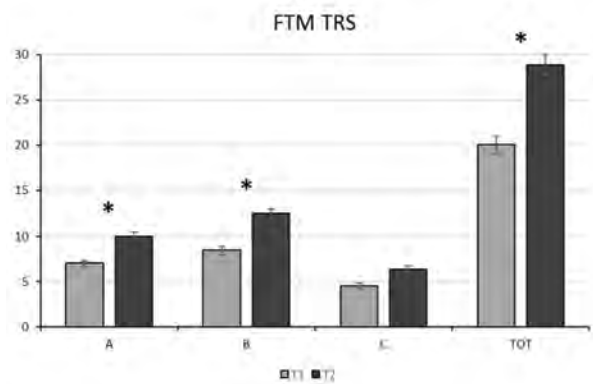
Fahn-Tolosa-Marin Tremor Rating Scale subscores A, B, C and Total in ET patients in baseline (T1) and follow-up (T2) evaluation. Vertical bars indicate standard error. Asterisks indicate P values <0.05.
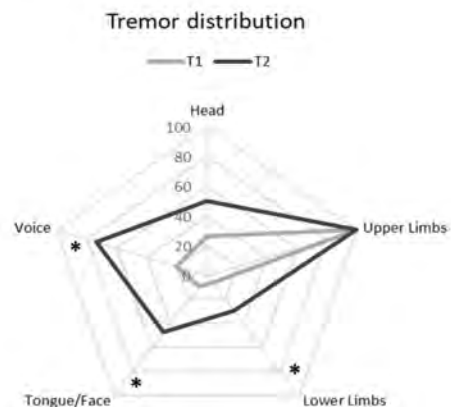
Percentage of patients with different body segments involvement in baseline (T1) and follow-up (T2) evaluation. Asterisks indicate P values <0.05.

Conclusion: ET is a progressive disorder characterized by tremor spread in multiple body segments over time and the emergence of soft signs. Further observations are needed to identify possible predicting factors.

Disclosure: The authors have no conflicts of interest to declare.

EPO-114

Circulating brain-enriched microRNAs for the discrimination of Parkinson's disease and atypical parkinsonian syndromes

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Background and aims: Multiple System Atrophy (MSA) and Progressive Supranuclear Palsy (PSP) are atypical parkinsonian syndromes (APS) with significant clinical overlap with idiopathic Parkinson's disease (iPD). Given their clinical diagnosis, biomarkers for early identification and separation of these distinct forms of parkinsonism are of great interest. Unlike protein biomarkers, microRNAs are stable molecules that can be quickly and precisely quantified using standard laboratory procedures such as RT-PCR. This study's goal was to uncover microRNA subsets with diagnostic potential for APS and iPD.

Methods: Initial selection of 28 brain-enriched miRNAs was based on expression data and validation in human tissues. RT-qPCR was then performed on plasma from 25 MSA (12MSA-C, 13MSA-P), 11 PSP, 25 iPD patients, and 25 healthy controls. Statistical methods identified the diagnostic biomarkers and their correlations with motor, cognitive/neuropsychiatric, and autonomic tests.

Results: 13 microRNAs were differentially expressed across the five groups. Between 1–4 microRNA classifiersbest differentiated MSA-C, MSA-P, PSP, and iPD from controls, with AUC values of 0.88, 0.92, 0.79, and 0.74, respectively. Combinations of two miRNAs differentiated MSA-C from MSA-P (0.76), MSA-C from PSP (0.83), MSA-C from iPD (0.93), MSA-P from PSP (0.91), and MSA-P from iPD (0.95); a single microRNA distinguished PSP from iPD (0.78). The levels of one microRNA were positively correlated with the LEDD score in the MSA-C group, whereas the levels of five microRNAs were negatively correlated with the SCOPA-AUT symptoms scale.

Conclusion: Our findings support the use of brain-enriched miRNAs as non-invasive biomarkers for parkinsonian diseases and suggest pathophysiological causes.

Disclosure: Nothing to disclose.

EPO-115

Real-life prognosis of neurologic complications of botulinum toxin: a French nationwide pharmacovigilance study

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Background and aims: The use of botulinum toxin in neurology is common. However its neurologic complications can lead to respiratory failure or death. This study aims to characterize clinical features and real-life prognosis of botulinum toxin related neurologic complications.

Methods: A nationwide study of all neurologic adverse drug reactions (ADRs) related to the use of botulinum toxin A and B in neurology between 1994 and 2020 from the French pharmacovigilance database, unique in its detailed narrative safety descriptions reported by healthcare professionals.

Results: 151 neurologic systemic complications and 40 with local complications were included, with a patient's age of 53 [36; 66] years; 56% were women. Except three miscellaneous cases, all cases presented symptoms belonging to the clinical spectrum of botulism, either as an isolated symptom (41%) or as multiple symptoms (59%), with a time to onset of 12 [7; 15] days after injection and a duration of 54 [28; 90] days. Eighty three percent of cases recovered spontaneously or were recovering on the date of notification. Reported drugs were not different between cases with local or systemic ADRs, although the doses were higher in cases with systemic ADRs (P < .001). Serious cases were more frequent for systemic ADRs (67% versus 34%; P < .001). Three complications resulted in death, all after treatment for cervical dystonia or sialorrhea.

Conclusion: In this pharmacovigilance study, botulism spectrum symptoms occurring after a botulinum toxin injection were frequent, often had a favorable outcome, though were often initially serious.

Disclosure: Allergan, Ipsen, Merz Pharma.

EPO-116

Levodopa-Carbidopa Intestinal Gel Improves Long-term Parkinson's Disease Symptoms: Final Analysis of the DUOGLOBE Study

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Background and aims: Levodopa-carbidopa intestinal gel (LCIG) reduced burden of motor and non-motor symptoms in clinical trials of patients with advanced Parkinson's disease (PD). We evaluated long-term LCIG effectiveness and safety in a real-world setting.

Methods: DUOGLOBE (NCT02611713) was a 3-year, global, observational, prospective study. LCIG-naïve patients treated in routine clinical practice were enrolled. The primary outcome was change in patient-reported "Off" time. Secondary outcomes included non-motor symptoms (NMSS), sleep and daytime sleepiness (PDSS-2 and ESS), and health-related quality of life (HRQoL; PDQ-8). Serious adverse events (SAEs) were also assessed. Final outcomes for month (M) 36 are presented here.

Results: Of 195 patients, 89 completed the 3-year follow-up. Baseline characteristics indicated substantial disease burden (Table 1). Concomitant use of oral levodopa derivatives, monoamine oxidase B inhibitors and, most prominently, catechol-O-methyltransferase inhibitors decreased (Table 2); approximately one-third of patients were treated with LCIG monotherapy or in combination with oral levodopa. "Off" time significantly improved through M36 (M36, 3.3 hours/day; p<0.001). Significant improvements through M36 were sustained for NMSS total scores (p<0.01), NMSS subdomains of sleep/fatigue (p<0.01), gastrointestinal tract (p<0.001), and miscellaneous (p<0.001); PDSS-2 (p<0.001), and ESS (p<0.01) (Table 1). HRQoL significantly improved until M24 (p<0.01). While 25% of patients discontinued due to AEs, non-safety reasons accounted for half of discontinuations. Falls and (worsening of) PD were the most common SAEs (Table 3).

Assessments,[a] mean ± SD	Baseline[b]	Change from Baseline to Month 36
"Off" time, hours/day	6.0 ± 3.4 (n = 164)	−3.3 ± 3.7*** (n = 80)
NMSS total score	88.2 ± 51.1 (n = 164)	−14.3 ± 40.5** (n = 79)
Cardiovascular, including falls	3.1 ± 4.4 (n = 169)	0.0 ± 5.0 (n = 82)
Sleep/fatigue	16.3 ± 10.5 (n = 169)	−3.7 ± 12.3** (n = 82)
Mood/cognition	15.7 ± 15.9 (n = 169)	−1.6 ± 13.4 (n = 82)
Perceptual problems/hallucinations	2.9 ± 5.3 (n = 169)	0.5 ± 5.9 (n = 82)
Attention/memory	8.2 ± 8.6 (n = 172)	−0.8 ± 8.7 (n = 84)
Gastrointestinal tract	9.5 ± 8.2 (n = 171)	−2.5 ± 6.1*** (n = 84)
Urinary	14.3 ± 11.0 (n = 170)	0.0 ± 11.0 (n = 84)
Sexual function	5.0 ± 7.1 (n = 171)	−0.6 ± 5.7 (n = 80)
Miscellaneous[c]	12.6 ± 9.7 (n = 171)	−3.9 ± 10.3*** (n = 84)
PDSS-2 score[d]	26.6 ± 11.7 (n = 171)	−5.8 ± 12.9*** (n = 85)
ESS score[d]	9.8 ± 5.3 (n = 171)	−1.8 ± 6.0** (n = 84)
PDQ-8 summary index score[e]	45.1 ± 18.1 (n = 171)	−2.5 ± 19.6 (n = 84)

[a] Analysis set included 164 patients.
[b] Defined as the first set of clinical data collected before starting LCIG treatment with optional NJ or permanent PEG-J tubes.
[c] Miscellaneous included pain, taste/smell, weight change, and excessive sweating
[d] Assessment for evaluating sleep and sleepiness symptoms.
[e] Assessment for HR-QoL.
ESS = Epworth Sleepiness Scale; HR-QoL = health-related quality of life; LCIG = levodopa-carbidopa intestinal gel; NJ = nasojejunal; NMSS = Non-Motor Symptoms Scale; PEG-J = perculaneous endoscopic gastrostomy with jejunal extension; PDSS-2 = Parkinson's Disease Sleep Scale; PDQ-8 = 8-item Parkinson's Disease Questionnaire. P < .001 (***), and P < .01 (**).

Table 1. Efficacy of Levodopa-Carbidopa Intestinal Gel at Month 36 of Routine Clinical Practice (DUOGLOBE Study)

Concomitant anti-PD medications, n (%)	Baseline N = 195	Month 31–36 N = 91
Levodopa derivatives[*]	155 (79.5)	59 (84.8)
Dopamine agonists	112 (57.4)	47 (51.6)
COMT inhibitors	97 (49.7)	12 (13.2)
MAO-B inhibitors	74 (37.9)	21 (23.1)
Amantadine	41 (21.0)	25 (27.5)
Anticholinergics	3 (1.5)	1 (1.1)

[*] Use with LCIG is common, as LCIG is intended primarily for 16-hour daily use.
COMT = catechol-O-methyltransferase; MAO-B = monoamine oxidase B; PD = Parkinson's disease.

Table 2. Proportion of Patients Taking Concomitant Anti-PD Medications

Assessments,[a] mean ± SD	Baseline[b]	Change from Baseline to Month 36
"Off" time, hours/day	6.0 ± 3.4 (n = 164)	-3.3 ± 3.7*** (n = 80)
NMSS total score	88.2 ± 51.1 (n = 164)	-14.3 ± 40.5** (n = 79)
Cardiovascular, including falls	3.1 ± 4.4 (n = 169)	0.0 ± 5.0 (n = 82)
Sleep/fatigue	16.3 ± 10.5 (n = 169)	-3.7 ± 12.3** (n = 82)
Mood/cognition	15.7 ± 15.9 (n = 169)	-1.6 ± 13.4 (n = 82)
Perceptual problems/hallucinations	2.9 ± 5.3 (n = 169)	0.5 ± 5.9 (n = 82)
Attention/memory	8.2 ± 8.6 (n = 172)	-0.8 ± 8.7 (n = 84)
Gastrointestinal tract	9.5 ± 8.2 (n = 171)	-2.5 ± 6.1*** (n = 84)
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Miscellaneous[c]	12.6 ± 9.7 (n = 171)	-3.9 ± 10.3*** (n = 84)
PDSS-2 score[d]	26.6 ± 11.7 (n = 171)	-5.8 ± 12.9*** (n = 85)
ESS score[d]	9.8 ± 5.3 (n = 171)	-1.8 ± 6.0** (n = 84)
PDQ-8 summary index score[e]	45.1 ± 18.1 (n = 171)	-2.5 ± 19.6 (n = 84)

[a]Analysis set included 164 patients.
[b]Defined as the first set of clinical data collected before starting LCIG treatment with optional NJ or permanent PEG-J tubes.
[c]Miscellaneous included pain, taste/smell, weight change, and excessive sweating
[d]Assessment for evaluating sleep and sleepiness symptoms.
[e]Assessment for HR-QoL.
ESS = Epworth Sleepiness Scale; HR-QoL = health-related quality of life; LCIG = levodopa-carbidopa intestinal gel; NJ = nasojejunal; NMSS = Non-Motor Symptoms Scale; PEG-J = percutaneous endoscopic gastrostomy with jejunal extension, PDSS-2 = Parkinson's Disease Sleep Scale; PDQ-8 = 8-item Parkinson's Disease Questionnaire. *P* < .001 (***), and *P* < .01 (**).

Table 3. Primary Reasons for Discontinuation and Serious Adverse Events From DUOGLOBE Through 36 Months of Routine Clinical Practice

Conclusion: These final, long-term DUOGLOBE results showed significant and sustained improvements in motor symptoms, non-motor symptoms, and HRQoL with LCIG treatment. Safety was consistent with the established LCIG safety profile.

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EPO-117

Status Update of EPSILON: a Phase III, Randomised, Placebo-Controlled Study of Opicapone in Early Parkinson's Disease

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Background and aims: Opicapone (OPC) proved effective for the treatment of end-of-dose motor fluctuations in patients with Parkinson's disease (PD). Co-administration of OPC with levodopa (L-dopa)/dopa decarboxylase inhibitor (DDCi) preparations inhibits the peripheral catechol-O-methyltransferase, thereby increasing L-dopa bioavailability and reducing motor fluctuations. This study aims to explore the potential of OPC to enhance the clinical benefit of L-dopa/DDCi in patients with early-stage PD without motor fluctuations.

Methods: Patients aged 30−80 years with idiopathic PD, treated with 3–4 daily oral doses of up to 500 mg L-dopa, with signs of motor disability will be randomised to receive OPC 50 mg once daily or placebo (1:1) during a 6-month double-blind follow-up period. The L-dopa/DDCi regimen should remain stable throughout this period, and at the end, patients may enter a 1-year, open-label period of OPC 50 mg treatment (Figure). A total of 162 patients per group are planned to be recruited.

Figure: Overall EPSILON study design (A) and timeline of study assessments (B)
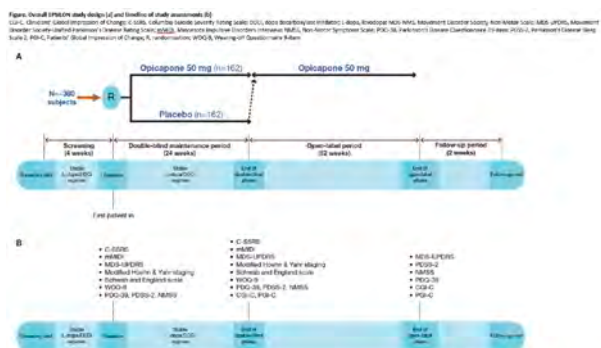
Results: The primary endpoint is change from baseline in the Movement Disorder Society-Unified Parkinson's Disease Rating Scale (MDS-UPDRS) Part III. Secondary endpoints include tolerability, motor and non-motor assessments and global impression of change. As of December 2021, 106 patients have been screened, 77 patients have been randomised and 57 study-initiation-visits in 11 countries have been performed. The study has been approved in all participating countries.

Conclusion: This study will evaluate the effect of OPC on motor symptoms when given as add-on to stable L-dopa/DDCi therapy in patients with early-stage PD.

Disclosure: Supported by Bial.

EPO-118

ADOPTION Study: Status Update of a Randomised, Open-Label Exploratory Trial of Opicapone in Parkinson's Disease

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Background and aims: Long-term treatment with levodopa (L-dopa) in Parkinson's disease (PD) patients is often associated with the development of wearing-off symptoms. The catechol-O-methyltransferase inhibitor opicapone (OPC) proved to be effective in reducing wearing-off symptoms. This study aims to evaluate the effect of OPC versus an additional dose of L-dopa/dopa decarboxylase inhibitor (DDCi) to optimise the L-dopa/DDCi regimen as first-line approach to treat wearing-off in PD patients.

Methods: ADOPTION is a randomised, open-label, exploratory clinical trial that will include patients aged ≥30 years with idiopathic PD, who received 3−4 daily oral L-dopa doses (up to 600 mg) and developed signs of wearing-off (<2 years). Patients will be randomised to OPC 50 mg once daily or to an additional dose of 100 mg/25 mg L-dopa/DDCI during a 4-week open-label follow-up period (Figure). Approximately 100 patients from 25 sites in 5 different countries are planned to be recruited.

Figure: Study design (a) and timeline of study assessments (b). CGI-C, Clinicians' Global Impression of Change; DDCi, dopa decarboxylase inhibitor; DDni, early discontinuation visit; s dose, levodopa; MDS, NMS, Movement Disorder Society-Non-Motor Scale; MDS-UPDRS, Movement Disorder Society-Unified Parkinson's Disease Rating Scale; PDQ-8, Parkinson's Disease Questionnaire 8-item; PGI-C, Patients' Global Impression of Change; R, randomisation; V, visit

Results: The primary endpoint is change from baseline in OFF-time measured by motor fluctuation diaries. Secondary endpoints include tolerability, motor and non-motor assessments (Movement Disorder Society (MDS)-Unified Parkinson's Disease Rating Scale, MDS-Non-Motor Symptoms, Parkinson's Disease Questionnaire-8), and Clinician and Patient Global Impression of Change. The study has already been initiated in two countries.

Conclusion: This study will evaluate the potential of adjunctive OPC versus an additional dose of L-dopa/DDCi as first-line approach to treat wearing-off in patients with PD.

Disclosure: Supported by Bial.

EPO-119

Oculomotor analysis as a predictor of long-term clinical disability in parkinsonism

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Background and aims: Parkinsonian Syndromes (PS) are neurodegenerative disorders that reflect abnormal function of basal ganglia–cortical circuits. Distinctive impairments lead to specific ocular abnormalities in each syndrome. We proposed to find independent oculomotor predictors of clinical disability in PS.

Methods: We retrospectively reviewed oculomotor and vestibular data from PS patients (Parkinson's disease [PD], Progressive Supranuclear Palsy [PSP], Multiple System Atrophy [MSA], and Cortico-Basal Syndrome [CBS]) who underwent detailed video-oculographic analysis and compared it between groups, correlated it with clinical data at baseline and after 1 year, and applied multivariate analysis to ascertain their value as independent predictors of clinical progression (UPDRS-III, Hohen & Yahr). Correction for multiple comparisons were applied.

Results: There were 50 patients (PD, n=14; PSP, n=18; MSA, n=8; CBD, n=10), with a mean age of 67.7±10.2 years (range 36–85), 31 were males (62%), Groups were age- and gender-matched. We found significantly greater fixation instability, slower and more hypometric saccades, and lower prevalence of positional nystagmus in PSP, and lower gain pursuit and more prolonged saccadic latency in CBS. Downward ocular pursuit gain constituted an independent predictor of motor disability at the time of eye movement assessment and 1 year later, across PS groups.

Conclusion: Ocular fixation, pursuit and saccade abnormalities abled us to differentiate between PSP, CBD from other PS. Vestibular analysis did not show additional discriminatory effect in our series. Vertical pursuit was an independent predictor of motor disability in PS, making it a potential diagnostic and clinical progression marker in parkinsonism, regardless of PS subtype.

Disclosure: Nothing to disclose.

EPO-120

Role of clinical assessment and kinematic analysis for bradykinesia detection in essential tremor

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Background and aims: Movement slowness (here specifically referred to as bradykinesia) is a common, yet still unrecognized movement abnormality in patients with essential tremor (ET). Here we to investigate whether reduced movement velocity in ET patients, as demonstrated by kinematic analysis of finger tapping, is also clinically detectable.

Methods: We retrospectively analyzed the video recordings of finger tapping performed by 58 patients with ET (further divided in two sub-groups: 30 'slow-ET' and 28 'non-slow-ET' according to kinematic analysis), 30 patients with Parkinson's disease (PD) and 30 healthy subjects (HCs). The video assessment was carried out by 4 blinded neurologists, according to the item 3.4 (finger tapping) of the Movement Disorders Society-Unified Parkinson's Disease Rating Scale. The inter-raters' agreement was calculated by the Fleiss' K. We compared the mean scores obtained in the three groups by a Kruskal-Wallis ANOVA.

Results: We found a moderate to substantial agreement between raters. Kruskal-Wallis ANOVA showed a significant difference in the blinded finger tapping evaluation between ET, PD and HCs ($p < 0.001$). Namely, the highest scores were observed in PD. In addition, ET had higher video scores than HCs. The analysis of the ET subgroups showed higher finger tapping scores in those kinematically categorized as 'slow-ET' compared to the 'non-slow. Among the 'slow-ET' patients, however, 8/30 patients (26.6%) had been considered normal or only slightly impaired at the blinded video evaluation.
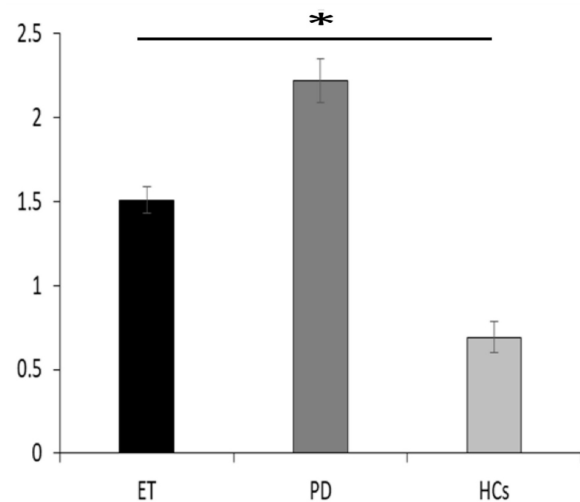
Finger tapping video rating scores in essential tremor (ET), Parkinson's disease (PD) and healthy controls (HCs). Bars indicate mean values. Error bars indicate standard error of the mean. Asterisks indicate $P < 0.05$.
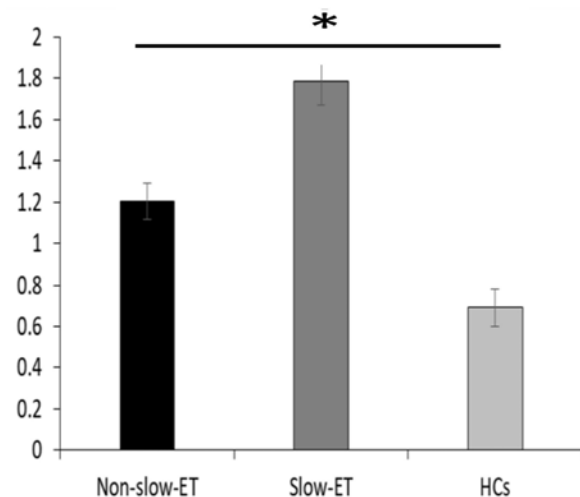
Finger tapping video rating scores in essential tremor (ET) patients as divided into two subgroups (non-slow and slow) according to the movement velocity values obtained with the kinematic analysis of finger tapping and in healthy controls (HCs).

Conclusion: The present results may be relevant when considering patients categorization into ET –plus, thus emphasizing the need of a careful clinical and kinematic assessment of bradykinesia in ET.

Disclosure: Nothing to disclose.

EPO-121

Patient journeys - visualising care needs of patients with rare neurological diseases

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Background and aims: Patient Journeys (PJs) are infographical overviews that visualize patients' needs in the care of their rare disease. Because PJs are designed from the patient's perspective, they allow clinicians to effectively address the needs of rare disease patients. PJs consider that patients' needs may differ at different stages of the disease - e.g., initial symptoms vs. treatment. They also reflect the patients' personal experiences, which may vary depending on the person, clinic and country.

Methods: The European Reference Network for Rare Neurological Diseases (ERN-RND) has started to develop PJs lead by patient representatives. ERN-RND was established in 2017, along with 23 other ERNs, by the European Commission with the goal of helping patients with rare neurological diseases in Europe receive faster diagnosis and access to adequate treatment and care. ERN-RND consists of healthcare professionals, representatives of patient organizations (ePAGs) and researchers in nearly all EU countries.

Results: ERN-RND ePAGs have worked with patient organizations and EURORDIS to develop PJs for: Friedreich's Ataxia, Hereditary Spastic Paraplegia, Cervical Dystonia, Huntington's Disease and Multiple System Atrophy.

Visualisation of a patient journey for Huntington's Disease

Conclusion: ERN-RND considers PJs working documents that patients and clinicians can use together to identify gaps in care and adapt care pathways to better meet the needs of patients living with these conditions. PJs can therefore be seen as a first step toward systematic patient engagement in the design of care pathways. Additionally, PJs are a useful resource for patients, families, non-specialist clinicians, and the general public to understand the care needs of patients living with a rare neurological disease.

Disclosure: Nothing to disclose.

EPO-122

A urodynamic study on the effects of levodopa-carbidopa intestinal gel on urinary symptoms in Parkinson's disease

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Background and aims: Dopaminergic transmission plays a key role in regulating bladder activity, through inhibition of micturition reflex via D1-GABAergic basal ganglia output pathways. Lower urinary tract symptoms (LUTS) severely impact quality of life of Parkinson's disease (PD) patients and may benefit from levodopa. Previous reports show that levodopa-carbidopa intestinal gel (LCIG) infusion is associated with improvement of LUTS as measured by clinical scales and voiding diaries, suggesting that continuous dopaminergic stimulation may produce stronger effects on micturition. However, we are unaware of any objective quantification of the changes in bladder dysfunction by LCIG in advanced PD patients. Here we report urodynamic findings before and six months after LCIG treatment in three PD patients suffering from LUTS.

Methods: All patients (79, 70, and 59 years-old) at baseline underwent the same urodynamic procedure: placement of a two-way 6-Ch bladder catheter, a 10-Ch rectal catheter with subsequent filling of the bladder with physiological solution at 50 mg/h in ON condition. Patients were evaluated with the same procedure after 6 months of LCIG therapy.

Results: Urodynamic evaluations were summarized in Table 1. Patient 1 showed an improvement in detrusor overactivity. Patient 2 and 3 presented mild improvement of detrusor hypocontractility decreased incontinence episodes, and reduction in urethral resistance, respectively.

	Patient 1		Patient 2		Patient 3	
	T0	T1	T0	T1	T0	T1
Pdet Opening (cmh2o)	81	92	92	36	66	53
Pdet - maximum flow (cmh2o)	69	58	86	35	72	53
Pdet - minimum flow (cmh2o)	53	102	84	22	105	60
Maximum flow (ml/s)	4.7	5.0	3.1	11.2	10.4	11.8
Ejected volume (ml)	135	56	48	135	94	91
Emptying time (s)	118	27	30	32	24	14
Flow time (s)	50	21	28	32	17	14
Medium flow (ml/s)	2.7	2.7	1.7	4.3	5.7	6.8
Time to reach maximum flow (s)	36	14	10	3	5	3
Pdet maximum (cmh2o)	99	103	97	57	118	66
Residual urine (ml)	N.A.	N.A.	N.A.	N.A.	N.A.	N.A.
Compliance (ml/ cmh2o)	10.2	1.6	1.7	6.5	1.4	0.8
Max cystometric capacity – Vinfus (ml)	154	131	185	108	104	106
Max cystometric capacity – Pdet (cmh2o)	19	72	106	18	68	122

Pdet: detrusor pressure; Vinfus: infusion volume; N.A: not applicable; T0: baseline urodynamic evaluation; T1: urodynamic evaluation performed after 6 months of LCIG treatment

Table 1. Collection of patients' urodynamic parameters before and after 6 months of LCIG treatment

Conclusion: Urodynamic parameters improve after switching from oral therapy to LCIG in PD patients, associated with improvement in detrusor overactivity, detrusor hypocontractility, and urethral resistance. This is the first quantitative analysis of LUTS assessed by objective parameters after switching from pulsatile to continuous dopaminergic therapy.

Disclosure: No disclosure to declare.

EPO-123

Amantadine use in patients with Parkinson's disease and effect on morbidity and mortality related to COVID-19 infection

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Background and aims: The current COVID-19 pandemic prompted not only the development of vaccines, but also the study of the effectiveness of some repurposed antiviral drugs such as the amantadine in Parkinson's disease (PD), a highly susceptible population.

Objective: To assess possible effect of amantadine on COVID-19 related mortality and morbidity in PD.

Methods: The study included 75 patients with PD (65.3% women), mean age 65 ± 7 years (37–88), duration of the disease mean 12 ± 7 years (1-25). Among this PD cohort, 22 (29.3%) had COVID-19 infection and 8 patients of them (36.4%) received amantadine for at least 3 months. On average, the duration of amantadine administration was 8 ± 5 months.

Results: Comparative morbidity and mortality data was collected on patients taking amantadine versus those not on amantadine. The two groups were similar in relation to gender, age, duration of the disease and concomitant pathology (p>0.05). PD patients who received amantadine were less likely to develop COVID-19 than those who did not take amantadine (p>0.05). The amantadine treated PD had low hospitalization rate, significantly lower rate of pneumonia (OR=3; 95% CI: 0.44–20.3) and there was no mortality.

Conclusion: The results of a retrospective study showed that the use of amantadine in patients with PD may have an effect on reducing morbidity and mortality during the COVID-19 pandemic. This is consistent with published clinical observations suggesting a possible protective effect of amantadine against coronavirus infection.

Disclosure: Nothing to disclose.

EPO-124

Initial experience with levodopa–entacapone–carbidopa intestinal gel infusion (LECIG) in clinical practice in Austria

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Background and aims: Levodopa–entacapone–carbidopa intestinal gel infusion (LECIG) is a device-aided Parkinson's disease (PD) therapy approved in Austria in 2021 for the management of patients with advanced disease. We report our experiences with initiating and treating patients with LECIG.

Methods: 18 patients were treated with LECIG in our centre in 2021 (treatment duration: 1–10 months). 14 patients (9 de novo, 5 switched from other pump systems) were cognitively able to participate in our written survey. The questionnaire included: • Client satisfaction with the device and effects on PD symptoms • Satisfaction with care delivered by application specialist and physician • Problems with various aspects of the device • Reasons for starting LECIG. Scoring was 1–5 (1= very dissatisfied, 5= very satisfied).

Results: 14 questionnaires were returned (100% return rate): 7 male, 7 female patients, Hoehn & Yahr stages 3 to 4. Average age: 76.9 years (range 70–84 years), average disease duration 15.21 years (range: 3–25 years). Overall satisfaction with effects on symptoms is reasonably high with average 4.29. Table During this short observation period, no patients discontinued treatments. Problems reported included issues with the following aspects: • Tube: 3 • Stoma: 4 • Connector: 1 Main reasons for switching to LECIG were: • Motor fluctuations (7) • Non-motor fluctuations (2) • Burden of oral medication (9) • Smaller pump (4).

Table 1: Satisfaction with:	Mean
… pump size	3.85
… weight of pump	3.92
… wearability of device	3.14
… using pump system	4.23
… changing flow rate	3.08
… application specialist	4.46
… physician	5.54
… effects of therapy on symptoms	4.29

Table: Satisfaction scores

Conclusion: Our experience during this short time suggest crucial roles for the treating physician and the application specialist. Individual answers also show that there is some room for improvement of some aspects of the device (e.g. wearability, changing flow rates).

Disclosure: Volker Tomantschger received lecture fees and consultancy remuneration from Stada and AbbVie.

MS and related disorders 1

EPO-125

TELE MS: A randomized controlled trial investigating satisfaction with remote visits for people with multiple sclerosis

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Background and aims: Continuous monitoring is the hallmark of managing chronic disease. Multiple sclerosis, in particular, requires patients to visit their treating neurologists (MSologists) typically twice a year, at least. The current global pandemic has manifested an urgent patient need in terms of remote disease monitoring.

Methods: This randomized controlled open trial investigated satisfaction with remote visits for people with multiple sclerosis (pwMS). We included 45 pwMS who were randomized to one of three groups (1:1:1) that would determine the modality of their next scheduled visit: (i) regular outpatient visit or (ii) visit over the phone or (iii) visit by means of video chat. We defined patient satisfaction determined by the telemedicine perception questionnaire (TMPQ, min: 17 and max: 85 points) as the primary endpoint with the assumption of non-inferiority of televisits compared to conventional visits. Physician satisfaction measured on the PPSM score (Patient and Physician Satisfaction with Monitoring, min: 5 and max: 25 points) was the secondary endpoint.

Results: The trial met both endpoints. Mean TMPQ scores in the individual groups were 58 (SD 6.7) points for conventional visits, 65 (SD 7.5) points for phone visits, and 62 (SD 5.5) points for video visits. Physician satisfaction over the whole cohort was similarly high. Median PPSM scores were 23 (range: 16-25) for the whole cohort, 19 (range: 16–25) for conventional visits, 25 (range: 17–25) for phone visits, and 25 (16–25) for video visits.

Conclusion: We conclude that televisits in multiple sclerosis yield a high level of satisfaction for both patients and treating physicians.

Disclosure: There are no direct conflicts of interests relevant to this clinical study.

EPO-126

GWAS Variants, Non-genetic Factors, and Transient Transcriptome in Multiple Sclerosis Etiopathogenesis

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Background and aims: A clinically actionable understanding of multiple sclerosis (MS) etiology requires GWAS interpretation, prompting research on gene regulatory models. Previous investigations suggested heterogeneity in etiology components, stochasticity in the interaction between genetic and non-genetic factors, and enrichment of binding sites for non-genetic agents in MS-associated DNA intervals. To find a unifying model, we focused on the recently mapped transient transcriptome (TT), including enhancers, intergenic and antisense intronic RNAs.

Methods: Through R and Phyton, we set up a pipeline to perform a colocalization analysis of three datasets: 601 MS-associated variants from the GWAS Catalog; DNA Binding Regions (DBRs) for MS-relevant human and Epstein-Barr Virus (EBV) transducers, namely EBNA2 (6,880 regions), EBNA3C (3,835 regions), activation-induced cytidine deaminase (AID, 4,823 regions), and Vitamin D Receptor (VDR, 23,409 regions); more than 4,5 million genomic intervals plausibly coding for the TT. Gene-enhancers maps of colocalization 'hotpots' were produced according to the Activity-By-Contact (ABC) model.
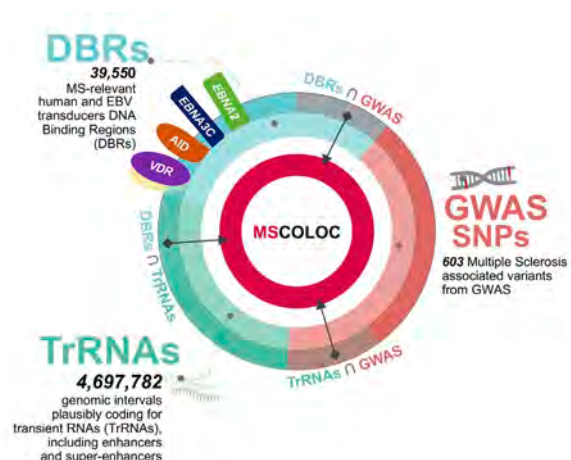
Schematic representation of the colocalization analysis.

Results: TT-coding regions were enriched for both MS-associated GWAS variants, and DBRs for molecular transducers mediating non-genetic etiopathogenetic factors (vitamin D deficiency, EBV infection, B cell dysfunction). We prioritized 275 genomic regions bound by at least 2 out

of 4 molecular transducers, containing 'hotspots' of interactions between genetic and non-genetic modifiers of MS risk/protection. ABC mapping of genes regulated by these 'hotspots' revealed cell-specific, pleiotropic effects.
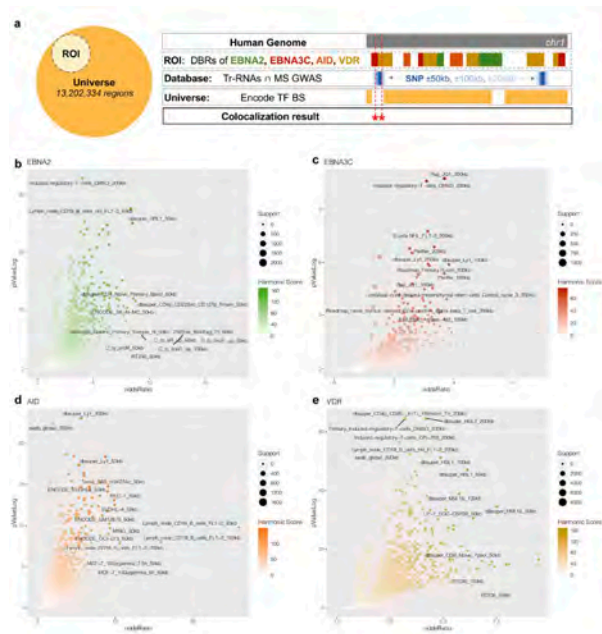
Colocalization analysis of DBRs for human (VDR, AID) and viral (EBNA2,EBNA3c) molecular transducers, MS-associated SNPs and DNA regulatory regions derived from databases.
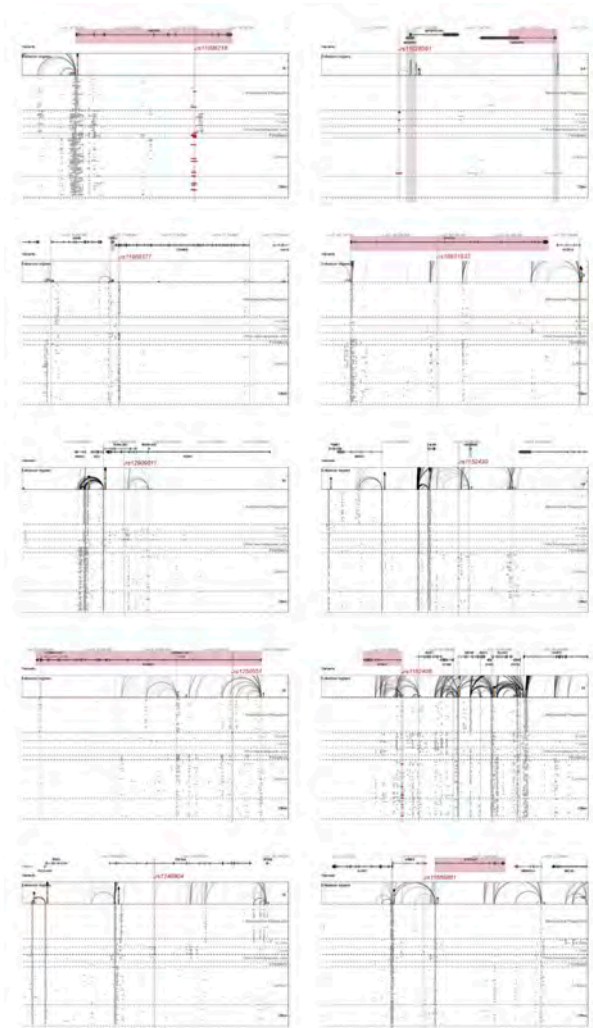
ABC gene-enhancer mapping of MS-trRNAs regulatory hotspots

Conclusion: Studies on the transient and persisting transcriptomes may integrate to clarify the interplay between genetic variability and non-genetic factors causing MS. To this purpose, our colocalization analysis also provides a freely available data resource at www.mscoloc.com.

Disclosure: Nothing to disclose.

EPO-127

Positive Association Between Baseline Brain Volume and Long-term Cognition in Patients With Relapsing Multiple Sclerosis

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Background and aims: Accelerated brain volume (BV), particularly thalamic volume (TV), loss in patients with relapsing multiple sclerosis (RMS) may be correlated with cognitive impairment. This exploratory analysis assessed relationships between baseline BV and long-term cognitive outcomes measured by Symbol Digit Modalities Test (SDMT) in ozanimod trials.

Methods: Adults with RMS who completed phase 3 SUNBEAM (NCT02294058) could enrol in the ongoing DAYBREAK trial (NCT02576717). In SUNBEAM, oral ozanimod 0.46mg/d or 0.92mg/d was compared with intramuscular interferon β-1a 30μg/wk. In DAYBREAK, all patients received ozanimod 0.92mg/d. Baseline TV, whole brain, and cortical grey matter volumes (WBV and CGMV, respectively) were classified as high, medium, or low tertile (high and low presented here) per numerical values in the SUNBEAM intent-to-treat population.

Results: At baseline, patients with high TV had higher mean SDMT scores than those with low TV; this trend was maintained throughout SUNBEAM and DAYBREAK (Figure 1). Differences in least-squares mean SDMT score changes from baseline between high vs low TV were significant at all time points (Figure 2). During DAYBREAK, differences in proportions of patients with high vs low TV who achieved clinically meaningful SDMT improvement were significant (Figure 3). Similar trends were observed for WBV and CGMV.

Figure 1. Mean SDMT Scores in High and Low TV Groups Over Time
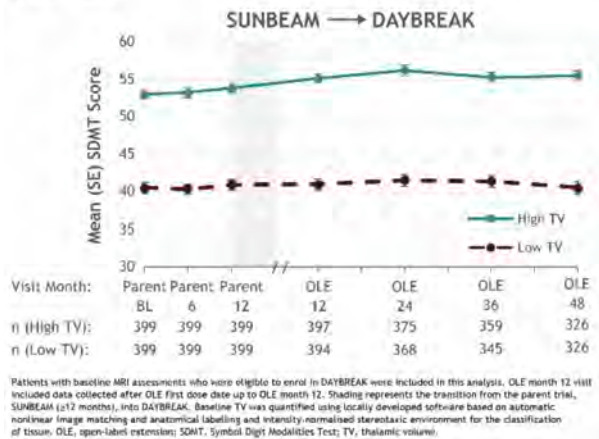
Figure 2. Change From Baseline in Least-Squares Mean SDMT Scores in High and Low TV Groups Over Time

Figure 3. Proportion of Patients With Improved, Stable, or Worsened SDMT Scores in High and Low TV Groups Over Time
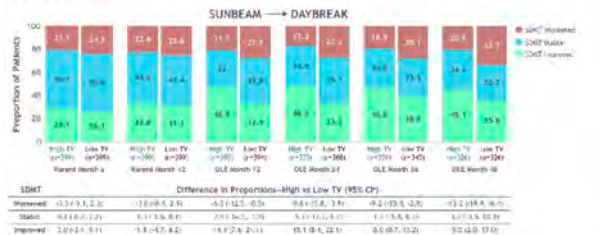
Conclusion: Patients with high baseline BV had higher baseline SDMT scores and were more likely to remain stable or improve over 4–5 years of ozanimod treatment than those with low baseline BV. Early ozanimod use demonstrated the greatest cognitive benefits in patients with preserved BV, supporting an association between preserved BV and improved long-term cognitive outcomes.

Disclosure: The SUNBEAM and DAYBREAK studies were supported by Celgene International II.

EPO-128

Progressive Multifocal Leukoencephalopathy with Natalizumab Extended or Standard Interval Dosing in US and ROW

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Background and aims: Progressive multifocal leukoencephalopathy (PML), an important identified risk for natalizumab, has been well characterized for standard interval dosing (SID; dosing interval every-4-weeks) using data from the US TOUCH Prescribing Program. Overall, information on PML with natalizumab extended interval dosing (EID, dosing interval >every-4-weeks), especially in the rest of the world (ROW), is limited. Study objective was to describe characteristics, risk factors, and clinical outcomes of natalizumab EID and SID PML cases in the US and ROW.

Methods: Global reports of confirmed cases of natalizumab PML were extracted from postmarketing, observational, and clinical trial data in the Biogen Global Safety Database and PML Case Management System, and were assessed using descriptive statistics.

Results: As of June 9, 2021, there were 857 confirmed natalizumab PML cases. In the US and ROW, SID accounted for 203/233 (87.1%) and 590/624 (94.6%) cases, and EID for 30/233 (12.9%) and 34/624 (5.4%), respectively (Table 1). Demographics of US and ROW PML cases were similar. For US and ROW EID PML cases, 56.7% and 44.1% had anti-JCV index >1.5, 20.0% and 11.8% received prior immunosuppressant therapy, and mean duration of natalizumab treatment at diagnosis was 90.0 and 70.2 months, respectively (Table 2). Clinical outcomes were similar for EID and SID PML cases (Table 3).

Conclusion: This analysis provides information on Biogen-confirmed natalizumab PML cases worldwide. Despite limitations including small numbers of EID cases, these results may help inform the medical community on PML in patients treated with natalizumab EID or SID in and beyond the US.

Disclosure: Supported by Biogen.

EPO-129

Levamisole as a major cause of acute disseminated encephalomyelitis: russian single-center experience

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Background and aims: Levamisole (LEV) is an immune stimulator. Nowadays it is mostly used as cocaine adulterant and as an antiparasitic drug in some countries. In Russia people often used LEV as an antiparasitic drug without doctors prescription LEV-associated multifocal inflammatory encephalopathy (LAMIE) is a very deteriorating side-effect of LEV and may be a diagnostic challenge for specialists in multiple sclerosis (MS) and other immune-mediated disorders. LAMIE has different phenotypes. One of them is acute disseminated encephalomyelitis (ADEM).

Methods: The aim of this retrospective study was investigating causes of ADEM in Russia (Moscow) and frequency of ADEM, associated with LEV. This study was performed at Bujanov Moscow City Clinical Hospital with ambulatory service for MS (reference center for MS and other immune-mediated neurological disorders) from South, South-West and New Moscow Districts of Moscow (>3,5 mln inhabitants). We retrospectively reviewed all medical records to find patients, who presented with ADEM during 2018–2020.

Results: Our analysis revealed 42 patients with ADEM. 31 of 42 patients (74%) used LEV at the beginning of the disease (from 1 to 3 months). Other established causes were albendazole usage in 1 patient. 1 patient was after measles vaccination. 9 ADEM were idiopathic (2 of them converted to MS). We will describe the case of recurrent LAMIE and the case of post-mortem LAMIE brain study.
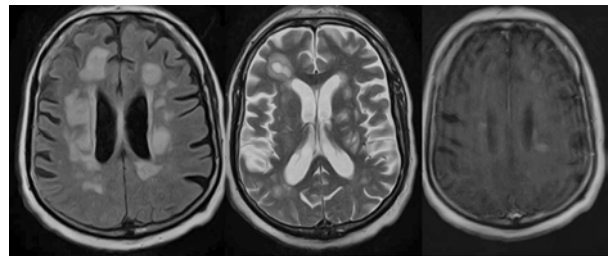
Fig.1 MRI of LAMIE patient.

Conclusion: LAMIE is a very important diagnostic consideration in the first demyelinating episode in Russia. LEV is the most frequent cause of ADEM at the South of Moscow.

Disclosure: Nothing to disclose.

EPO-130

Primary Results from 8–11 Years' Follow-up in CLASSIC-MS Show Long-term Efficacy With Cladribine Tablets in ORACLE MS

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Background and aims: The exploratory Phase IV CLASSIC-MS study (NCT03961204) was a long-term efficacy follow-up of patients originally enrolled in Phase III studies of cladribine tablets (CladT). We report long-term mobility+disability beyond treatment courses received in ORACLE MS.

Methods: This analysis represents ORACLE MS patients in CLASSIC-MS with a first clinical demyelinating event (FCDE) who had received ≥1 course of CladT or placebo. Primary objective: Long-term mobility (no wheelchair use in previous 3 months [EDSS<7]/not bedridden at any time prior to first visit in CLASSIC-MS). Further objectives: Long-term disability status (EDSS<6; i.e. no requirement for ambulatory device at any time since last parent study dose [LPSD]), and time-to-conversion to clinically definite multiple sclerosis (CDMS). Descriptive analyses and findings presented as exposed/never exposed to CladT.

Results: Cohort comprised 227 patients: mean EDSS score 2.15 at CLASSIC-MS baseline; median time since LPSD, 9.5 (range 8.2–11.2) years. CladT exposed: 68.7% (n=156). Conversion to CDMS occurred in 50.0% (n=78) of CladT exposed and 77.5% (n=55) of never exposed patients; median time to conversion was 3.36 (range 0–11.1) and 1.21 (range 0–10.7) years, respectively (Table). Over half of CladT exposed patients (53.2%) remained relapse-free since LPSD vs. 28.2% of never exposed patients. Patients not using a wheelchair/bedridden: CladT exposed, 98.7%; never exposed, 94.2% (Figure). Patients with no requirement for ambulatory device: CladT exposed, 97.4%; never exposed, 94.4%.
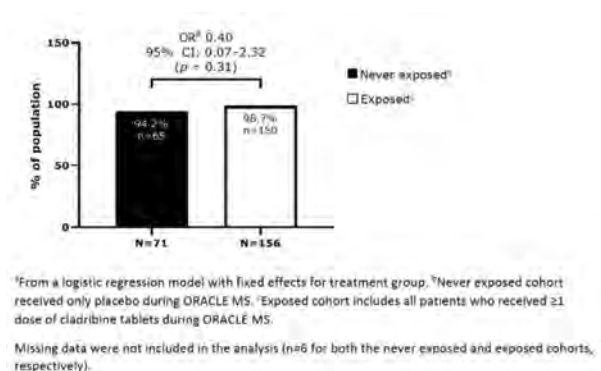
Figure: Primary Endpoint: Long-term Mobility. Patients who were not using a wheelchair (EDSS<7) in the previous 3 months or bedridden at any time prior to first visit in CLASSIC-MS.

Variable	Never exposed to cladribine (n=71)	Exposed to cladribine (n=156)
Patients who converted to CDMS, n (%)		
Yes	55 (77.5)	78 (50.0)
No	16 (22.5)	77 (49.4)
Unknown	0 (0)	1 (0.6)
Time to conversion to CDMS, years		
Patients with event, n	55	78
Mean ± SD	2.15 ± 2.64	3.57 ± 2.72
Median (range)	1.21 (0–10.7)	3.36 (0–11.1)

Table: Tertiary Endpoint: Conversion to CDMS Since First Parent Study Dose.

Conclusion: With a median 9.5 years' follow-up, findings suggest FCDE patients exposed to CladT experienced sustained efficacy (long-term mobility+disability) with delayed conversion to CDMS.

Disclosure: This study was sponsored by Merck (CrossRef Funder ID: 10.13039/100009945).

EPO-131

Analysis of Multiple Sclerosis (MS) Relapse Following Discontinuation of Ozanimod in DAYBREAK

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Background and aims: Patients discontinuing MS disease-modifying therapy (DMT) are at risk of disease reactivation. Rebound, characterized by severe return of disease activity and permanent disability, is a concern with some DMTs. This analysis characterises relapses following ozanimod discontinuation during the DAYBREAK trial, including in a subset of patients who discontinued for family-planning purposes.

Methods: DAYBREAK (NCT02576717) is a phase 3, single-arm, open-label extension trial of ozanimod 0.92 mg/d that enrolled patients with relapsing MS who completed a phase 1–3 ozanimod trial. DAYBREAK began Oct 2015 and is ongoing (data cutoff: Feb 2021). Confirmed MS relapses after permanent ozanimod discontinuation were analysed for severity and disability.

Results: Of 2,494 enrolled patients, 439 (17.6%) discontinued DAYBREAK; mean ozanimod 0.92 mg exposure during DAYBREAK among those who discontinued was 25.6 months (standard deviation [SD], 14.7; range, 0.03–57.6 months). Of 439 patients who discontinued ozanimod, 10 (2.3%) subsequently relapsed in the absence of a DMT (Tables 1 and 2). 76 (17.3%) discontinued for family-planning purposes, of whom 6 (7.9%) relapsed (Table 3). Overall, relapses generally occurred 49–76 days after discontinuation (median 54.5 days); none were severe or associated with severe sustained increase in disability. Seven patients (including all 6 who discontinued for family planning) fully recovered; 3 partially recovered.

Table 1. Characteristics of Posttreatment Relapse After Discontinuing Ozanimod in DAYBREAK (n=10)

Follow-up duration[a]	n/N (%)
≤28 days	439/439 (100)
29–60 days	295/439 (67.2)
61–90 days	183/439 (41.7)
>90 days	102/439 (23.2)
Timing of relapse after ozanimod discontinuation	n/Number with follow-up (%)
≤28 days	0/439 (0)
29–60 days	7/295 (2.4)
61–90 days	2/183 (1.1)
>90 days	1[b]/102 (1.0)
	n/Number with posttreatment relapse (%)
≤28 days	0/10 (0)
29–60 days	7/10 (70)
61–90 days	2/10 (20)
>90 days	1[b]/10 (10)
Time since last dose to relapse	Days
Median (range)	54.5 (34[c]–141[b])
Mean (SD)	64.1 (29.5)
Ozanimod exposure in DAYBREAK	Months
Median (range)	34.2 (25.5–48.8)
Mean (SD)	34.8 (7.7)
Severity of relapse[d]	n/Number of those with posttreatment relapse (%)
Mild	5/10 (50)
Moderate	5/10 (50)
Severe	0
Increase in EDSS during relapse, points	
Median (range)	1 (0–2.5)
Mean (SD)	1.05 (0.76)
Recovery from relapse[e]	n/Number of those with posttreatment relapse (%)
Partial	3/10 (30)
Complete	7/10 (70)
Duration of relapse	Days
Median (range)	20 (6–51)
Mean (SD)	22.4 (14.7)
Steroids used for posttreatment relapse, n	0[f]
Switched to a different DMT,[g] n	0

[a]Protocol-defined safety follow-up after ozanimod discontinuation was increased from 28 to 75 days (2015 amendment) and then 90 days (2019 amendment). [b]The long outlier case (141 days after discontinuation) was associated with the patient not being able to return to the site after running out of study drug 4 months earlier due to travel restrictions during the COVID-19 pandemic. [c]In the months prior to the stated discontinuation date, the patient with a relapse at 34 days postdiscontinuation had absolute lymphocyte count values suggesting an inconsistent administration of ozanimod; thus, this patient may have discontinued earlier than stated. [d]Severity was determined at the investigator's discretion. [e]Recovery from the relapse was assessed based on a patient's function 30 days after relapse start. [f]Three patients received steroids as inpatients. [g]Treatment with certain DMTs at the investigator's discretion was permitted after 28 days of safety follow-up. DMT, disease-modifying therapy; EDSS, Expanded Disability Status Scale; SD, standard deviation.

Table 2. Demographic Characteristics and Reasons for Discontinuation Among Those Who Relapsed and All Patients Who Discontinued DAYBREAK

Characteristic	Posttreatment Relapse (n=10)	All Patients Who Discontinued Ozanimod (N=439)
Age at MS symptom onset, mean (SD), y	21.9 (4.8)	28.0 (9.0)
Age at DAYBREAK baseline, mean (SD), y	28.3 (6.1)	35.6 (9.8)
Sex, n (%)		
Female	9 (90.0)	311 (70.8)
Male	1 (10.0)	128 (29.2)
Race, n (%)		
White	9 (90.0)	435 (99.1)
Black	0	2 (0.5)
Asian	0	1 (0.2)
Other	1 (10.0)	1 (0.2)
EDSS at DAYBREAK baseline, mean (SD)	2.3 (1.7)	2.7 (1.4)
Number of relapses during DAYBREAK, mean (SD)	0.9 (1.7)	0.6 (1.2)
Reason for discontinuation, n (%)		
Lack of efficacy	1 (10.0)	61 (13.9)
Adverse events[a]	1 (10.0)	74 (16.9)
Other	8 (80.0)	304 (69.2)
Family planning (intent to conceive)	6 (60.0)	76 (17.3)[b]
Became pregnant[c]	0	25 (5.7)
Sponsor/physician decision	1 (10.0)	20 (4.6)
Voluntarily withdrew	1 (10.0)	157 (35.8)
Lost to follow-up	0	26 (5.9)

[a]Includes deaths. [b]Includes 5 men who discontinued due to desire to procreate. [c]Ozanimod dosing was suspended if urine pregnancy test was positive, and patient was discontinued from the trial if pregnancy was confirmed. EDSS, Expanded Disability Status Scale; MS, multiple sclerosis; SD, standard deviation.

Table 3. Characterisation of Relapses (n=6) Among Patients Who Discontinued for Family-Planning Purposes (N=76)

Duration of follow-up[a]	n/N (%)
≤28 days	76/76 (100)
29–60 days	66/76 (86.8)
61–90 days	44/76 (57.9)
>90 days	23/76 (30.3)
Timing of relapse after ozanimod discontinuation	**n/Number with follow-up (%)**
29–60 days	4/66 (6.1)
61–90 days	2/44 (4.5)
	n/Number of those with posttreatment relapse (%)
29–60 days	4/6 (66.7)
61–90 days	2/6 (33.3)
Time since last dose to relapse	**Days**
Median (range)	55 (49–76)
Mean (SD)	59.7 (11.8)
Severity of relapse[b]	**n/Number of those with posttreatment relapse (%)**
Mild	5/6 (83.3)
Moderate	1/6 (16.7)
Increase in EDSS during relapse, points	
Median (range)	0.75 (0.0–2.5)
Mean (SD)	0.92 (0.86)
Recovery from relapse[c]	**n/Number of those with posttreatment relapse (%)**
Partial	0/6 (0)
Complete	6/6 (100)
Duration of relapse	**Days**
Median (range)	15 (8–38)
Mean (SD)	18.7 (11.7)
Steroids used for posttreatment relapse, n	5[d]

[a]Protocol-defined safety follow-up after ozanimod discontinuation was increased from 28 to 75 days (2018 amendment) and then 90 days (2019 amendment). [b]Severity was determined at the investigator's discretion. [c]Recovery from the relapse was assessed based on a patient's function 30 days after relapse start. [d]One patient received steroids as an inpatient. EDSS, Expanded Disability Status Scale; SD, standard deviation.

Conclusion: A small number of patients, including those who discontinued for family-planning purposes, had confirmed relapse after ozanimod discontinuation. There was no evidence of disease activity or disability indicative of disease rebound. All relapses were reported as mild or moderate, with most patients experiencing a complete recovery.

Disclosure: DAYBREAK was supported by Celgene International II.

EPO-132

WHITE MATTER LESIONS AND COMORBIDITIES IN MULTIPLE SCLEROSIS: CENTRAL VEIN SIGN AND DIFFUSION MRI

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Background and aims: Despite the similar features shared by MS, migraine and Small Vessel Disease (SVD)-related white matter (WM) T2-hyperintensities, ex-vivo studies demonstrated their heterogeneous histopathology. We investigated SVD and migraine impact on the assessment of the Central Vein Sign (CVS) in a MS patients' cohort and applied the Spherical Mean Technique (SMT) to evaluate whether perivenular (CVS+) and non-perivenular lesions (CVS-) show distinctive microstructural features.

Methods: 120 MS patients stratified into 4 Age Groups performed 3T brain MRI. WM lesions were classified in CVS+ and CVS- by visual inspection of FLAIR* images; mean values of SMT metrics (INTRA, EXTRATRANS, EXTRAMD) were extracted.

Results: 68.7% lesions were perivenular. Significant differences were found between CVS+ and CVS- volume in the whole brain (p<0.001) and between CVS+ and CVS- volume and number in all the four subregions (p<0.001 for all). The percentage of CVS+ decreased from youngest to oldest patients (79.7%–57.7%), with the deep/subcortical WM of oldest patients as the only where CVS+ number was lower than CVS-. Older age and migraine were predictors of a lower percentage of CVS+ (p<0.001 and p=0.013 respectively). Whole brain CVS+ showed higher EXTRAMD, EXTRATRANS and lower INTRA (p=0.001, p=0.001, p=0.02 respectively).

Conclusion: Age and migraine have a relevant impact in reducing the percentage of CVS+. SMT may differentiate CVS+, characterized by higher inflammation, demyelination and fiber disruption, from CVS-. The development of new CVS-, especially in the deep/subcortical WM of older patients, should be considered a "red flag" for a different -other than MS-pathophysiology.

Disclosure: Authors report no disclosures.

EPO-133

Ponesimod Effects on Relapse Severity: A Post Hoc Analysis of the OPTIMUM Study

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Background and aims: Ponesimod is a sphingosine 1-phosphate receptor 1 (S1P1) modulator indicated for the treatment of relapsing forms of multiple sclerosis (RMS) in adults. In the ~2-year phase 3 OPTIMUM study (NCT02425644), ponesimod 20 mg was significantly superior to teriflunomide 14 mg in reducing annualised relapse rate in adults with RMS. This post hoc analysis of OPTIMUM examined relapse severity in both treatment groups over the ~2-year observation period.

Methods: Relapses were categorised by maximum severity: high/moderate, ≥1 functional domain was affected and corticosteroid use was required, treatment was withdrawn (high only), and/or patient was hospitalized (high only); low, all other relapses. Proportions of patients with high/moderate and low maximum relapse severity were calculated, and incidence rates were examined using odds ratios.

Results: In total, 389 patients experienced ≥1 relapse (ponesimod: 166 of 567 patients [29.3%]; teriflunomide: 223 of 566 patients [39.4%]). Compared with patients treated with teriflunomide, patients treated with ponesimod had a 42% reduction in odds of experiencing high/moderate maximum relapse severity (OR 0.58; 95% CI, 0.44–0.76) (Figure). Among a subgroup of patients with baseline Expanded Disability Status Scale score ≤3, patients treated with ponesimod had a 56% reduction in odds of experiencing high/moderate maximum relapse severity (OR 0.44; 95%, CI 0.30–0.64). Odds of experiencing low relapse severity were similar among treatment groups (overall and EDSS ≤3).
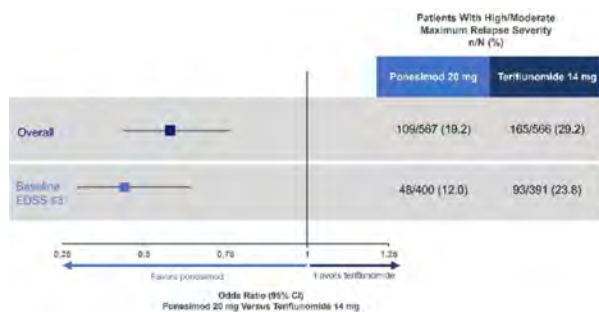
Figure 1. Odds of Experiencing High/Moderate Maximum Relapse Severity in OPTIMUM

Conclusion: In OPTIMUM, patients receiving ponesimod 20 mg were less likely to experience moderate-to-severe relapses than patients receiving teriflunomide 14 mg, and effects were more pronounced in the early illness population (EDSS score ≤3).

Disclosure: This research was funded by Janssen Scientific Affairs, LLC.

EPO-134

iPad-based application CogEval® as a predictor of Multiple Sclerosis in patients with Clinically Isolated Syndrome

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Background and aims: Cognitive impairment in patients with Clinically Isolated Syndrome (CIS) has been associated with a higher risk of conversion to Multiple Sclerosis (CIS-MS) compared to those patients remaining as a CIS (CIS-CIS). Our aim is to study the prognostic value of the iPad®-based application Processing Speed Test (PST) CogEval® in patients with a CIS to predict the accuracy to discriminate a MS.

Methods: Single-center prospective study of patients with a CIS from October 2019 to January 2022. We included patients with a CIS and ≥1 PST performed within the first 5 years since first symptom. Z scores adjusted by age, sex and level of education were obtained.

Results: 219 patients were included, 153 women (69.9%) with a mean (±SD) age of 37.7 (±10.3) years and a mean time from the first symptom to the first PST of 2.7 (±1.5) years. 190 patients (86.8%) fulfilled MS criteria (CIS-MS). CIS-MS patients had a higher radiological activity (p<0.001) and a higher proportion of IgG oligoclonal bands (p<0.001) compared to CIS-CIS patients. CIS-MS patients had a significantly lower Z score (mean [SD] -0.2 [±0,9] in CIS-MS vs 0.4 [±0,7] in CIS-CIS group, p=0.001) despite a similar EDSS between both groups (mean [SD] 2.0 [±0,9] vs 1.5 [±0,6] respectively, p=0.41).

Conclusion: iPad-based® PST CogEval® is a simple and easy tool in real-world setting with a potential prognostic value to discriminate CIS patients with higher risk of MS.

Disclosure: Nothing to disclose.

EPO-135

The impact of high-efficacy disease-modifying therapies in cognitive impairment in Multiple Sclerosis patients

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Background and aims: Information processing speed (IPS) impairment is one of the cognitive domains affected most and earliest in multiple sclerosis (MS). Cognitive decline could be slowed by early administration of high-efficacy disease-modifying therapies (heDMTs), despite few studies have assessed this topic. Our aim is to study the effect of heDMTs in preventing IPS impairment in MS patients.

Methods: Single-center prospective study measuring IPS with the Processing Speed Test (PST) CogEval® in MS patients from October 2019 to January 2022. We defined heDMTs as treatment with natalizumab, alemtuzumab, ocrelizumab or rituximab. Raw scores (RS) and Z-score adjusted by age, sex and level of education were obtained. Cognitive decline was defined as a baseline Z-score below (or including) -2 and/or ≥10% RS deterioration after one year. Multivariate regression models were used.

Results: 847 patients were included, 419 (68.1%) women, with a mean (±SD) age of 45 (±11.4) years. Relapsing MS patients (79.1%) had higher baseline Z-scores and lower radiological activity and EDSS scores than progressive MS patients (20.9%). For each year delaying the start of a heDMT, we observed -0.01 points less in baseline Z-score (ß=-0.01 [CI95% -0.02 to -0.004], p=0.01), with a weak correlation (r=-0.21). In patients with at least one year of follow-up (n=158), the multivariate model showed that only EDSS progression during that year predicted a higher risk of ≥10% deterioration in RS (OR=5.84 [CI95% 2.09–16.84], p=0.001).

Conclusion: Early administration of heDMTs could potentially prevent IPS impairment in MS, although this effect may require a prolonged time.

Disclosure: Nothing to disclose.

EPO-136

Self-reported and clinician-rated measures in multiple sclerosis care: looking for a complementary assessment approach

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Background and aims: Relapsing-remitting multiple sclerosis (RRMS) patients experience disability in different domains affecting their quality of life even in early stages of the disease. This study aimed to evaluate if patient-reported outcomes (PROs) are able to capture disability in early-stage RRMS.

Methods: A multicentre, non-interventional study was conducted. Adult patients with RRMS diagnosis, disease duration ≤3 years, and Expanded Disability Status Scale (EDSS) score between 0–5.5 were included. 9-Hole Peg Test (9-HPT), NeuroQoL Upper Extremity (NeuroQoL-UE), Timed 25-Foot Walk (T25-FW), Multiple Sclerosis Walking Scale (MSWS-12), Symbol Digit Modalities Test (SDMT), and Perceived Deficits Questionnaire (PDQ-5) were used to measure hand function, gait, and cognition, respectively.

Results: A total of 189 patients were included (mean age: 36.1±9.4 years, 71.4% female, mean disease duration: 1.2±0.8 years, median EDSS score: 1.0 [IQR=0.0–2.0]). A proportion of 12.6% (n=23/183) and 23.4% (n=43/183)

patients reported a moderate-to-extreme limitation in walking and running ability on the MSWS-12, respectively. 24.6% of patients (n=45/183) spent ≥6 seconds in T25-FW. All but one of MSWS-12 item scores were significantly correlated with T25-FW score. Seven patients (3.7%, n=7/188) spent >33.3 seconds completing 9-HPT. Each individual NeuroQoL-UE item and total scores had a significant correlation with 9-HPT score (p≤0.002). 81 patients (43.1%, n=81/188) had information processing speed problems (cut-off score ≤49). Attention, planning/organisation and prospective memory PDQ-5 items were significantly correlated with SDMT score (p<0.05).

Conclusion: PROs can enable RRMS patients to communicate their perceived disability in different domains often not detected in early stages, assisting clinicians in disease monitoring and decision making.

Disclosure: This study was funded by the Medical Department of Roche Farma Spain. R. Gómez-Ballesteros and J. Maurino are employees of Roche Farma Spain. None of the other authors report any conflict of interest.

EPO-137

Could Kappa Free Light Chains Represent a Marker of Cognitive Impairment in Multiple Sclerosis Patients?

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Background and aims: Pathophysiology of cognitive impairment (CI) in Multiple Sclerosis (MS) is still unclear and cortical grey matter pathology may be influenced from early stages by meningeal B cell aggregates. Oligoclonal bands (OBs) allow an early diagnosis and have a negative prognostic value. Cerebrospinal fluid (CSF) Kappa free light chains (KFLCs) and KFLCs-Index (K-Index) were proved a reliable diagnostic marker of intrathecal synthesis, but its prognostic role is unknown. We explored the correlation of B-cells activity biomarkers and CI in MS patients at diagnosis.

Methods: Cognition in 50 newly-diagnosed MS patients was evaluated using Brief International Cognitive Assessment for MS (BICAMS) battery. CSF Lambda FLCs (LFLCs), KFLCs, and K-Index (CSF-serum KFLC-albumin ratio) were determined with nephelometry. OBs were determined with isoelectrofocusing and immunoblotting.

Results: 26% of our patients showed CI. 92% of our patients had OBs and mean CSF KFLC 0.619 ± 0.085 g/dl and K-Index 96.82 ± 96.84. Patients with impaired verbal memory (VM) and CI showed high CSF KFLCs (respectively p:0.0002 and p<0.0001) and K-Index (respectively p:0.02 and p:0.002). Cognition correlated with CSF KFLCs (r:-0.39 p:0.004) and K-Index (r:-0.28 p:0.04). No differences or correlations were observed for CSF LFLCs. Patients with or without OBs displayed similar cognitive performances (p>0.05).

Conclusion: Our preliminary results suggest that KFLCs and K-Index may have a prognostic role in identifying patients with CI. Few data are reported in literature of correlation between cognition and IgG intrathecal synthesis markers, and to our knowledge, those are the first results indicating a possible role of KFLCs in that process.

Disclosure: No disclosures related to this study.

EPO-138

Disability progression of active and nonactive primary and secondary progressive multiple sclerosis patients in the US

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Background and aims: This study describes the physician-reported disability progression of active and nonactive primary progressive multiple sclerosis (PPMS) and secondary progressive multiple sclerosis (SPMS) patients in the United States (US).

Methods: Physicians who participated in the Adelphi Disease Specific Programme reported the disease progression of their patients with active and nonactive PPMS and SPMS in the annual cross-sectional survey in the US from 2013–2021.

Results: A total of 851 active PPMS, 1677 nonactive PPMS, 293 active SPMS, and 486 nonactive SPMS patients were evaluated. Most patients had a current EDSS scores <7 and were on a current disease-modifying treatment (Table 1). In both active and nonactive PPMS, 5% were reported as improving while 6% of active SPMS and 2% of nonactive SPMS were reported as improving. Majority (60–70%) of the active and nonactive PPMS and SPMS patients were deteriorating slowly and 2-11% were deteriorating rapidly (Table 2).

Endpoints	Active PPMS	Nonactive PPMS	Active SPMS	Nonactive SPMS
Baseline EDSS Score				
0–5	57%	57%	58%	54%
5.5–6.5	23%	22%	26%	26%
7+ or unknown	20%	21%	15%	20%
Treatment				
On a current DMT	77%	59%	89%	74%
Not on a DMT	23%	41%	11%	26%

DMT=disease-modifying treatment; EDSS=Expanded Disability Status Scale; PPMS=primary progressive multiple sclerosis; SPMS=secondary progressive multiple sclerosis.

Table 1: Baseline EDSS Score by patient type

Disability progression	Active PPMS	Nonactive PPMS	Active SPMS	Nonactive SPMS
Improving	5%	5%	6%	2%
Stable	19%	31%	22%	29%
Deteriorating slowly	70%	60%	61%	68%
Deteriorating rapidly	6%	3%	11%	2%

PPMS=primary progressive multiple sclerosis; SPMS=secondary progressive multiple sclerosis; Question asked was "Which of the following profiles best describes the patient's disease progression?"

Table 2: Physician-reported disability progression

Conclusion: This study showed that most active and nonactive PPMS and SPMS patients were deteriorating, demonstrating the high unmet need despite patients being on disease-modifying treatments. In the nonactive population, only 5% of PPMS and 2% of SPMS patients were reported as improving. There continues to be a high unmet need for additional treatments for patients with PPMS and SPMS that are safe and effective; this is especially true in nonactive populations, where there are limited options.

MS and related disorders 2

EPO-139

Evaluation of the potential newborn exposure to glatiramer acetate (Copaxone) via lactation

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Background and aims: Glatiramer acetate (Copaxone, GA), a subcutaneous (SC) treatment of relapsing forms of multiple sclerosis (MS), is a heterogeneous mixture of peptides. The risk of neonate exposure to GA via breast milk was assessed.

Methods: GA systemic exposure was assessed using polyclonal ELISA method following a 60mg SC injection of GA in healthy volunteers (HV) (n=20), 30mg/kg SC injection and oral 600mg/kg in cynomolgus monkeys (n=4), and 3mg/kg SC injection in beagle dogs (n=3). Standard Relative Infant Dose (RID) was calculated using Cmax values and factored to account for the oral absorption.

Results: Limited PK data from HV and animals demonstrated that systemic exposure to GA occurs only for a short period after dosing (Table 1). Oral Cmax and AUC relative to SC administration in monkey were <2.6% and <0.5%, respectively. Human RID was calculated considering worst-case scenario in which maximum drug concentration in breast milk is similar to Cmax. The RID was 9%; when adjusted to account for low oral absorption, RID dropped to 0.2% (Table 2).

Table 2:   RID Calculations for Humans

Dose in human mg	Dose in human mg/kg[a]	C_{max} in human ng/mL[b]	Milk intake mL/kg/day	Total infants daily dose intake by ng/kg/day[c]	RID% [d]	Total daily dose absorbed orally by infants ng/kg/day	Absorption based RID%[e]
20	0.333	202[c]	150	30,300 (0.03 mg/kg/day)	9	788 (0.000788 mg/kg/day)	0.2
40	0.666	404[c]	150	60,600 (0.06 mg/kg/day)	9	1,576 (0.001576 mg/kg/day)	0.2

[a]Assuming 60 kg average women's body weight
[b]Extrapolated from the highest C_{max} (606 ng/mL) following 60 mg dose in HV study
[c]GA concentration in milk is assumed to be as C_{max}, total daily dose = C_{max} in human ng/mL*milk intake mL/kg/day
[d]RID% = infant daily dose/mother dose * 100
[e]RID factored by 2.6% to account for oral absorption, based on the cynomolgus monkey study

Conclusion: Known GA physiochemical properties (high charge, protein binding and molecular weight) suggest that it is unlikely to be transferred to breast milk. The PK data demonstrate that there is limited time in which GA can be transferred to milk and it is poorly absorbed from the GI. The RID for GA is 0.2% when poor oral absorption is factored, a value considered 'safe' by the World Health Organization. The data indicates that the potential newborn exposure to GA via milk is unlikely.

Disclosure: Authors are employees of Research and Development, Teva Pharmaceutical Industries, Ltd. Author Details.

Table 1. T_{max} and exposure duration following SC injection

Species	Number with GA detected/ total number sampled	T_{max} and exposure duration
Human HVs[a]	9/17[b]	Up to 30 min in 8 subjects and 240 minutes in 1 subject
Cynomolgus Monkeys	4/4	T_{max} range = 15 to 30 min; serum GA concentrations ≤ LOQ (50 ng/mL) at 4 hours postdose
Beagle dogs	3/3	T_{max} range = 30 to 60 min; serum GA concentration returned to baseline at 6 hours

[a]Blood samples were collected for PK purposes at 5, 15, 30, 60, 120, 240 and 360 minutes post injection
[b]Levels in the remaining 8 volunteers were below the assay limit of quantitation LOQ (50 ng/mL)

EPO-140

Pathophysiological Mechanisms and Electroencephalographic Biomarkers of Fatigue in Multiple Sclerosis

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Background and aims: Fatigue is the most common symptom in patients with Multiple Sclerosis (pwMS). Motor fatigue assessment in pwMS is purely based on clinical scales and no objective assessment has been validated so far. Also, the mechanism underlying motor fatigue in pwMS is poorly understood. We investigated whether pwMS show more motor fatigue than healthy controls (HC), and tested the hypothesis that increased motor fatigue in pwMS is generated at central nervous system level. Finally, we explored whether motor fatigue in pwMS is associated with specific changes in the excitability of the motor cortical network.

Methods: 11 patients with relapsing-remitting MS, and 15 age and sex-matched HC performed repeated blocks of maximal voluntary contraction with the first dorsal interosseous muscle (FDI) until exhaustion. Peripheral and central motor fatigue were assessed by a neuromuscular assessment based on the superimposed twitch technique. Motor cortical network excitability was assessed by measuring the local mean field amplitude (LMFA) of transcranial magnetic stimulation (TMS)-evoked EEG potentials before and after the fatiguing task.

Results: We found early fatigability , significantly higher central motor fatigue, and no differences in peripheral motor fatigue in pwMS compared to HC Motor fatigue was associated with a decrease in LMFA only in HC and not in pwMS.
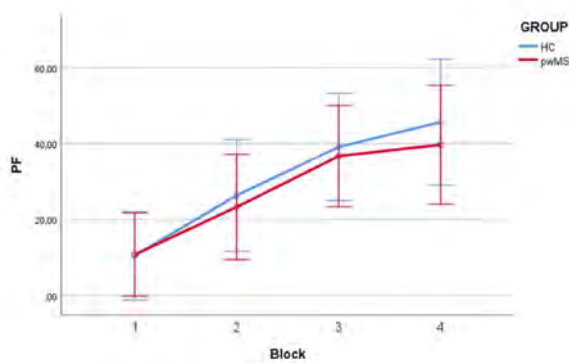
Periferal fatigue (PF) significantly increased as a function of factor block (F(3,30) = 32.15, p<0.001), but we found no significant group*block interaction (F(3,72) =0.37, p=0.69) and no significant effect of factor group (F=0.1, p=0.8).
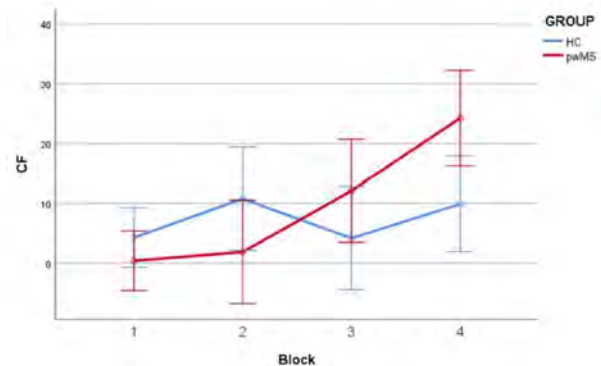
Central Fatigue (CF) significantly increased as a function of factor block (F(3,72) = 7.92, p<0.001),). A significant difference in CF between pwMS and HC only on task failure (4th block) (45.3±4.37 vs 20.96±3.74 %, p<0.001).
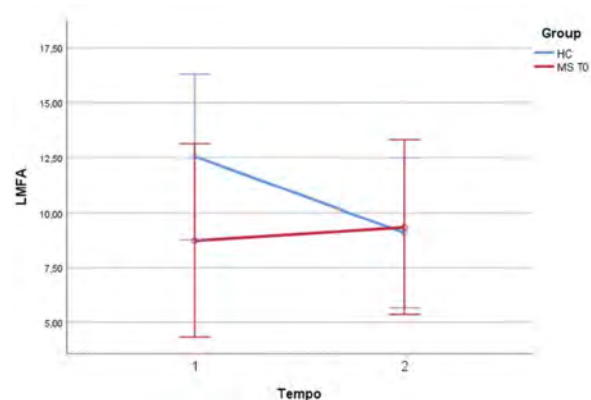
HC showed a reduction of LMFA values post-fatigue (2) compared to pre-fatigue (1) (9.08±7.07 vs 12.54±8.48, p 0.031). pwMS showed no signficant change in LMFA pre(1) vs post-fatigue (2)

Conclusion: Central mechanisms play a major role in motor fatigue in pwMS. Motor fatigue is associated with abnormal modulation of motor cortical network excitability in pwMS. Our results could be used to develop new treatments targeting motor fatigue in pwMS.

Disclosure: Nothing to disclose.

EPO-141

Investigating the epigenetic signature of Multiple Sclerosis and immunological imprint of ocrelizumab via miRNA analysis

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Background and aims: MicroRNAs (miRNA) are promising biomarkers in relapsing-remitting multiple sclerosis (RRMS). We investigated the epigenetic signature of RRMS and the immunological effects of ocrelizumab, an anti-CD20 monoclonal antibody, via miRNA expression profile.

Methods: MiRNA and immune-related gene expression was analysed in peripheral blood mononuclear cells of 6 naïve RRMS patients (OCRE cohort) at baseline (T0) and 12 months after ocrelizumab (T12), and in 6 healthy controls (HCs), using TaqMan Array MicroRNA Cards and Immune Panel Arrays (discovery phase). Differentially expressed miRNAs and genes, along with in silico predicted miRNA targets, were analysed by qPCR in 10 naïve RRMS patients (NMS cohort), 9 RRMS patients who switched from fingolimod to ocrelizumab (FTO cohort), and additional 10 HCs (validation phase).

Results: Let-7i was upregulated in the OCRE (T0) and NMS cohorts compared to HCs. In the NMS cohort, mRNA levels of Bcl-2, a Let-7i target, were also upregulated. Bcl-2 was also downregulated at baseline in the FTO cohort. miR-181a-5p and miR-181c-5p were upregulated, and transcriptional levels of IL-6, a miR-181a target, were downregulated, in both OCRE and FTO patients at T12 versus T0.
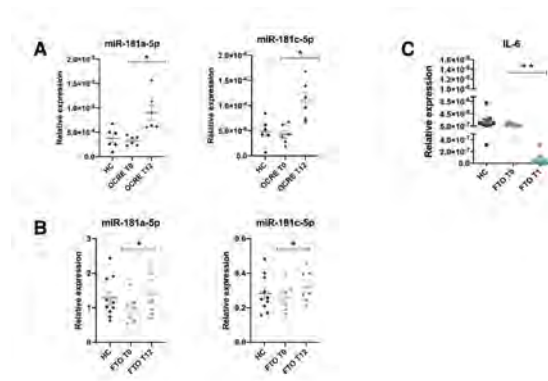
miR-181a-5p and -181c-5p levels (Mean ± SEM) at T12 versus T0 in OCRE cohort (p=0.0312) (A) and in FTO cohort at T12 versus T0 (p=0.0312, p=0.046 respectively) (B). Transcription levels of IL-6 (Mean ± SEM) in FTO cohort at T12 versus T0 (p=0.004)

Conclusion: Let-7i could participate in MS pathogenesis, by upregulating Bcl-2 and inhibiting apoptosis of autoreactive immune cells. Ocrelizumab could modulate inflammation and T lymphocytes' function beyond B cell depletion, by upregulating miR-181a/c, which are involved in the T cell receptor signalling, and downregulating IL-6. Data validation in a wider patients' cohort is needed.

Disclosure: The authors declare no relevant or material financial interests related to the study.
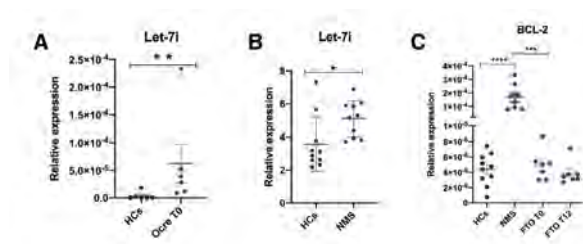
Let-7i levels (Mean ± SEM) in OCRE cohort at T0 (A) versus healthy controls (HCs) (p=0.087) and in NMS cohort versus HCs (p=0.01) (B). Bcl-2 levels (Mean ± SEM) in NMS cohort versus HCs (p=0.01) (B). Bcl-2 levels (Mean ± SEM) in NMS cohort versus HCs (p<0.0001) and in FTO cohort at T0 versus NMS (p=0.0003) and T12

EPO-142

Is Autonomic Dysfunction in Relapsing Remittent Multiple Sclerosis Correlated with Vagus Nerve Cross-Sectional Area

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Background and aims: Autonomic dysfunction is being increasingly recognized as an important aspect of multiple sclerosis (MS) at the clinical, neurophysiological and molecular level. The aim of this work was to correlate the disability, fatigue and autonomic dysfunction in patients with relapsing remittent MS (RRMS) with the sympathetic skin response (SSR) and the cross-sectional area (CSA) of vagus nerves on both sides.

Methods: This case case-control study was conducted on 50 RRMS patients and 50 controls. The patients were clinically assessed using Expanded disability status score (EDSS). Fatigue was assessed using Modified Fatigue Impact Scale (MFIS) and the autonomic dysfunction was assessed using Composite Autonomic Symptom Score (COMPASS 31). SSR and vagal nerve CSA were measured for both patient and controls.

Results: Patients with RRMS had significantly more delayed latency and smaller amplitude of SSR on both Rt and Lt side in comparison to controls (p-value ≤0.001 in all parameters). Patients with RRMS had also significantly smaller CSA of both Rt and Lt vagus in comparison to controls (p-value ≤0.001, ≤0.001). There were statistically significant correlations between SSR latency and amplitude on both Rt and Lt side, and the disease duration, the total number of relapses, EDSS, MRI lesion load, and COMPASS. There were statistically significant negative correlations between the CSA of both Rt and Lt vagus, and both COMPASS (p-value ≤0.001, 0.001) and MFIS (p-value ≤0.001, ≤0.001).

Conclusion: The autonomic dysfunction in patients with RRMS is correlated with the SSR and the vagus nerves CSA.

Disclosure: Nothing to disclose.

EPO-143

Evaluation of Clinical and Radiological Characteristics of TDLs, Long-Term Follow-up Results

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Background and aims: Tumefactive demyelinating lesions(TDLs) are a variant of the spectrum of inflammatory demyelinating diseases(IDDs).It can occur alone or during the course of multiple sclerosis (MS).We aimed to determine the clinical and radiological features of TDLs,and to obtain information that clinicians use for diagnosis,and treatment approaches.

Methods: Clinical,and imaging characteristics,treatments and Expanded Disease Status Scale(EDSS) scores of 41 patients with TDLs followed up in our clinic(1981-2021) were retrospectively analyzed.

Results: 30 (73.2%)of the patients were female and 11 (26.8%) were male. 10 (24%) of the patients had childhood-onset.The mean age at onset was 26.9±13.8 years.The mean follow-up period was 9.5±6.5 years.There were 29 (70.7%) patients with TDL alone and 12 (29.3%) patients with MS. The most common initial findings were motor and sensorimotor findings.Oligoclonal bands were detected in 42.4%.Localizations of the lesions were most frequently in the frontal and parietal lobes.Of TDLs 34.1% had open-ring enhancement. Of the patients 34% with TDL alone were diagnosed with MS in a median of 20 months. qEight patients (27%) remained monophasic.The median of the initial and final EDSS were 3.0 and 2.0, respectively.The median final EDSS in patients with monophasic course was found to be significantly lower than in patients with relapsing course(p=0.007). Of the patients 76% were receiving DMTs.

	n (%)
Total number of the patients	41
Childhood-onset	10 (24.4%)
Gender (F/M)	3/1
Female	30 (73.2%)
Male	11 (26.8%)
Childhood-onset female/male ratio	10/0
History of epilepsy	15 (36.6%)
TDL alone	29 (70.7%)
TDL developed in MS course	12 (29.3%)
Age at 2021 (mean±SD)	37.29±12.8
Age at disease onset (mean±SD)	26.9±13.8
Follow-up duration (yr) (mean±SD)	9.5±6.5
Disease duration (yr) (median, IQR)	8 (5-15)
Disease course (monophasic/relapsing)	
Monophasic	8 (19.5%)
Relapsing	32 (78%)
Oligoclonal Bands (OCBs)	
Positive	14 (42.4%)

Medians of last EDSS scores patients with relapsing course and monophasic
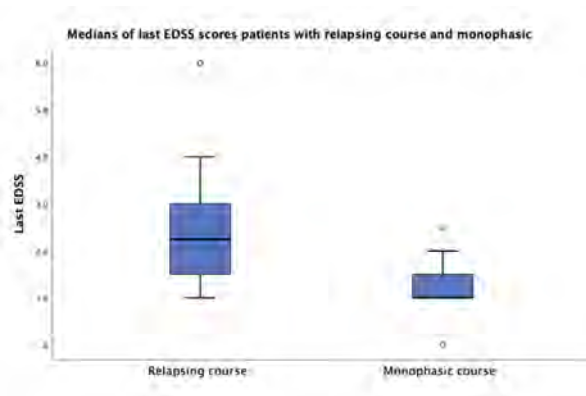
Conclusion: TDLs are a spectrum of IDDs with characteristic radiological findings. It is important to differentiate from neoplasms. DMTs should be initiated early for the patients who fulfilled the criteria for dissemination in time and space from the beginning. Multicenter, larger, prospective studies of patients would be most informative and helpful for a better understanding of these clinical pictures.

Disclosure: Nothing to disclose.
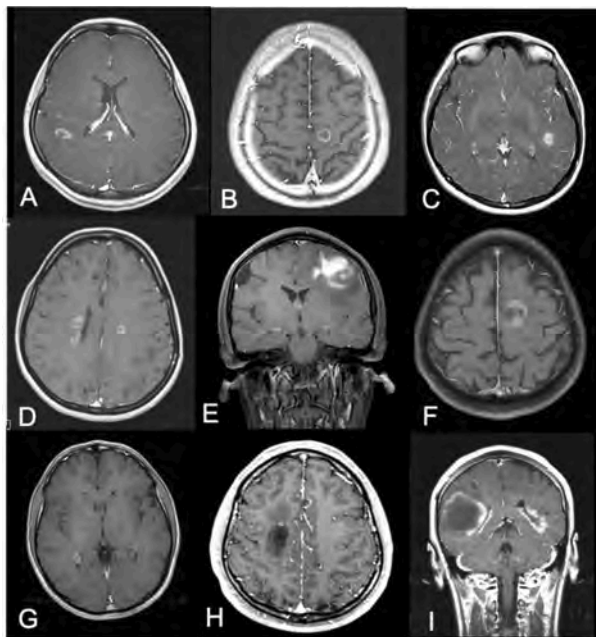
EPO-144

Real-World Analysis Affirms High Persistence and Adherence with Diroximel Fumarate after Switch from DMF to DRF in MS

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Background and aims: Diroximel fumarate (DRF) is an oral fumarate approved for the treatment of relapsing forms of MS (RMS). It has the same pharmacologically active metabolite as dimethyl fumarate (DMF) and a similar efficacy and safety profile. DRF has improved gastrointestinal (GI) tolerability and lowlow (<1%) treatment discontinuation due to GI adverse events (AEs) in clinical trials. There is limited data characterising persistence to DRF in the real-world, especially in patients who have switched to DRF from DMF.

Methods: This retrospective analysis of the AcariaHealth Specialty Pharmacy Program included patients with MS who initiated DRF from 01-December-2019 through 30-January-2021, focusing on a subset of patients with DMF as their most recent disease-modifying therapy. This analysis evaluated patient persistence, measured as overall proportion of patients remaining on therapy; discontinuation rate due to GI AEs; and adherence measured by proportion of days covered (PDC).

Results: 433 patients were included who had previously been treated with DMF and switched to DRF. The most common reason for discontinuing DMF was due to GI AEs (37 of 89 discontinuations, 41.6%). Median (range) DRF treatment duration was 6.9 (0.6–18.6) months. 31 (7.2%) patients discontinued DRF, 15 (3.5%) due to GI AEs. Mean PDC was 90.7% (95% CI: 88.0–93.5) and proportion of patients with PDC ≥80% was 84.8% (95% CI: 81.4-88.1).

Conclusion: Of 433 patients who switched from DMF to DRF, most (>90%) were able to tolerate and persist on DRF after switching; patients also had a high rate of adherence to DRF, with low treatment discontinuation due to GI AEs.

Disclosure: Supported by Biogen.

EPO-145

The effect of smoking on long-term grey matter atrophy and clinical disability in patients with early multiple sclerosis

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Background and aims: The relationship between smoking, long-term brain atrophy and clinical disability in patients with multiple sclerosis (MS) is unclear. We aimed to assess the long-term effects of smoking by assessing MRI and clinical outcome measures after ten years in smoking and non-smoking patients with relapsing-remitting MS (RRMS).

Methods: 85 RRMS patients participating in a 10-year follow-up visit following a clinical trial were included. Smoking was defined by serum cotinine levels measured regularly for two years during the clinical trial, and by retrospective patient self-reporting. At the 10-year follow-up visit, clinical tests were repeated, and brain atrophy measures were obtained from MRI using FreeSurfer. Differences were investigated by two-sample t-tests for normally distributed variables, otherwise by Mann-Whitney U tests.

Results: After ten years, RRMS patients who smoked early in the disease course had lower deep grey matter (p=0.017) and total white matter (p=0.015) volumes and higher T2 lesion volumes (p=0.014), than non-smoking patients (Table 1a and Figure 1). Smokers had a higher score (higher walking impairment) on the timed 25-foot walk (T25FW) test (p=0.031), and a larger decrease in paced auditory serial

addition test (PASAT) (attention) scores (p=0.042) (Table 1b and Figure 2). The results were similar for smoking defined by cotinine levels and by patient self-reporting.

Table 1a MRI measures in smokers and non-smokers (defined by cotinine level) at the 10-year follow-up visit.

MRI measure	Non-smokers (mean, SD)	Smokers (mean, SD)	Mean difference	95% conf. interval	p-value
Total GM volume (mL)	643.62 (55.76)	621.83 (47.51)	21.785	-3.220, 46.791	0.087
Total WM volume (mL)	465.33 (54.98)	435.76 (42.33)	29.577	5.961, 53.192	**0.015**
Total deep GM volume (mL)	57.73 (4.98)	54.59 (5.50)	3.139	0.586, 5.691	**0.017**
Thalamus volume (mL)	8.08 (1.02)	7.67 (1.00)	0.41	-0.08, 0.90	0.096
Mean Cth (mm)	2.55 (0.13)	2.52 (0.12)	0.03	-0.03, 0.09	0.329
T2 Lesion volume (mL)	3.11 (3.07)	6.63 (9.68)			**0.014**
T2 Lesion count	19.70 (7.61)	21.62 (9.85)	-1.918	-6.115, 2.278	0.365

Table 1b Clinical measures in smokers and non-smokers (defined by cotinine level) at the 10-year follow-up visit, and change between month 24 and the 10-year follow-up visit.

Clinical measure	Non-smokers (mean, SD)	Smokers (mean, SD)	Mean difference	95% conf. interval	p-value
EDSS[1]	2.5 (1.5)	2.0 (1.6)			0.306
Change in EDSS[1]	0.5 (2.0)	0.0 (1.13)			0.505
T25FW[1]	3.88 (1.29)	4.43 (1.47)			**0.031**
Change in T25FW[1]	-0.01 (1.30)	0.31 (1.23)			0.202
D9-HPT[1]	20.02 (6.59)	21.31 (5.68)			0.167
Change in D9-HPT[1]	2.41 (3.11)	3.11 (4.65)			0.480
ND9-HPT[1]	20.68 (6.59)	23.23 (7.27)			0.130
Change in ND-9HPT[1]	3.14 (4.80)	4.08 (6.11)			0.307
PASAT	49.06 (8.40)	45.11 (10.68)	3.95	-0.43, 8.32	0.077
Change in PASAT	-3.91 (7.20)	-7.26 (6.70)	3.35	0.13, 6.57	**0.042**

[1]Difference analysed by Mann-Whitney U test, median and interquartile range reported.
Abbreviations: SD=standard deviation; conf=confidence; GM=grey matter; mL=millilitre; WM=white matter; Cth=cortical thickness; EDSS=expanded disability status scale; T25FW=timed 25-foot walk; D9-HPT=dominant hand 9-hole peg test; ND9-HPT=non-dominant hand 9-hole peg test; PASAT=paced auditory serial addition test; SDMT=symbol digit modalities test.
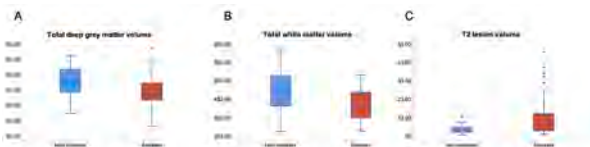
Figure 1. Boxplots illustrating the total deep GM volume (mL) (A), total WM volume (mL) (B) and total T2 lesion volume (mL) (C) in non-smokers and smokers (defined by cotinine levels) at the 10-year follow-up visit. The boxes represent the lower quartile (25th percentile), the median, and the upper quartile (75th percentile), the whiskers represent the largest observed value within the 1.5 interquartile range, measured from the lower and upper quartile.
Abbreviations: GM=grey matter; WM=white matter; mL=millilitre.
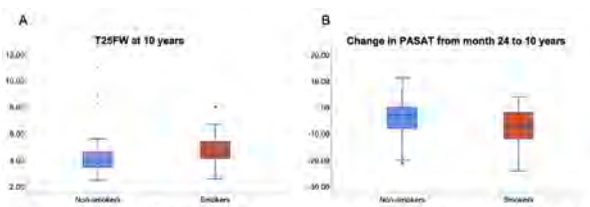
Figure 2. Boxplots illustrating the T25FW (s) at the 10-year follow-up (A) and change in in PASAT score from month 24 to the 10-year follow-up (B) in non-smokers and smokers (defined by cotinine levels). The boxes represent the lower quartile (25th percentile), the median, and the upper quartile (75th percentile), the whiskers represent the largest observed value within the 1.5 interquartile range, measured from the lower and upper quartile.
Abbreviations: T25FW=timed 25-foot walk; s=second; PASAT=paced auditory serial addition test.

Conclusion: Smoking early in the disease course was associated with lower brain tissue volumes, higher lesion load and disability accrual after ten years in RRMS patients. The findings imply that patients should be aided in smoking cessation upon diagnosis, to prevent long-term disability progression.

Disclosure: The authors of this manuscript declare no relationships with any companies, whose products or services may be related to the subject matter of the article.

EPO-146

Voxel-wise multimodal MRI reveals specific patterns of brain damage in the main multiple sclerosis phenotypes

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Background and aims: Advanced magnetic resonance imaging (MRI) techniques can be used to detect demyelination and neurodegeneration affecting gray (GM) and white matter (WM) in multiple sclerosis (MS). In this study, we applied a multimodal MRI approach to investigate in vivo the heterogeneous pathological processes occurring in the main MS clinical phenotypes.

Methods: 57 MS patients (42 relapsing-remitting [RR], 15 secondary progressive [SP]) and 47 healthy controls (HC) underwent brain 3T MRI. Voxel-wise differences of brain GM and WM atrophy, T1weighted (w)/T2w-ratio, quantitative susceptibility mapping (QSM), neurite density index (NDI) and magnetization transfer ratio (MTR) maps in the main study groups were investigated.

Results: Compared to HC, RRMS showed significantly lower MTR of posterior periventricular and infratentorial WM, deep GM and frontal cortex, widespread lower T1w/T2w-ratio, atrophy of deep GM, insular cortex and WM, widespread lower NDI in supratentorial WM and cerebellum, small GM/WM clusters with either significantly increased or decreased QSM (p<0.001). Compared to RRMS, SPMS patients showed significantly lower MTR of periventricular WM, deep GM and cerebellum, lower T1w/T2w-ratio of fronto-temporal regions, widespread cortical atrophy, widespread lower NDI of WM, increased QSM in the pallidum and striatum and increased T1w/T2w-ratio of the pallidum (p<0.001).

Conclusion: By combining advanced MRI techniques, we found that demyelination and irreversible neuro-axonal loss are already present in RRMS and become more severe and widespread in SPMS. Higher T1w/T2w-ratio and QSM in pallidum and striatum, possibly reflecting iron accumulation and neurodegeneration, may represent relevant MRI markers able to discriminate SPMS from RRMS.

Disclosure: Nothing to disclose.

EPO-147

Real-world adherence and persistence of pts with MS treated with ocrelizumab over 3 yrs: CONFIDENCE interim analysis

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Background and aims: Ocrelizumab has been approved in the EU for the treatment of relapsing MS (RMS) and primary progressive MS (PPMS) since 2018. Adherence and persistence to an effective disease-modifying therapy (DMT) is critical for achieving multiple sclerosis (MS) treatment goals. Here, we present preliminary real-world adherence and persistence data of patients with RMS and PPMS treated with ocrelizumab over 3 years.

Methods: CONFIDENCE (ML39632, EUPAS22951) is an ongoing, non-interventional, post-authorization safety study assessing patients in Germany with RMS or PPMS newly treated with ocrelizumab or other selected DMTs for up to 10 years. Persistence was assessed by time to treatment discontinuation, and patients without discontinuation were censored with their last recorded visit prior to the datacut (8 Oct 2021); adherence was assessed by median time between dosing intervals.

Results: Here, 2023 patients with RMS and 473 patients with PPMS treated with ocrelizumab and ≥1 post-initiation assessment visit were analyzed. Average baseline EDSS scores (SD) were 3.14 (1.88) and 4.43 (1.60) for patients with RMS and PPMS, respectively. Mean ocrelizumab exposure was 1.60 years for both MS phenotypes. The persistence rates for patients with RMS at one, two and three years were 95%, 91% and 89%. Patients with PPMS had one-, two- and three-year persistence rates of 93%, 88% and 86%. The median interval between doses was ~6 months for both MS phenotypes.

Conclusion: These preliminary data show that patients treated with ocrelizumab under real-world conditions demonstrated high treatment persistence over 3 years and adhered to the recommended 6-month treatment schedule.

Disclosure: The CONFIDENCE study is sponsored by Roche Pharma AG (Grenzach-Wyhlen, Germany). Ashfield MedComms GmbH (Mannheim, Germany) provided medical writing support for this abstract, funded by Roche Pharma AG.

EPO-148

Efficacy of inebilizumab in the European Union subpopulation of the N-MOmentum trial

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Background and aims: N-MOmentum was a phase 2/3 trial that assessed the efficacy and safety of inebilizumab in neuromyelitis optica spectrum disorder (NMOSD), with a 28-week randomized controlled period (RCP; 3:1 to inebilizumab 300 mg or placebo) and an optional open-label extension (OLE; >2 years; inebilizumab 300 mg every 26 weeks). This post hoc analysis reports efficacy data in European Union (EU) vs non-EU participants of N-MOmentum.

Methods: Aquaporin-4-immunoglobulin G–seropositive participants were stratified into EU (n=50; Bulgaria, Czech Republic, Estonia, Germany, Hungary and Poland) and non-EU (n=163) groups. Endpoints included NMOSD attack rates, disability-related outcomes and cumulative magnetic resonance imaging (MRI) lesion activity in the RCP and OLE.

Results: During the RCP, reduction in relapse rates was greater in those receiving inebilizumab vs placebo (EU: 12.5% [5/40] vs 30.0% [3/10]; p=0.1640; non-EU: 10.7% [13/121] vs 45.2% [[19/42]; P<0.0001). Rates of worsening Expanded Disability Status Scale score were lower in those receiving inebilizumab vs placebo (EU: 15.0% vs 30.0%, p=0.3191; non-EU: 14.9% vs 35.7%, p=0.0084). Reduction in mean (standard deviation) active MRI lesions was greater in those receiving inebilizumab vs placebo (EU: 1.11 [0.32] vs 1.33 [0.52], p=0.2612; non-EU: 1.84 [1.12] vs 2.48 [1.29], p=0.0152), as were mean NMOSD-related hospitalizations (EU: 1.0 vs 2.0, p=0.2778; non-EU: 1.0 vs 1.33, p=0.0360). There were no significant differences from baseline in low-contract visual acuity binocular scores for either subgroup. Data from the OLE will be reported.

Conclusion: Inebilizumab was associated with reduced risk of NMOSD attacks and disability in EU and non-EU cohorts of N-MOmentum.

Disclosure: Editorial assistance was provided by MedThink SciCom. This data presentation is sponsored by Horizon Therapeutics. Full author disclosures will be reported in the poster presentation.

EPO-149

Tumefactive demyelinating lesions after 2 cycles of alemtuzumab in MS. Dynamics of the immune cell populations.

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Background and aims: Paradoxical multiple sclerosis (MS) activation has been reported after alemtuzumab, but the appearance of tumefactive demyelinating lesions (TDLs) is exceptional.

Methods: We report a patient who developed TDLs 24 months after the 2nd cycle of alemtuzumab. Peripheral blood lymphocyte subpopulations were analysed using flow cytometry.

Results: A 24-year-old woman with relapsing MS (RMS) discontinued fingolimod after 2 years due to gestational desire. Two months later, she experienced severe disease activation requiring methylprednisolone and plasma exchange. Alemtuzumab was initiated. Nine months after the 1st cycle, she experienced a relapse. MRI demonstrated 12 Gd+ lesions. An increase of total B-cell and a decrease of T-cell subpopulations were observed with no changes in minor T- and B- subsets. 24 months after the 2nd cycle, she developed cognitive impairment. Brain MRI showed multiple Gd+ lesions, including TDLs. We found again an increase of B-cells, but also of CD4+ Th1 central memory. Interestingly, Th1/Th17 cells were increased 3 months before the LTDs detection. B-cell dysregulation has been associated with the pathogenic mechanism of paradoxical disease activation being the re-population a possible trigger of disease activity. CD19+CD24hiCD38hi cells have been proposed as putative biomarker of disease activation. We analysed transitional B cells but no differences were found.

Conclusion: This would be the first case describing TDLs in MS after 24 months of the 2nd cycle of alemtuzumab. The TDLs detection was associated with changes in immune cell populations being the increment of Th1/Th17 cells a candidate biomarker of TDLs in MS patients treated with alemtuzumab.

Disclosure: NRL received a training grant from Merck ("1er Concurso interhospitalario de casos clínicos para residentes de Neurología. Neurochallenge noreste").

EPO-150

Changes in lymphocytes, neutrophils and immunoglobulins in year-1 cladribine treatment in multiple sclerosis

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Background and aims: Cladribine is a nucleoside analogue, approved for the treatment of active multiple sclerosis (MS). Looking at clinical trial results, during cladribine treatment, there is a marked and long-lasting CD19 B-cell depletion and a modest T-cell depletion. Immunoglobulin (Ig) levels were never explored. In our real-world study, we evaluated changes in lymphocytes, neutrophils and immunoglobulins over the first 12 months of cladribine treatment.

Methods: This observational retrospective study has been conducted on prospectively collected data from 2018 to 2021. Clinical and laboratory data at baseline and after 2, 6 and 12 months were included.

Results: Using baseline as reference, total lymphocyte count was lower after 2, 6, and 12 months. Neutrophils were lower after 2 and 6 months, but not after 12 months. We observed no changes in IgG, IgM and IgA over 12 months. CD19 B-cell count was lower after 2 and 6 months, but not after 12 months. CD8 T-cell count was lower after 2 and 6 months, but not after 12 months. CD4 T-cell count was lower after 2, and 6 months, but not after 12 months.

Conclusion: We observed a significant decrease in total lymphocyte count from 2 months after cladribine treatment start until the end of year 1. After 12 months, we observed complete reconstitution of CD19 B-lymphocytes. Immunoglobulins remained stable over year-1 cladribine treatment that is also in line with observed normal antibody production to COVID-19 infection and vaccination in patients treated with cladribine.

Disclosure: The authors have no conflict of interest. No funds was received.

EPO-151

Fast but not furious: rapid ocrelizumab infusion for Multiple Sclerosis patients' management during COVID-19 pandemic

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Background and aims: Highly-effective disease modifying therapies, including ocrelizumab (OCR), modified Multiple Sclerosis (MS) course. COVID-19-pandemic challenges MS clinicians to be innovative in delivering therapies. We describe our experience with OCR-rapid infusions (OCR-RIs) in patients with MS (pwMS), evaluating infusion-related reactions (IRRs) and patients' experiences.

Methods: We implemented OCR-RI protocol for pwMS with prior OCR-exposure for at least one year: infusion time was reduced from 3.0 to 2.0 hours. Demographic and clinical data were collected, along with IRRs frequency, severity, treatment and patients' opinion. IRRs were categorized according to common terminology criteria for adverse events.

Results: Table 1 shows baseline characteristics of OCR-subjects (n=292). We performed 160 OCR-RIs (54.8%). None of eligible patients, that is stable pwMS with prior OCR-exposure for at least one year, declined OCR-RIs. 4/160 subjects (2.5%) experienced IRRs: throat irritation and/or headache. All IRRs occurred during infusion-time and were classified as mild. No IRRs during post-infusion observational time or post patients' discharge were reported. When IRRs occurred, infusions were temporarily stopped, physiological solution and/or symptomatic medications were given and infusions were subsequently resumed at standard velocity. All IRRs resolved and no OCR-treatment was discontinued (Table 2). Patients with IRRs were scheduled for standard-velocity infusion for the following OCR-administrations. Patients were willing to continue with OCR-RIs and found them safe and time-saving.

OCR-RI	Total, N (%) = 160 (54.8)	During infusion, N (%)	Post-infusion, (%)	N Post-discharge, N (%)	Grade	Outcome
Total - IRR	4	4	0	0	1 MILD	RESOLVED
Throat	4	4	0	0	1 MILD	RESOLVED
Headache	1	1	0	0	1 MILD	RESOLVED
Mono-symptomatic	3	3	0	0	1 MILD	RESOLVED
Multiple symptoms	1	1	0	0	1 MILD	RESOLVED

Table 2. Number and summary of IRRs during rapid infusion protocol of OCR. IRR grade was categorized according to common terminology criteria for adverse event.

Conclusion: In our cohort, IRRs frequency was reduced compared to literature (8%) (1), whereas severity and management were comparable. No severe/life-threatening IRRs were observed. In the pandemic scenario, RI protocols represents a strategy to improve patients' management.

Disclosure: CZ, CB, SG, AN: no disclosures. MAR:Bayer, Biogen, Bristol Myers Squibb, Celgene, Genzyme, Merck Serono, Novartis, Roche, Teva. LM: Merck-Serono, Novartis, Roche, Sanofi. MF: Biogen, Merck-Serono, Novartis, Teva, Roche.

Total N, (Female N, %)	292, (168, 57.5%)
Age (Y), mean ± SD (min-max)	41.9 ± 10.5 (19.9 – 69.7)
MS duration (Y), mean ± SD (min-max)	11.5 ± 8.2 (0.2 – 41.6)
EDSS, median (min-max)	3.5 (0.0 – 7.5)
MS clinical phenotype, N (%)	RRMS= 233 (79.8) PPMS= 55 (18.8) SPMS= 4 (1.4)
Treatment characteristics	Naïve, number (%) = 76 (26.0%) Switch from 1° line DMDs, number (%) = 54, (18.5%) Switch from 2° line DMDs, number (%) = 152, (52.1%) Other, number (%) = 10, (3.4%)
OCR-treatment duration (Y), mean ± SD (min-max)	2.6 ± 7.5 (0.008 – 122.1)
Rapid OCR-pwMS N, (Female N,%)	160 (87, 54.4%)
Age (Y), mean ± SD (min-max)	42.8 ± 10.3 (19.9 -69.7)
MS duration (Y), mean ± SD (min-max)	11.8 ± 7.4 (1.4 – 41.6)
EDSS, median (min-max)	3.5 (0.0 – 7.5)
MS clinical phenotype, N (%)	RRMS= 129 (80.6) SPMS= 0 (0) PPMS= 31 (19.4)
Treatment characteristics	Naïve, number (%) = 34 (21.3%) Switch from 1° line DMDs, number (%) = 26, (16.3%) Switch from 2° line DMDs, number (%) = 93, (58.1%) Other, number (%) = 7, (4.4%)
N. Rapid OCR- infusions, mean ± SD (min-max)	2.1 ± 0.6 (1.0 -4.0)

Table 1. Demographic and clinical characteristics of population at baseline.

EPO-152

Potential Role of Arginine as a Biomarker of Acute Inflammatory Process in Multiple Sclerosis

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Background and aims: Multiple sclerosis (MS) is a chronic autoimmune disease of the central nervous system (CNS). L-arginine plays an important role as precursor of neurotransmitter of nitrite oxide (NO), which has a potential role in the pathogenesis of MS. At the sites of inflammation, the NO is produced in high concentrations, thus arginine could be lowered. The aim of this study was to verify changes in levels of arginine in cerebrospinal fluid (CSF) of patients in early stages of MS.

Methods: We have collected CSF of 19 patients (16 females, aged 19–55 years) with newly diagnosed MS and CSF of 19 healthy controls (16 females, aged 19-55 years). CSF samples were analysed using HPLC-MS/MS method in ESI+ and –mode. Data were processed with AB Sciex software. Further, the results were processed with Metaboanalyst database and verified by targeted analysis with analytical standards. Verified results were compared between the both groups.

Results: In patients in early phases of MS with no specific or corticosteroid treatments the levels of arginine were significantly decreased in CSF in comparison to healthy controls.

Conclusion: The decreased levels of arginine in CSF in the early stages of MS can be a potential biomarker of ongoing inflammation in MS. Further analysis is necessary.

Disclosure: Supported by University Hospital Královské Vinohrady, GAUK and project COOPERATIO of Charles University.

Muscle and neuromuscular junction disorder 1

EPO-153

DOK7-associated congenital myasthenic syndrome: a differential diagnosis of core myopathies?

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Background and aims: DOK7 is a postsynaptic protein associated with acetylcholine receptor clustering pathway. DOK7 mutations lead to a defective protein production, causing neuromuscular transmission failure. DOK7 mutations accounts for 10–15% of all Congenital Myasthenic Syndromes (CMS) and although its clinical picture may be diverse, most patients display a limb-girdle pattern of weakness and ptosis without ophthalmoparesis.

Methods: To present a clinical case of a DOK7-associated congenital myasthenic syndrome with core-like areas on muscle biopsy.

Results: 22-year-old male presented with a 3-year-history of progressive proximal limb weakness. Despite an unremarkable medical history, he reported difficulty running as a child. There was no family history of consanguinity or neuromuscular disease. Neurological examination disclosed bilateral facial weakness without ptosis or opthalmoparesis, bilateral sternocleidomastoid muscle atrophy, upper limb and proximal predominant proximodistal tetraparesis (G2-3/5UL G4/5LL), mild waddling gait and no myotonia. Needle electromyography revealed myopathic potentials in the muscles studied and muscle biopsy was myopathic, with type-2 fibre atrophy and core-like areas. Genetic study identified a DOK7 gene mutationc.1124_1127dupTGCC (p.(Ala378Serfs*30)). Repetitive nerve stimulation showed a >10% decrement in spinal accessory nerve. The patient started salbutamol with significant clinical improvement.
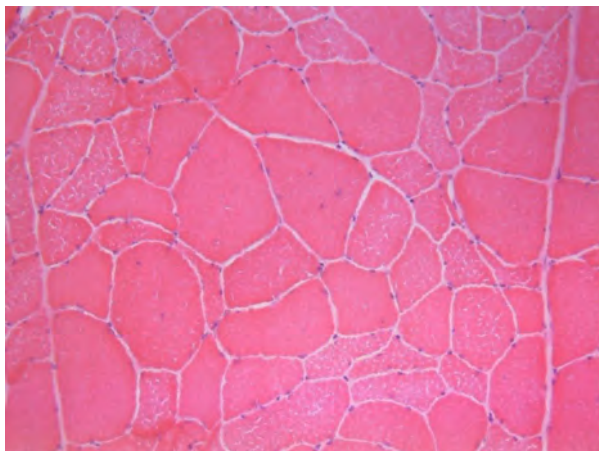
Muscle biopsy (haematein-eosin, 200x)

Conclusion: Core myopathies are clinically, pathologically, and genetically heterogeneous muscle diseases and are an important differential diagnosis of limb-girdle CMS. Biopsy results may be misleading in cases like the one we present. There are scarce reports of core-like areas in muscle biopsy of patients with DOK7 mutations and their pathogenesis in CMS is unknown. It may be necessary to include DOK7 mutations in the differential diagnosis of core myopathies.
Disclosure: Nothing to disclose.

EPO-154

Clinical aspects of Myopathy in HIV infection: female sex and forearms involvement as predictive factors

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Background and aims: The involvement of the central and peripheral nervous system is frequent in HIV infection. Myopathy related to HIV has a heterogeneous spectrum of muscle injury and is often subclinical and consequently underdiagnosed. The present study sought to investigate the prevalence of clinical aspects of myopathy and describes the pattern and severity of muscle involvement among HIV-infected patients admitted to a tertiary referral center.

Methods: A census, cross-sectional, and analytical study was conducted in southern Brazil. A total of 144 patients hospitalized between February 2019 and February 2020 were interviewed and submitted to physical examination and dynamometry of the limbs.

Results: The prevalence of clinical findings of myopathy was 11.1%, and it was associated with female sex (OR=6.9; 95% CI=2.2 to 21.3; p<0.01). The circumference ≤20 cm (adjusted OR=7.4; 95% CI=1.4 to 37; p=0.02) and dynamometry ≤ 18Kgf (adjusted OR=7.4; 95% CI=0.9 to 62.4; p=0.07) of forearms were found as possible predictive factors of myopathy.

Conclusion: The prevalence of clinical aspects of myopathy in HIV-infected patients is notable and associated with the female sex. Patients with myopathy symptoms showed diffuse damage to muscle groups, especially in the forearms. Further studies are warranted to evaluate the relationship between physical examination data and the histopathologic confirmation of HIV myopathy.
Disclosure: Nothing to disclose.

EPO-155

Adults living with Duchenne Muscular Dystrophy: emerging challenges in 14 patients in their fourth and fifth decade.

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Background and aims: Improvements of multidisciplinary treatments are prolonging the life expectancy of DMD patients, yet unveiling new clinical challenges.

Methods: We present a single-centre cohort of DMD patients aging >30 years to describe specific clinical features and possibly underrated domains.

Results: In a population of 40 adult DMD patients, we selected 14 cases aging 30–48 years (mean 36.57+5.6), all with a confirmed diagnosis of absence of dystrophin in muscle biopsy and/or out-of-frame gene mutation. All of them but three were home-assisted. In most cases we observed a severe cardiomyopathy, with only 3/14 showing an EF% >55%; 5/14 were ventilated via tracheostomy; 8/14 via NIV 18–24h; 1/14 nocturnal NIV only; all of them had feeding complications (5/14 via PEG or via J-tube; 9/14 adapted per os nutrition). We also observed a high frequency of severe generalized pain (9/14), 3 of them using opioids with/without acetaminophen/NSAIDs; 2 patients manifested generalized epileptic seizures; psychiatric disorders were frequently observed (8/14 ranging from anxiety, depression, panic attacks, OCD, psychosis and ASD). 2/14 were on daily prednisone for >15 years; other few patients had been on therapy for some years, often not regularly and following varying dosages, mostly due to limiting adverse effects.

Conclusion: A complex clinical scenario of long-living DMD patients is emerging, with multi-system complications requiring careful monitoring and complex management. New issues are encountered, such as severe pain and psychiatric disorders, still lacking of safety data about drug therapies. Moreover, the family burden has dramatically increased in this growing DMD population.

Disclosure: Nothing to disclose.

EPO-156

Acoustic analysis of speech in patients with neuromuscular diseases (NMD): results of the study

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Background and aims: Bulbar disorders are found in many neuromuscular diseases. The development of analytical methods can simplify and standardize the assessment of dysarthria in patients with bulbar disorders. Aim. Evaluate the results of a persistent vowel phonation test to detect dysarthria associated with bulbar disorders.

Methods: Voice recordings of 83 people were analyzed (41 healthy controls - 23 men, 18 women, the average age 41.9 years; 42 patients with NMD: of them 22 patients with ALS (7 men, 15 women) and 20 patients with other NMD (SMA, MG) - 8 men, 12 women), the average age 57.3 years. Bulbar disorders were detected in 18 (21%) patients. We have developed a prototype of a mobile application with the ability to record, process voice and display the results of voice analysis. As a speech probe, a lingering pronunciation of the vowel sound /a/ is used, from which acoustic signs are extracted (trembling, flickering, the degree of pathology of vibrato, etc.). The result of the application is the values of the acoustic parameters.

Results: High levels of accuracy of 90.4%, sensitivity of 83.3% and specificity of 92.3% of the method of using acoustic analysis of the speech signal in patients with NMD were found. The results obtained indicate that the acoustic analysis of the voice and the obtained objective parameters are a promising direction for solving this problem.

Conclusion: The developed method can be used to assess the state of voice function in patients with bulbar disorders. This method will improve diagnostics and help prevent aspiration complications.

Disclosure: Nothing to disclosure.

EPO-157

Acute flaccid quadriparesis due to hyperkalemia without significant cardiological changes or renal failure

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Background and aims: The differential diagnosis of rapidly progressive quadriparesis includes muscle membrane disorders that can be caused by severe electrolyte imbalances, mainly hypo or hyperkalemia. We aim to present a case that reminds neurologists of this possibility in the emergency room (ER).

Methods: Description of a clinical case.

Results: An 80-year-old woman with past medical history of hypertension treated with spironolactone, an angiotensin receptor blocker, and a beta-blocker, diabetes with polyneuropathy treated with metformin and auricular fibrillation treated with acenocumarol presented to the ER with weakness of all extremities. She had fallen to the floor the previous day and referred an episode of urinary incontinence. Physical exam was significant for a blood pressure of 97/45 mmHg and tachypnea. Neurological exam showed an MRC grade 0-1 in all extremities and with neck flexion, absent reflexes, hypoesthesia in all extremities and trunk. Initial bloodwork revealed a severe metabolic acidosis (pH 6.95), a potassium of 9.3 mEq/L, creatinine 181.26 umol/L, and CK was 604 U/L. ECG showed auricular fibrillation with peaked T waves. A body-CT with contrast showed no signs of cervical spinal trauma or acute thoracic syndrome. Immediate measures to lower potassium were initiated (IV bicarbonate, insulin, and salbutamol) followed by hemodialysis. The patient quickly recovered and showed normal muscle force with a control potassium the following day of 5.54 mEq/L.

Conclusion: Electrolyte disturbances are associated with a myriad of neurological symptoms and signs. Hyperkalemia is mainly associated with cardiological complications, but muscular weakness is also common and can be severe.

Disclosure: Authors have no clonficts of interest to disclose.

EPO-158

Rituximab for the treatment of late-onset generalized and refractory myasthenia gravis

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Background and aims: Myasthenia gravis (MG) is considered refractory in 20% of cases. Rituximab has been used "off-label" in refractory cases, particularly in young-onset patients with anti-MuSK antibodies. Our aim is to describe and analyse the efficacy and safety of rituximab for the treatment of late-onset generalized and refractory MG patients.

Methods: A monocentric, retrospective and cross-sectional study included late-onset generalized and refractory MG patients followed in our centre between January 2012 and August 2021. Demographic and clinical profiles were evaluated, and response to rituximab treatment was assessed using the Myasthenia Gravis Foundation of America (MGFA) score.

Results: Four patients [3 men; mean age 62.5±4.7 years (49–61)] were included. Mean onset age was 57.3±4.6 years (51–63), and mean disease duration was 4.75±2.86 years (1–8). All patients had bulbar and axial symptoms as well as serum anti-AChR antibodies. Thoracic CT revealed thymic pathology in 2 patients (50%), having both been timectomized. Baseline MGFA score was between IIIA and IVB and, after a mean of 134±139,54 weeks (4–354), there was a sustained clinical improvement, with MGFA score between I and IIIB. One patient developed pneumocystosis, 4 weeks following treatment starting.

Conclusion: Rituximab treatment appears to be effective in late-onset generalized and refractory MG with serum anti-AChR antibodies. However, potential side effects related to chronic immunosuppression should be considered, particularly in older ones. Further studies are needed to assess the efficacy and safety of rituximab in this age group.

Disclosure: Nothing to disclose.

EPO-159

An atypical case of periodic paralysis with an unreported mutation in the CACNA1S gene

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Background and aims: CACNA1S gene mutations are known to be associated with malignant hyperthermia, thyrotoxic periodic paralysis, hypokalemic periodic paralysis, and congenital myopathy, but not with myotonia.
Methods: We studied the case of a patient with overlapping episodic weakness and stiffness by medical history, neurological examination, laboratories, electrophysiology, MRI and genetic analysis.
Results: A 21-year-old man disclosed at age 14 years episodes of painful muscle stiffness immediately after exercise, first in the upper limbs which spread to the legs and trunk muscles, after a few months, while neck and head were spread. After two years he began to experience episodes of severe generalized weakness (lasting several hours), more common in cold weather, the day after hard labor, sometimes after a carbohydrate-rich meal. Interictal neurologic examination showed hyperreflexia, exercise induced paradoxical myotonia and fasciculations, there was no evidence of weakness at rest. CPK, thyroid hormones and serum electrolytes levels were normal at rest, while hypokalemia appeared at maximum effort during cycloergometry. Autoimmune disorders were excluded. EMG revealed spontaneous activity at multiple sites but not myotonia at rest which appeared after exercise test. Brain and spine MRI was normal. NGS analysis demonstrated a novel missense variant in CACNA1S p.Arg557Cys (c.1669 C>T, of uncertain pathological significance at bioinformatic analysis; segregation analysis found the same variant in the patient's mother, who reported a similar clinical picture, pointed to its likely pathogenicity.
Conclusion: We report on a novel likely pathogenic mutation of CACNA1S, associated with a clinical phenotype combining paradoxical myotonia and hypokalemic periodic paralysis.
Disclosure: Nothing to disclose.

EPO-160

Oculopharyngeal muscular dystrophy in Sesimbra Municipality: first known cluster in Portugal

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Background and aims: Oculopharyngeal muscular dystrophy (OPMD) is globally rare, but there's clusters of higher prevalence. It's the most frequent muscular disease in our Neuromuscular outpatient clinics.
Methods: Demographic, clinical and laboratory data were retrospectively collected from OPMD patients followed at our institution since May 2017.
Results: We follow 16 patients, 8 men, median age 71 years (49–79). All but one were from the municipality of Sesimbra. All have positive family history. 70% have the GCN-10/13 genotype and 30% the GCN-10/14 genotype. The median age of clinical presentation was 52 years (40-73). The most prevalent initial symptom was eyelid ptosis (62.5%), followed by dysphagia (25%) and proximal weakness of the lower limbs (12.5%). All patients developed eyelid ptosis and dysphagia (median age at presentation 55 and 58 years, respectively). Nine patients underwent blepharoplasty (56.3%). Two patients (12.5%) placed percutaneous endoscopic gastrostomy (PEG). Most patients have paraparesis (87.5%), with a median age of presentation of 65 years. Other symptoms present were proximal limb weakness superiors (31.3%), dysphonia (56.3%), fatigue (31.3%), sialorrhea (18.7%). Of the patients with CK assay (50%), it ranged between 111 and 746 IU/L. Six patients underwent EMG (37.5%), that revealed a myopathic pattern in all, and only one had a muscle biopsy.
Conclusion: In our series, the high prevalence of paraparesis may be due to a referral bias or to specific epigenetic or environmental factors of this population. We estimate that the prevalence of this disease in Sesimbra is possibly higher than 1:1000.
Disclosure: There are no conflict(s) of interest that may have a direct bearing on the subject matter. This research didn't have any commercial or institutional support.

EPO-161

Eyelid neuromyotonia in a patient with Myasthenia Gravis

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Background and aims: Neuromyotonia is part of a spectrum of peripheral nerve hyperexcitability syndromes and is characterized by continuous and spontaneous muscle activity, which can be manifested in the form of myokymia, fasciculations, cramps and pseudomyotonia. It usually has an acquired etiology, and it is typically associated with autoimmune diseases, particularly Myasthenia Gravis.

Methods: A 59-year-old female with history of hypertension, atrial fibrillation, glaucoma and chorioretinopathy, presented in 2018 fluctuating episodes of ptosis and diplopia. Anti-acetylcholine receptor antibody was detected, and she was diagnosed with Ocular Myasthenia Gravis. Thymoma was excluded. In 2019 she developed generalized muscle weakness, requiring treatment with intravenous immunoglobulin. During hospitalization, the patient reported that sometimes she had involuntary contractions of the right eyelid and difficulty performing fast and complete eye opening, particularly after a vigorous eye closure. On neurological examination, she presented myotonia of the orbicularis oculi bilaterally, more evident on the right and with a "warm-up" phenomenon. EMG did not detect myotonic or neuromyotonic discharges but identified fasciculations and myokymia. Anti-VGKC antibody screening was positive and she was started on carbamazepine which resulted in a sustained symptom remission.
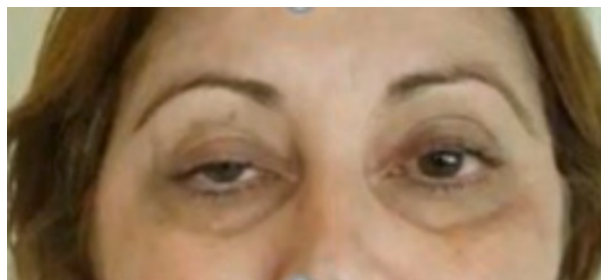
Patient showing difficulty performing complete eye opening after a vigorous eye closure, particularly on the right

Results: N/A

Conclusion: We herein report a case of eyelid neuromyotonia in a patient with Myasthenia Gravis without thymoma. The coexistence of this syndrome with Myasthenia Gravis can represent a diagnostic challenge, mainly due to the need to distinguish eyelid neuromyotonia from myasthenic eyelid ptosis. We intend to highlight the importance of recognizing these subtle symptoms, as they require specific pharmacological treatment.

Disclosure: Nothing to disclose.

EPO-162

Management of Lambert-Eaton Myasthenic Syndrome in the context of immunecheckpoint-inhibitor treatment - A Case Report

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Background and aims: Lambert-Eaton-Myasthenic Syndrome is considered the most common paraneoplastic disease in neurological patients. With increasing usage of cancer immunotherapy, the prevalence of immunotherapy-related-neurological adverse events (irNAE) is rising.
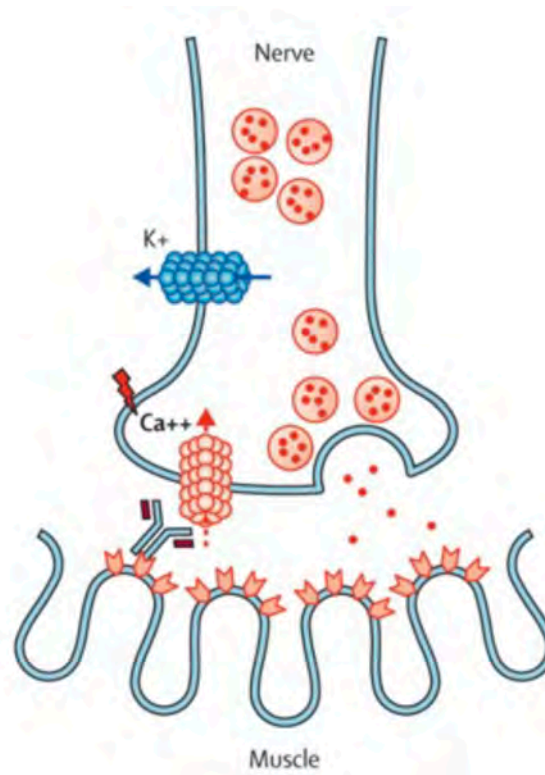
(1) In LEMS antibodies against presynaptic voltage-gated calcium channels reduce the influx of calcium and therefore the release of acetylcholine in the neuromuscular junction.

Methods: A 61-year old male presented with muscular weakness in the extremities for two months.. He did not recognize a worsening during day and had no further symptoms.

Results: Initial neurological examination disclosed no pathological findings. Electrodiagnostic studies (EDX) revealed a decrement after repetitive nerve stimulation and an increment after maximal muscle contraction. Electromyography was unremarkable, CK was slightly

elevated. Acetylcholine receptor antibodies were normal, anti-voltage gated calcium channel antibodies (VGCC-Ab) were elevated, anti-SOX-1-Ab were positive. This led to the diagnosis of a LEMS. Positive SOX-1-Ab were suspicious of paraneoplastic origin. A chest-CT-scan led to the diagnosis of a SCLC. Chemotherapy and adjuvant thoracic irradiation was initiated. The patient improved and staging disclosed partial remission. Under maintenance therapy with the anti-PDL-1 immune checkpoint inhibitor (ICI) Atezolizumab muscular weakness recurred. Neurological examination showed proximal paraparesis, reflexes showed facilitation despite a decrease of VGCC-Ab as a result of tumor-specific therapy. A symptomatic therapy with 3,4 Aminopyridine was initiated, Atezolizumab was discontinued.

(2) Electrophysiological studies support the diagnosis of LEMS: Ulnar motor study recording the ADM muscle at rest (2a) and after brief maximal exercise with facilitation of the CMAP (2b).
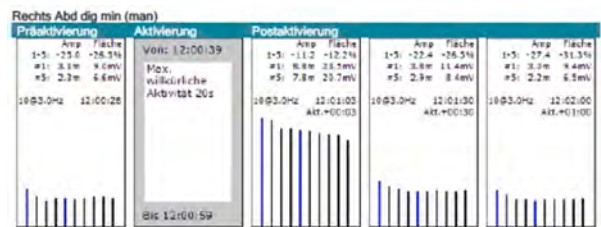
(3) Repetitive Nerve Stimulation (RNS) with the pathognomonic decrement-increment pattern for LEMS. Any decrement >10% comparing the first and fifth CMAP amplitude and an increment >40% after brief maximal exercise are abnormal.

Conclusion: Beside tumor-specific therapy being the treatment of choice, modern oncology offers the possibility of ICI-therapy. Downside of treatment is a high rate of severe autoimmune phenomena. In our case, even a single course of Atezolizumab lead to clinical relevant exacerbation. Pro and cons of this therapeutic dilemma and possible management options are discussed.
Disclosure: Nothing to disclose.

EPO-163

Myasthenia gravis treated in the neurology intensive care unit: a 14-year single centre experience

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Background and aims: Severe myasthenia gravis (MG) exacerbation with respiratory failure and/or dysphagia usually require monitoring and treatment in the Neurology Intensive Care Unit (NICU). The aim of our study was to identify all patients with severe MG exacerbation treated in the NICU in order to assessed potential factors affecting patients' need for mechanical ventilation, occurrence of complications and the final outcome.
Methods: We retrospectively included all patients with severe exacerbation of MG who required management in the NICU during a 14-year period. Baseline sociodemographic and clinical features, data on medication, comorbidities, and outcome were obtained by reviewing medical records and institutional databases.
Results: Our study comprised 130 severe MG exacerbations detected in 118 patients. Median age of patients was 61.5 years and women accounted for 58.5% of the patients. Half of the patients required mechanical ventilation during hospitalization. Lethal outcome was observed in 12.3% of severe MG exacerbations. Only elder age was an independent negative predictor of survival (OR 0.89, 95% CI 0.82–0.97, p<0.01). Complications during hospitalization were detected in 50% of patients. A higher number of comorbidities (OR 1.09, 95% CI 1.60–2.35, p=0.01) and mechanical ventilation (OR 28.48, 95% CI 8.56–94.81, p<0.01) were independent predictors of complications during hospitalization.
Conclusion: Patients with a severe MG exacerbation who do not require mechanical ventilation have a good outcome after treatment in the NICU. Elder age is an independent predictor of lethal outcome in patients with severe MG exacerbation. Mechanical ventilation and a higher number of comorbidities lead to more frequent complications.
Disclosure: Nothing to disclose.

Neuroepidemiology

EPO-164

The correlation between acute symptomatic post stroke seizures in children and the risk of developing epilepsy

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Background and aims: Stroke occurs in an estimated 3.8 per 100,000 children annually, and is an important cause of childhood brain injury and epilepsy. Estimation of seizure incidence after childhood stroke vary widely, in part due to variation in study referral populations and limitations of scope, sample size and length of follow-up, but the clinical features and effects on the outcome of early-onset seizures have not been studied enough.

Methods: The study included age groupe of children 1 month-18 years old, who were hospitalized in the Neurology Department and IMSP Mother and Child Institute and selected according to the presents of neurological symptoms especially those who associated seizures and epilepsy, presenting with first-time and image-confirmed arterial ischemic stroke.

Results: A total of 78 survivors of arterial ischemic stroke were enrolled. 20 (25.6%) had early-onset seizures, and 90% were initial presentation. Younger children (mean, 3.4±3.9 versus 9.0±6.2 years; p<0.001) and cortical involvement (5% versus 63.8%; p=0.01) are more likely to have early-onset seizures. 13 of 20 survivors with early-onset seizures had late-onset seizures after the acute stage, and 12 of them were diagnosed as poststroke epilepsy.

Conclusion: Children frequently develop remote seizures and epilepsy after a stroke, and clinical factors such as age, stroke type, stroke location and acute seizures at the time of stroke affect their risk. Early-onset seizures occurred in 25.6% of children with arterial ischemic stroke. Young age and cortical involvement were risk factors for early-onset seizures, 65% of children with early-onset seizures develop later on seizures after the acute stage.

Disclosure: Nothing to disclose.

EPO-165

Door to CT Scan time delay is related to delayed time of arrival in stroke patients

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Background and aims: Delay in hospital admission after stroke is the first obstacle to develop correctly care and acute therapy, The aim of this study was to describe delay in hospital admission of patients with stroke subtypes and association with door to computed tomography (CT) scan time.

Methods: We conducted a retrospective, single-center study in México City. We included electronic medical files of patients with stroke admitted to ER from January 2019 to October 2021. Patients were allocated in 2 groups: early arrival time and late arrival time (more or less than 3 hours). Demographic, radiological, and clinical variables were obtained.

Results: We enrolled 410 patients with baseline characteristics described in Table 1. The median admission delay was 283 minutes (140–506). 383 (93.4%) patients were admitted within 24 h. CVT was the stroke subtype with more time delayed. Statistical analysis showed that delay in hospital admission >3 hours increase the risk (OR 2.1, CI 95% 1.37–3.3) of delay in door to CT scan time (p=0.001). There was not association with other variables (Table 2).

Table 1. Baseline characteristics of 410 patients included in this study

Variable	No cases	%
Mean age (SD) 63.3 (16.7)		
Female	217	52.9
Diabetes	140	34.1
Hypertension	233	56.8
Dyslipidemia	24	5.9
AF	36	8.8
Smoking	57	13.9
Stroke subtype		
TIA	49	12
IS	154	37.6
ICH	56	13.7
SAH	130	31.7
CVT	21	5.1
Recurrent stroke	38	9.3

Table 1. Baseline characteristics of 410 patients included in this study

Table 2. Clinical patterns and stroke subtypes of 410 included in this study

Variable	Arrival time ≤ 3 h n= 138	Arrival time > 3 h n= 272	p value
Years, mean (SD)	64.8 (16.6)	62.6 (16.7)	0.21**
Sex, female (%)	80 (58)	137 (50)	0.14*
NIHSS >10, n (%)	57 (41)	110 (40)	0.86*
Stroke subtype			
TIA, n (%)	22 (16)	27 (10)	0.076*
IS, n (%).	51 (37)	103 (38)	0.85*
ICH, n (%)	16 (11)	40 (15)	0.38*
SAH, n (%)	7 (58)	5 (63)	1.0*
CVT, n (%)	2 (1)	19 (7)	0.016*
Stroke onset	4 (33)	5 (63)	0.43*
Morning, n (%)	39 (28)	71 (26)	
Afternoon, n (%)	61 (44)	109 (40)	
Night, n (%)	38 (28)	92 (34)	

* Chi square test
** t student te

Table 2. Clinical patterns and stroke subtypes of 410 included in this study

Conclusion: There was association between admission delay in stroke patients and door to CT scan time delay. There is a considerable admission delay in CVT in comparison with arterial stroke subtypes.

Disclosure: Centro Medico Nacional Siglo XXI, Neurology department To present the casuistry of stroke in a third level hospital in Mexico.

EPO-166

Modifiable risk factors for cerebrovascular disease in patients aged 40-65 in Poland, Podlasie province.

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Background and aims: Searching for modifiable risk factors and their elimination is crucial for prevention of cerebrovascular diseases. The aim of our study was to analyze the modifiable risk factors of cerebrovascular diseaeses in patients examined under the prevention program.

Methods: We enrolled 120 patients (56 males and 54 females) in the age range 40–65, which were referred to our neurological outpatient clinic in 2019 by a primary care physician, without history of cerebrovascular event. Patients had physical and subjective examination, full lipidogram, glucose concentration, heart echo, usg carotid and vertebral arteries, CT scan of the head and 24 hours ekg holter monitoring.

Results: The most common risk factors was hyperlipidemia (86.7%), next was high body mass index (BMI) and abdominal obesity (80%), hypertension (75.8%) (50% had poorly controlled hypertension), atherosclerosis 58.3% (14.3% had significant stenosis), diabetes 17,5%, atrial fibrillation 4.2%, PFO (2.5%), ASD II (0.8%). No physical activity was found in 67.5%, smoking in 24.2%, 73.3% population used alcohol (8.3% more than once a week), recommended daily consumption of vegetable and fruit was declared by 7% of respondents, 65% used sweet fizzy drinks. Has also been shown that male gender predisposes to the development of atherosclerotic lesions in the carotid arteries and fasting glucose supplementation, female gender to abdominal obesity and low HDL concentration.

Conclusion: Modifiable risk factors for cerebrovascular disease, such as dyslipidemia, smoking and hypertension are highly prevalent in the population age 40-65. Preventive programs are important in primary prevention of cerebrovascular disease.

Disclosure: Nothing to disclose.

EPO-167

Consequences of surgeries suspension during the pandemic to brain tumor diagnosis and mortality in a developing country

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Background and aims: In the scenario of crisis in the Brazilian health system, one of the measures taken to optimize resources and reduce the hospital transmission rate was the suspension of elective surgeries. Therefore, it is important to analyze the effect of canceling this treatment modality on the diagnosis and mortality from malignant brain tumors.

Methods: A cross-sectional quantitative study was carried out using the open database of the Brazilian Ministry of Health (DATASUS) and the IBM SPSS statistical software. The information regarding the detailed diagnosis and the mortality rate concerning malignant brain tumors from January 2016 to November 2021 were analyzed.

Results: A mean annual mortality rate of 169.1 and several 2,969.6 diagnoses were observed between July 2016 and July 2019, while in 2020 the mortality rate was 3.5% lower and the diagnostic rate 12, 4% higher. For 2021, 14% and 17.5% were observed for both variables, respectively. The p-value for comparing the mortality rate from January to July 2021 compared to the same period in 2019 resulted in 0.99966.
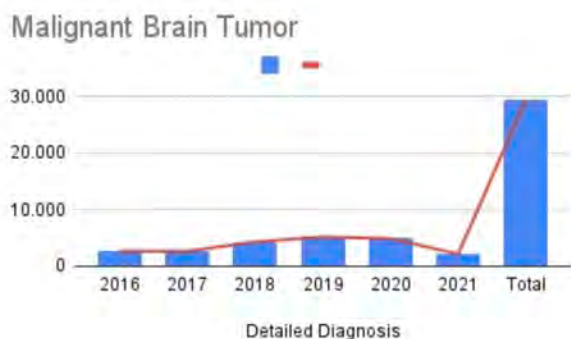
Detailed diagnosis of malignant brain tumors from 2016 to 2021 in Brazil.

The mortality rate of malignant brain tumors from 2016 to 2021 in Brazil.

Conclusion: According to the analysis, there was an increase in the number of diagnoses of malignant brain tumors during the pandemic period, with the mortality rate increasing only in 2021. However, the calculated p-value (p = 0.99966) pointed to an irrelevance between the numerical differences described, and it is not possible to conclude that there is an association between suspensions and the number of diagnoses and deaths.

Disclosure: The authors report no conflict of interest.

EPO-168

Neurologic Syndromes and mortality in COVID-19

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B. Labella [1], G. Ceccardi [1], M. Toffali [1], D. Arici [1],
A. Lupini [1], I. Libri [1], M. Giunta [1], M. Di Cesare [1],
M. Bolchini [1], V. Mazzoleni [1], D. Pezzini [1], B. Risi [1],
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Background and aims: Neurological syndromes have been reported in Severe-acute-respiratory-syndrome-coronavirus2(SarsCov2) infection. However, the association between neurological syndromes and COVID-19 outcomes need further investigations. The aim of this study was to assess whether neurologic manifestations are associated with COVID-19 severity and inpatient mortality.

Methods: The study prospectively included patients with documented Sars-Cov2 infection admitted to Brescia Hospital between February 2020-October 2021. Sociodemographic variables, preexisting comorbidities and presence of neurologic manifestations were evaluated as potential factors associated with COVID-19 severity and in-hospital mortality.

Results: A total of 1,672 patients were analyzed including 405 (24%) with neurological manifestations. The most common diagnosis were cerebrovascular diseases (n=123), delirium or encephalopathies (n=98) and seizures (n=41). The presence of any neurological manifestation was significantly associated with less severe COVID-19, expressed as Brescia-COVID-Respiratory-Severity-Scale(BCRSS) >2 (OR 0.45, p <0.001), need of any oxygen supply (OR 0.35, p <0.001) or need of Non Invasive Ventilation(NIV)/Invasive Ventilation(IV) (OR 0.64, p=0.026). Conversely, neurological patients exhibited a higher rate of in-hospital mortality at univariate analysis (17% vs 12%, p=0.007). This association was not confirmed at multivariate analysis including age, premorbid conditions and severity of COVID-19 (OR 0.85, p 0.52). In diagnosis-specific analyses, cerebrovascular diseases were associated with higher risk of in-hospital mortality independently from premorbid conditions and severity of COVID-19 (OR 3.83, p=0.03).

Conclusion: Neurological manifestations appeared to be associated with less severe COVID-19 disease and does not impact in-hospital mortality when adjusted for the effect of age, premorbid conditions and COVID-19 severity. Conversely, cerebrovascular diseases were specifically associated with higher risk of mortality.

Disclosure: Nothing to disclose.

EPO-169

Clinical Manifestations and Outcomes of Toxoplasma Encephalitis as the Initial Presentation of Patients with AIDS

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Background and aims: The aim of the study is to profile, evaluate and describe the clinical manifestations and outcomes of toxoplasma encephalitis as initial manifestation of Acquired Immune Deficiency Syndrome.

Methods: This is a prospective cohort study that profiled patients with toxoplasma encephalitis at presentation and are newly diagnosed with Acquired immune Deficiency syndrome between January 2019 – December 2020.

Results: There were 45 patients who presented with central nervous system infection and 11 patients were seen to satisfy the inclusion criteria and were not excluded in the study. The study shows that toxoplasma encephalitis can be the only OI present among patients with AIDS. The most common non-focal neurological presentation in 10 (90%) patients was headache and 7 (64%) patients confusion/psychotic disturbances Focal neurological manifestation is motor weakness which was the most common presentation. Patients had improved MRS scores after 2 weeks of discharge. Patients discharged with MRS 4 and 5 still had the same MRS score. After 6 months of follow-up, the patient`s MRS score improved. The study shows that those with lower MRS scores 2 and below had better outcomes.

Conclusion: Good outcomes were seen with more than 2 weeks treatment and hospitalization within 3 weeks. Those with poor MRS on admission and discharge had poorer outcome. Those who completed Cotrimoxazole treatment and started on antiretroviral therapy were seen to have improvement in MRS within 6 months.

Disclosure: Financial support: None. Nothing to disclose.

EPO-170

Challenges Faced By Neurophysiotherapist While Consultation Through Tele-rehabilitation – A Cross Sectional Study

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Background and aims: The COVID-19 pandemic has up-stretched a lot of constraints for both neuro-physiotherapists (NeuroPT) and their clients. Majority of the NeuroPT have been shifted towards tele-consultation mode for their client's consultations and monitoring purposes. The current study intended to explore the various challenges faced by the Indian neuro-physiotherapists, during their tele-consultation sessions with their clients.

Methods: A self-structured and validated questionnaire having a reliability of (Cronbach's alpha) – 0.9 were used in which 17 questions framed to obtain responses from the NeuroPT and these primarily constructed to explore challenges faced by neurophysiotherapist during consultations of their clients. The domains were-Satisfaction, Time-constraints, Handiness and Cost-effectiveness of Tele-rehabilitation mode over traditional way of consultations.

Results: The responses obtained through this cross-sectional survey point out that the major challenges faced by NeuroPT are that, tele-rehabilitation is not a better option over orthodox consultations as their clients were not able to define their health condition accurately. In contrast to this, about 85% of NeuroPT agreed on the point that this mode is beneficial and very much cost-effective.

Conclusion: The prominent challenges reported by NeuroPT's were time-consuming process, poor satisfaction and description of their health condition percentiles and network issues.

Disclosure: Nothing to disclose.

EPO-171

A population-based study on incidence and prevalence of Multiple Sclerosis inthe Province of Palermo, Sicily.

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Background and aims: Recent studies on Incidence and prevalence of Multiple Sclerosis (MS) indicate increasing trends of disease frequency, but updated large population-based studies in Sicily are lacking.

Methods: MS incidence had been previously investigated in several Sicilian municipality by multi source methodology. In the present study, we investigated MS frequency in the Province of Palermo at June 30th 2018 (prevalence day) in a population of 1,252,588 inhabitants. Incidence rates were calculate for the period 2000–2018 (18,875,588 person/years). We obtained clinical and demographical data for each patient by MS clinics and centers in the study area, by Hospital and Neurological Departments and by general practitioners. We calculated Age and sex specific onset adjusted prevalence and incidence rates with 95% confidence intervals.

Results: Crude onset adjusted prevalence was 169.9/100,000 inhabitants (95% CI 161.7–177.1), it was 114.5 in men and 221.8 in women (W:M ratio 1.94), with a peak of nearly 300/100,000 in the age classes between 35 and 45 years of age. Mean annual incidence rates were 6.3/100.000 inhabitants (95% CI 6.0–6.7) for the whole population, with a peak of 13.8/100,000 in the age class between 25 and 29 year of age. Incidence was 4.1/100,000 in men (95% CI 3.7–4.5) and 8.5/100,000 (95% CI 8.0–9.1) in women.

Conclusion: This is the largest population-based study performed in Sicily. The present study revealed Prevalence and incidence rates considerably higher compared to all previous studies performed in the same area, and within the highest among other studies performed in the mediterranean area.

Disclosure: Dr Ragonese received research funding by Almirall and Roche; he also received travel grants and honoraria for speaking by: Biogen, Genzyme Sanofi, Merck, Novartis, Roche.

EPO-172

Overview of rabies virus infections in Brazil over 14 years

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Background and aims: Rabies is an infectious disease caused by a virus of the Rhabdoviridae family capable of causing serious complications in the Central Nervous System. Our objective is to analyze the panorama of this disease in Brazil.

Methods: The temporal analysis was based on the historical series of monthly hospitalizations for rabies (RD) (ICD-10: A82) in Brazil from November 2007 to November 2021, based on data from the Hospitals' Information System of the Unified Health System. the variables "number of hospitalizations", "deaths", "average length of hospital stay" and "average expenses per hospitalization". We accomplished statistical modelling using Stata/MP 14.0 software. Prais-Winsten regression was used to analyze the behaviour of variables over time.

Results: : In the analyzed period, Brazil registered 1,104 hospitalizations for rabies. Of these, 76 died (Figure 1). The mean length of stay was 10.6 days, and the mean value of hospitalizations was BRL 2,025.33 (USD 384.86). The result of the Prais-Winsten regression showed stability in the number of hospitalizations (p-value>0.05). Mean expenses and hospital stay were statistically increasing (p-value<0.05; beta>0), even with low increment rates (Table 1).

Prais-Winsten AR(1) regression		Hospitalizations	Average value of hospital expenses	Average hospital stay
β		-0.0012	0.0028385	0.0007343
SD		0.0007	0.0004539	0.0003258
p-value		0.119	<0.0001	0.025
Average annual increment (%)		-0.003	0.007	0.002
CI95%	LL	-0.006	0.004	0.0002
	UL	0.001	0.009	0.0032
Interpretation		Stable	Increasing	Increasing

Table 1: Analysis of the time series of the number of hospitalizations, hospital expenses and average hospital stay due to rabies from 2008 to 2021

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Conclusion: Despite having increased spending on fighting rabies, the Health System is still experiencing a stabilization in the number of hospitalizations and an increase in the average hospital stay.

Disclosure: Nothing to disclose.

Figure 1: Hospitalizations and deaths due to rabies in Brazil from 2007 to 2021

EPO-173

Epidemiological study of multiple sclerosis in "La Mancha Centro", Spain

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Background and aims: Studying the epidemiology of MS is interesting, given the presumable influence of environmental and genetic factors on its development. This study is proposed to determine the prevalence and incidence of MS, as well as the clinical and sociodemographic profile of MS patients in La Mancha Centro Health Area (HA).

Methods: Retrospective and observational, cross-sectional study of patients diagnosed with MS in the neuroimmunology clinic of the hospitals of our HA, to determine the prevalence and distribution of patients according to age, sex, EDSS and clinical phenotype. Subsequently, a longitudinal design is carried out to determine the incidence of the disease in the 2006–2020 period.

Results: 257 patients with a diagnosis of MS were recruited. The prevalence is 137.28 cases/100,000 inhabitants. The average incidence in the 2006–2020 period is 7.9 cases/ 100,000 inhabitants / year. The distribution by sex was 68% women and 32% men, with 30% being in the 41–50 age group. The predominant clinical phenotype is relapsing-remitting MS, in 75%. The most common EDSS score is 1.

Conclusion: The prevalence of MS in our HA is higher than that described in the different studies published so far in Europe. Likewise, the incidence figure in our SA is above the average incidence in Europe. However, the clinical and demographic characteristics of our patients are similar to those of the studies published so far in our continent.

Disclosure: Nothing to disclose.

EPO-174

Temporal analysis of meningitis and its sociodemographic risk factors in Brazil over the last decade

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Background and aims: This paper aims to evaluate the risk factors for hospitalizations for meningitis in Brazil and whether COVID-19 has an influence on this process.

Methods: The patients' data is from the Notifiable Diseases Information System of Brazil's Ministry of Health. The lethality and odds ratio analyses were performed in the OpenEpi software using the Taylor Series with an IC95%. The temporal analysis is from January 2010 to November 2021, collected from the Hospitals' Information System of the Unified Health System. The statistical modelling used Gretl software and the US Census Bureau's X-13-ARIMA-SEATS tool (1.1). The adjustment statistics were calculated using MS Excel. We also checked the influence of COVID-19 on the subject.

Results: Aetiology, age, ethnicity, region and municipal income were considered statistically significant risk factors for unfavourable outcomes in meningitis. The sex category did not show a significant difference in meningitis lethality (Table 1). Regarding the temporal analysis, the best ARIMA models were $(0,1,1)$ x $(0,0,0)$ for the North region and $(0,1,1)$ x $(0,1,1)$ for the others regions. All models proved to be more efficient than the naive prediction (MASE <1; Theil's U<1) and obtained R^2 above 85% (Table 2). The trend of hospitalizations has been negative since 2020. Least squares regression showed that the COVID-19 was statistically significant in reducing hospitalization values in all Brazilian regions.

Variable		Hospital discharge	Death from meningitis	Meningitis lethality	OR
Etiology					
	BM	21335	3900	15.45	12.82 (11.97 - 13.73)
	MM	5755	909	13.64	11.08 (10.11 - 12.14)
	MCC	2866	1951	40.50	47.74 (43.96 - 51.85)
	MM+MCC	4141	1050	20.23	17.78 (16.25 - 19.46)
	PM	6518	3114	32.33	33.51 (31.15 - 36.05)
	TBM	2369	707	22.98	20.93 (18.89 - 23.2)
	VM	77921	1111	1.41	
	HM	973	217	18.24	15.64 (13.35 - 18.33)
	AEM	4535	1555	25.53	24.05 (22.14 - 26.12)
	USM	21894	2957	11.90	9.47 (8.82 - 10.17)
Age					
	< 1y	23431	1986	7.81	2.08 (1.92 - 2.25)
	1 - 4y	30056	1336	4.26	1.09 (1.002 - 1.188)
	5 - 9y	23029	938	3.91	
	10 - 14y	12105	800	6.20	1.62 (1.47 - 1.79)
	15 - 19y	7985	908	10.21	2.79 (2.54 - 3.07)
	20 - 39y	27831	4021	12.62	3.54 (3.30 - 3.81)
	40 - 59y	17170	4631	21.24	6.62 (6.15 - 7.12)
	60 - 64y	2551	930	26.72	8.95 (8.10 - 9.89)
	65 - 69y	1820	695	27.63	9.37 (8.41 - 10.46)
	70 - 79y	1997	826	29.26	10.15 (9.15 - 11.27)
	> 80y	732	447	37.91	14.99 (13.11 - 17.15)
Ethnicity					
	White	67911	6864	9.18	
	Yellow	694	96	12.15	1.36 (1.10 - 1.70)
	Brown	43687	6358	12.70	1.44 (1.39 - 1.49)
	Black	5455	1191	17.92	2.16 (2.01 - 2.31)
	Indigenous	364	97	21.04	2.63 (2.10 - 3.30)
Sex					
	Male	87988	10278	10.46	
	Female	60841	7255	10.65	1.02 (0.98 - 1.05)
Brazilian major region					
	South	29702	2701	8.34	
	Southeast	80529	9455	10.51	1.29 (1.23 - 1.35)
	Northeast	26066	3152	10.79	1.33 (1.26 - 1.40)
	Midwest	6576	1056	13.84	1.76 (1.63 - 1.90)
	North	5973	1171	16.39	2.15 (2.00 - 2.32)
Extreme poverty municipality					
	Yes	1125	384	25.45	2.94 (2.61 - 3.30)
	No	147721	17151	10.40	

*VM: viral meningitis; USM: unspecified meningitis; MM: meningococcal meningitis; BM: bacterial meningitis; HM: meningitis due to *Haemophilus influenzae*; MM: meningococcal meningitis + meningococcemia; TBM: tuberculous meningitis; AEM: meningitis due to another etiological agent; PM: pneumococcal meningitis; MCC: meningococcemia.
Table 1: Epidemiological profile of patients with an unfavorable outcome for meningitis

Table 1: Epidemiological profile of patients with an unfavorable outcome for meningitis
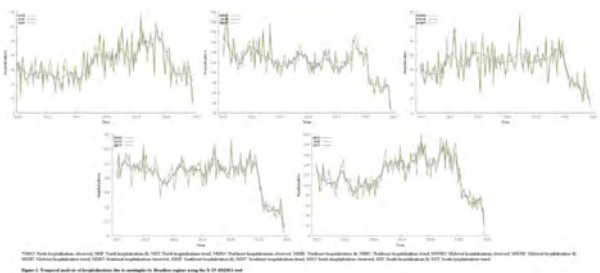
Figure 1: Temporal analysis of hospitalizations due to meningitis by Brazilian regions using the X-13 ARIMA tool

Time series	Optimal model	MASE	RMSE	R²	Goodness-of-fit Theil's U	AIC	BIC
North hospitalizations	(0,1,1) × (0,0,0)	0.38	0.30	-0.89	0.37	1019.2225	1025.0479
Northeast hospitalizations	(0,1,1) × (0,1,1)	0.50	0.18	0.37	0.48	1120.9376	1135.2753
Midwest hospitalizations	(0,1,1) × (0,1,1)	0.38	0.38	0.86	0.58	973.9972	985.4673
Southeast hospitalizations	(0,1,1) × (0,1,1)	0.61	0.37	0.87	0.64	1261.1442	1272.6144
South hospitalizations	(0,1,1) × (0,1,1)	0.56	0.08	0.89	0.61	1148.9405	1157.5431

*MASE: mean absolute scaled error; RMSE: root mean square error; AIC: Akaike information criterion; BIC: Bayesian information criterion.
Table 2: Adjustment of the X-13 ARIMA model to analyze the historical series of hospitalizations due to meningitis in Brazil over the last decade

Table 2: Adjustment of the X-13 ARIMA model to analyze the historical series of hospitalizations due to meningitis in Brazil over the last decade

Conclusion: It is possible that the measures against Sars-CoV-2 have contributed to reducing the hospitalizations by meningitis.
Disclosure: Nothing to disclose.

Neuroimaging 1

EPO-175
Abstract withdrawn

EPO-176
MRI investigation of caudate networks in the normal aging

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Background and aims: Subventricular zone (SVZ) neuron precursor cells possibly modulate striatal neuronal activity via the release of soluble molecules. Neurogenesis decay in SVZ may result in structural alterations of brain regions connected to the caudate, particularly to its medial component. The aim of this study was to investigate how the functional organization of caudate networks relates to structural brain changes with aging.

Methods: 50 "young" (20–35 years [YC]) and 93 "old" (36–85 years [OC]). In YC, stepwise functional connectivity (SFC) was used to characterize regions that connect to medial and lateral caudate at different levels of link-step distances. Atrophy of medial- (MCR) and lateral- (LCR) caudate connected regions was estimated in OC.

Results: In YC, medial- and lateral-caudate showed direct connectivity to basal ganglia, superior and caudal middle frontal and inferior parietal gyri, cingulate cortex, precuneus, pericalcarine and insula. With subsequent steps, caudate parts were also connected to precentral and superior temporal gyri and cuneus. In YC, medial-caudate showed higher direct connectivity to basal ganglia, superior, middle and inferior frontal and inferior parietal gyri (MCR) relative to the lateral-caudate. Considering the opposite contrast, lateral-caudate showed a stronger connectivity to basal ganglia, orbitofrontal, rostral-anterior cingulate and insula cortices (LCR) compared to medial-caudate. In OC, MCR showed greater atrophy relative to LCR. Splitting OC into two groups, the analysis showed that atrophy differences are driven by OC older than 60-years of age.

Conclusion: SFC analysis can be useful to evaluate the role of the SVZ in the network disruptions in age-related neurodegenerative disorders.

Disclosure: Supported by European Research Council (grant: StG-2016_714388_NeuroTRACK).

EPO-177
Functional connectivity of gray and white matter in olfactory-related brain regions in Parkinson's disease

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Background and aims: Before the onset of motor symptoms, Parkinson's disease will involve the anterior olfactory nucleus and olfactory bulb and cause olfactory disturbance, and hyposmia is a common clinical manifestation in the early stage of PD. Accumulating evidence has shown that BOLD signals in white matter change correspondingly after olfactory disorders and related stimuli, and the signal changes in brain white matter pathways show a certain degree of specificity, which can reflect changes of early olfactory function in Parkinson's disease.

Methods: In the present study, we developed a new method to decode functional connectivity of gray and white matter in olfactory-related brain regions in Parkinson's disease.

Results: Our results show that bilateral dorsolateral prefrontal cortex, and left frontoorbital cortex had the most significant differences in functional connectivity with white matter in patients with Parkinson's hyposmia, and these three brain regions are closely related to the superior temporal gyrus, middle temporal gyrus, and insula.
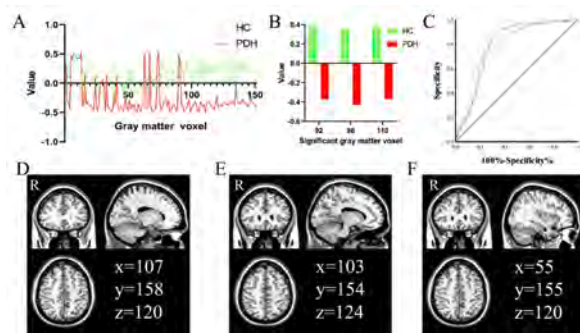
Figure1: Functional covariance connection gray matter characteristics
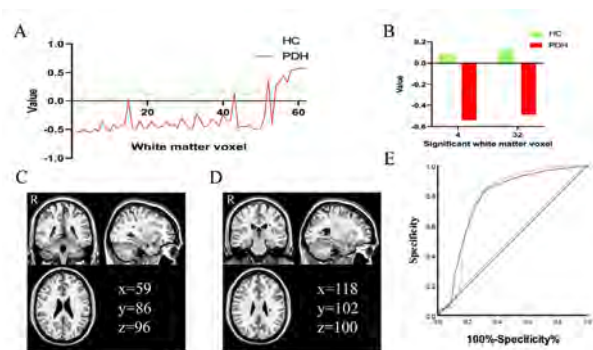
Figure2: Functional covariance connection white matter characteristics
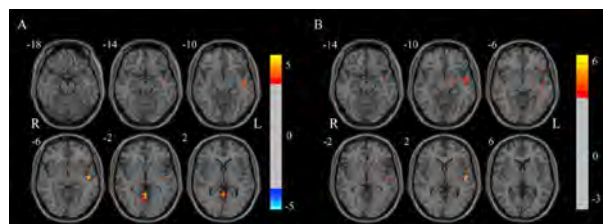
Figure3: Whole-brain functional connection based on seed points

Conclusion: These results demonstrate that alterations in functional connectivity of gray and white matter in olfactory-related brain regions can reflect the change of olfactory function in the early stage of Parkinson's disease, so as to be used as a potential neuroimaging marker for early diagnosis and disease progression.

Disclosure: The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

EPO-178

Amyloid-related imaging abnormalities and beta-amyloid targeting antibodies: a systematic review

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Background and aims: The aim of this systematic review was to summarize available evidence on amyloid-related imaging abnormalities (ARIA) from randomized clinical trials (RCTs) testing anti-β-amyloid monoclonal antibodies (mAbs) in patients with Alzheimer's disease (AD), and provide a comprehensive update about risk factors, clinical correlates and implications for treatment withhold/re-initiation.

Methods: A literature search of MEDLINE/PubMed, Embase and Cochrane and ClinicalTrials.Gov was conducted through September 15, 2021. Publications describing RCTs, re-analyses of RCTs data, and case reports of ARIA were included. Strengths of clinical data were graded according to the Oxford Centre for Evidence-Based Medicine.

Results: 22 RCTs publications, 11 RCTs reanalysis studies and one case report, including in total 15,508 adult patients, were selected for inclusion. ARIA-E (parenchymal edema and sulcal effusion) and ARIA-H (hemosiderin deposits) are thought to be expression of increased vascular fragility caused by mAbs therapeutic effect. Apolipoprotein-E (ApoE) ε4 genotype was the main risk factor for both ARIA types; ARIA-E incidence was further associated with treatment dose, affecting up to 55% of ε4 carriers treated with aducanumab. Both ARIA types manifested early during study course and symptomatic cases accounted for the 6.1–39.3% of ARIA-E cases at higher treatment doses across RCTs, whereas ARIA-H were generally asymptomatic. The majority of ARIA-E resolved with treatment withhold, although anecdotally requiring steroid administration. ARIA-E recurrence after dose re-initiation/adjustment varied from 13.8% to 25.6% across RCTs.

Conclusion: Evidence suggests that ARIA are frequent, collateral events of amyloid-modifying therapies and supports the notion that treatments can be continued with careful monitoring and possible dose adjustment.

Disclosure: Nothing to disclose.

EPO-179

Deep grey matter atrophy in teriflunomide-treated patients with multiple sclerosis

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Background and aims: Two large randomized, placebo-controlled phase III trials, TEMSO (NCT00134563) and TOWER (NCT00751881), showed that teriflunomide reduces the risk of disability worsening in relapsing-remitting multiple sclerosis. Furthermore, whole-brain atrophy was significantly slowed in a post-hoc SIENA analysis in TEMSO. However, potential effects on deep grey matter (dGM) structures have not been evaluated. The effect of teriflunomide on various dGM structures were examined using an advanced multi-template-based segmentation algorithm, MAGeT-brain.

Methods: TEMSO baseline, 1- and 2-year follow-up T1w MRI were segmented with MAGeT-brain. Thalamic and basal ganglia percentage volume change (PVC) was compared between treatment groups using rank ANOVA. Differences between PVC of these regions and whole brain (SIENA) were analysed using Mann–Whitney U tests.

Results: 932 patients were included in the study with 916 (year 1) and 808 patients (year 2) available at follow-up. During quality assessment prior to SIENA/MAGeT analyses, 13.7% whole brain, 21.9% thalamic, and 31.8% basal ganglia datasets were removed from the analyses. The treatment effect on whole brain atrophy was replicated, but only a non-significant effect on PVC was observed for the thalami (see figure). A treatment-independent comparison showed that atrophy was more pronounced in the basal ganglia compared to whole brain.

Conclusion: In contrast to whole brain analyses, dGM atrophy treatment effects were non-significant in this relatively heterogeneous T1w MRI dataset, likely driven by a greater susceptibility of smaller volumes to noise. To improve detection of treatment effects in the dGM, MRI sequences should be standardized and optimized for structural contrasts in these areas.
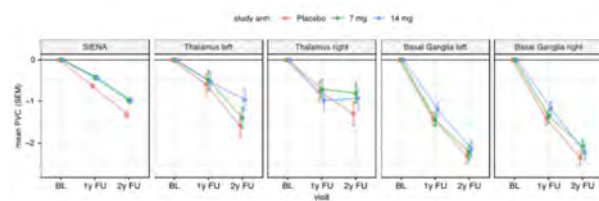
Disclosure: Editorial support was provided by Gleb Baida, PhD, and Katie Crosslin, PhD of Elevate Medical Affairs, which was sponsored by Sanofi Genzyme

EPO-180

Anatomical predictors of trigeminal neuralgia: influence on the recurrence rate in the postoperative period

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Background and aims: According to modern literature data, trigeminal neuralgia has a multifactorial nature, and the presence of trigeminal nerve compression is not a sufficient condition for the development of pain syndrome and requires the additional presence of one or more additional anatomical predictors. However, studies proving the influence of various combinations of anatomical predictors on the frequency of redaction in the postoperative period are few and contradictory.

Methods: A clinical study of 32 patients with trigeminal neuralgia was conducted. The studied patients were aged from 21 to 74 years. All patients underwent microvascular decompression using retrosigmoid access. The following anatomical predictors were considered: vasoneural conflict, volume and cross-sectional area of the cerebellum, volume, length, cross-sectional area of the trigeminal nerve and intertrihemial angle. Relapse assessment was carried out in the postoperative period for 1–2 years after surgical treatment.

Results: Vascular compression was identified in all the studied patients as the main anatomical predictor of trigeminal neuralgia. The absence of a positive effect after microvascular decompression was observed in 9,4% of patients. In 12,5% of patients who additionally had anatomical predictors such as a more acute intertrihemial angle of 34,6° (22,8/52,4)° before surgery, a resumption of pain syndrome with MR signs of vascular compression was revealed during the first 3–6 months after surgical treatment (p<0,05).

Conclusion: The combination of vascular compression with an acute intertrihemial angle may lead to a higher recurrence rate.

Disclosure: Nothing to disclose.

EPO-181

Dynamic functional connectivity changes in the triple network in mild traumatic brain injury

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Background and aims: A triple network model consisting of a default network, a salience network, and a central executive network has recently been used to understand connectivity patterns in cognitively normal versus dysfunctional brains. This study aimed to explore changes in the dynamic connectivity of triplet network in mild traumatic brain injury (mTBI) and its relationship to cognitive performance.

Methods: A total of 31 mTBI patients and 30 healthy controls were included in this study. The three networks were identified by group space independent component analysis, and the dynamic FC was analyzed by sliding window method and k-means clustering algorithm. Furthermore, we analyzed the relationship between changes in dynamic FC parameters and clinical variables in mTBI patients.

Figure 1.
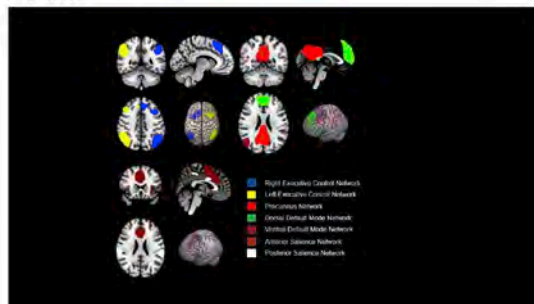
Group-level independent component analysis was used to identify these networks. Maps are displayed at Z> 2.0 (p < 0.01, FWE corrected).

Figure 2.
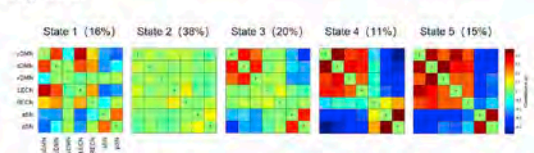
Cluster centroid and its total number of occurrence (percentage) for each state. The color bar represents z value of functional connectivity. Abbreviations: aDMN, anterior default mode network; LCEN, left central executive network; pDMN, posterior default mode network; RCEN, right central executive network; aSN, anterior Salience; pSN, post Salience.

Figure 3.
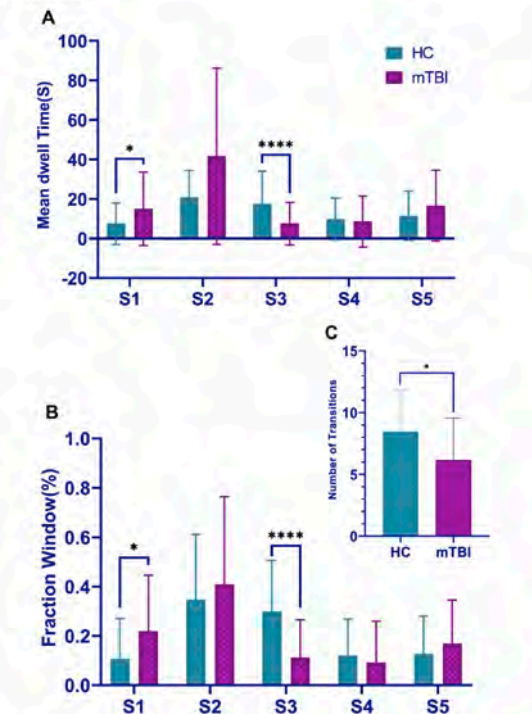
Between-group differences in temporal properties of dynamic functional connectivity states. Significant effects after correction for multiple comparisons (pFDR < 0.05, ** for p < 0.0021; *** for p < 0.0002, **** for p < 0.0001).

Figure 4.
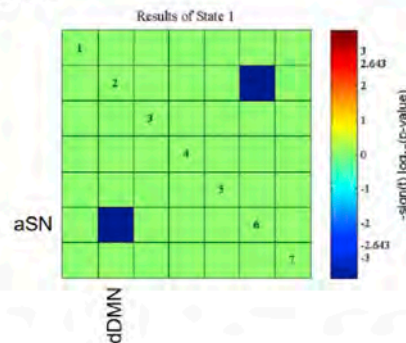
The functional connectivity of aSN to dDMN was significantly reduced in state 1 in mTBI patients compared with healthy controls. Blue rectangles indicate significance (p < 0.05, FDR corrected).

Figure 5.
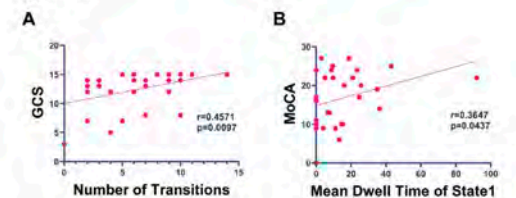
Results of partial correlation analysis between time characteristics and clinical indicators of significant differences between groups. For mTBI patients, (A) the number of transition positively correlated with the GCS score , (B) and the mean dwell time in State 1 positively correlated with MoCA. Abbreviations: GCS, Glasgow Coma Scale; MoCA, Montreal Cognitive Assessment.

Figure 1–5. Group-level independent component analysis was used to identify these networks.

Results: Brain triple network dynamic functional connectivity is clustered into five states. Compared with HC, mTBI patients spent longer in state 1, which is characterized by weakened dDMN and aSN connectivity, and state 3, which is characterized by a positive correlation between DMN and SN internal connectivity. mTBI patients had fewer metastases in different states than HC patients. In addition, the mean residence time in state 1 correlated with MoCA scores in mTBI patients; the number of transitions between states correlated with GCS in mTBI patients.

Conclusion: Our findings suggest that the dynamic properties of FC in the triplet network of mTBI patients are abnormal, and provide a new perspective on the pathophysiological mechanism of cognitive impairment from the perspective of dynamic FC.

Disclosure: Figure 1–5.

EPO-182

Brain metabolic correlates of process-specific CSF biomarkers in MCI due to Alzheimer's disease

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Background and aims: Cerebrospinal fluid (CSF) biomarkers can reflect several molecular aberrations and pathological changes in Alzheimer's disease (AD), e.g., neuronal death, synaptic and axonal injury. [18] F-fluorodeoxyglucose-PET(FDG-PET) brain metabolism might disclose a peculiar topography when correlated with the levels of some CSF proteins reflecting specific pathological processes.

Methods: We focused on some emergent CSF biomarkers, namely post-synaptic neurogranin (Ng), pre-synaptic α-and β-synuclein (α-and β-syn), and neurofilament light chain (NfL), as a marker of axonal damage, and explored the sites of correlation (volumes of interest, VOIs) of their levels with brain metabolism in a group of 26 patients with prodromal AD (16 females; age 75.4±6.6; MMSE score 26.1±1.9). We further assessed whether-and how extensively- these VOIs overlapped the hypometabolic areas resulting from comparing AD patients with 40 matched healthy controls (HC).

Results: Ng-VOI and α-syn-VOI encompassed left precuneus/posterior cingulate cortex (PC/PCC) and partially overlapped hypometabolism at those sites. β-syn-VOI and NfL-VOI regarded either left or right lateral temporal areas, respectively, with partial overlap with hypometabolism for the β-syn-VOI, whereas the NfL-VOI did not include hypometabolic regions (Figure 1).
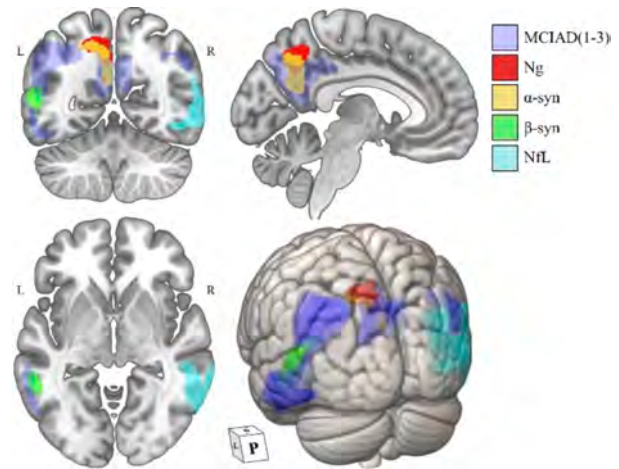
2D representation (axial, coronal, and sagittal cuts) and 3D rendering of the significant VOIs related to Ng (red), α-syn (yellow), β-syn (green), and NfL overlayed to the hypometabolic clusters (MCIAD1, MCIAD2, and MCIAD3 from left to right, in purple)

Conclusion: We speculate that CSF levels of Ng and α-syn express an already established hippocampal damage leading to PC/PCC deafferentation and hypometabolism. β-syn may represent the progression of synaptopathy in the temporal lobe, while NfL the axonal injury in less affected right temporal regions where neuronal loss is still subthreshold. These findings complement the information on the distribution of hypometabolism related to neuronal loss, which differs from the metabolic changes reflecting synaptic or axonal injury.

Disclosure: This work received support from the Italian Ministry of Health (Fondi per la Ricerca Corrente, 2020). This research did not receive any specific grant from funding agencies in the commercial or not-for-profit sectors.

EPO-183

Peri-ictal neuroimaging of Status Epilepticus: preliminary results of a prospective study

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Background and aims: Peri-ictal MRI abnormalities (PMAs) following status epilepticus (SE) show variable prevalence (12–100%) in literature. These alterations are frequently transitory, but the timing of appearance and disappearance is poorly investigated. We aimed to further characterize the type and timing of the MRI findings associated with SE.

Methods: We enrolled consecutive patients with SE, cluster of seizures or single seizure. Primary outcome was the presence, at MRI acquired during or immediately after epileptic event, of cortical high DWI signal. Subjects with MRI abnormalities underwent further studies until normalization.

Results: 54 patients were recruited, mean age was 61 years. Nineteen 35.2%) had SE, 15 (27.8%) had cluster of seizures and 20 (37%) had a single seizure. First MRI was positive in 13 cases (68.4%) from the SE group, 7 (27.8%) for the cluster group and 10 (50%) for the single seizure group. There was no statistical difference amongst the three groups for baseline outcome (p value=0.3672). Thirteen patients completed the follow-up MRI. In seven cases the follow-up was terminated for identification of a different etiology of the lesion (vascular, neoplastic). In three patients the alterations were no longer present (confirming as PMAs). Three patients had persistent anomalies and follow-up is still ongoing.

Conclusion: Our findings emphasize that PMAs are not specific to SE, given the non-significant differences in prevalence between the three groups investigated. These preliminary data warrant further investigation.

Disclosure: Nothing to disclose.

EPO-184

Brain volume measures in adults with MOG-antibody associated disease: a longitudinal multicenter study

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Background and aims: Myelin oligodendrocyte glycoprotein associated disease (MOGAD) features may overlap with relapsing-remitting multiple sclerosis (RRMS). Little is known about brain atrophy occurrence in MOGAD. This study compares rates of brain volume change over time in MOGAD and RRMS patients.

Methods: 18 adult MOGAD patients (10 females) were selected from a multicentric observational involving 7 centers in Italy, and subsequently extended to other 10 Italian centers. Patients were age-and sex-matched to 33 RRMS patients (17 females) recruited in the Verona MS centre. Availability of two brain MRI scans performed 6–30 months apart and a clinical follow-up ≥6 months were mandatory for each patient. The same MRI protocol and scanner at both timepoints was used for each patient. Annualized percentage brain volume change (PBVC/y) between the two MRI timepoints, baseline global brain, grey and white matter (WM) were compared between groups.

Results: Mean PBVC/y was lower in MOGAD than in RRMS in a subgroup of patients aged <60 years and with a disease duration ≤10 years (p=0.046). Overall, mean global brain volume was higher in MOGAD (p=0.021) as well as mean WM volume (p<0.001). Median T2-lesion volume at timepoint 1 was lower in MOGAD (p<0.001); T2-lesion volume increased between the 2 MRI timepoints in RRMS (p<0.001) but not in MOGAD (p=0.11).

Conclusion: MOGAD displays less global brain and WM atrophy than RRMS, as well as less brain volume loss and lesion load over time, suggesting different neuropathogenic mechanisms underlining the two diseases.

Disclosure: Nothing to disclose.

EPO-185

Increased midbrain sodium levels in progressive supranuclear palsy

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Background and aims: Progressive supranuclear palsy (PSP) is a debilitating neurodegenerative disease with high disease aggressiveness. A timely differential diagnosis is crucial for developing pathophysiology-orientated and potentially disease-modifying therapies. Current neuroimaging biomarkers mainly rely on structural changes implying that extensive atrophy already occurred. Sodium imaging (23Na-MRI) is a promising method for investigating neurodegeneration in vivo. The differentiation of total and intracellular-weighted 23Na-MRI signals substantially improves the interpretability of observed changes.
Methods: We enrolled ten patients with PSP and 19 age- and gender-matched healthy control subjects. All participants underwent a neurological examination, whole-brain structural and (total and intracellular-weighted) 23Na-MRI.
Results: Voxel-wise analyses revealed a marked increase of the brainstem total sodium content. This increase was positively correlated with symptom severity. The ROI-wise analyses demonstrated a pronounced total sodium disequilibrium in the midbrain, pons/medulla, and pallidum. These findings were present in the absence of any intracellular-weighted signal alterations or volumetric differences in these regions.
Conclusion: 23Na-MRI yields substantial benefits for the diagnostic workup of patients with PSP and fosters a deepened understanding of disease mechanisms.
Disclosure: The authors declare no conflict of interest.

EPO-186

Lesion network-symptom-mapping of eye-opening apraxia

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Background and aims: Eye-opening apraxia is the inability to voluntarily open the eyes. It is caused by a lack of supranuclear control, and may occur with ischemic stroke, neurodegenerative disorders, traumatic frontal lobe injuries and medications. Despite reports dating back to 1907, the anatomic and functionally responsible networks remain unknown. To test whether the heterogeneous lesion locations are linked in a common network, we applied 'lesion network-symptom-mapping'.
Methods: Stroke patients with eye-opening apraxia following endovascular therapy were prospectively enrolled. In addition, a systematic literature search identified cases of acquired eye-opening apraxia with CT or MRI images of sufficient quality. The lesions were mapped as 2D masks onto a standard brain atlas. Using available resting-state functional MRI data from 1,578 healthy adults, we investigated overlapping brain regions and networks common to lesions leading to eye-opening apraxia.
Results: In addition to the six patients admitted to our hospital, we identified 28 cases of eye-opening apraxia across 24 studies (total n=34). 65% of the lesions were in the right hemisphere, 24% bilateral or in the midbrain, and 12% in the left hemisphere. All hemispheric lesions involved the frontoparietal lobes, thalamus, or basal ganglia. Data analysis is ongoing, and the full data set will be presented at the EAN conference.
Conclusion: Brain lesions in various localizations lead to eye-opening apraxia. These are predominantly in the right hemisphere, and we hypothesize that lesion network-symptom-mapping will allow us to identify a common network that combines all the underlying locations.
Disclosure: The authors have none to declare.

EPO-187

Imaging of Glutamate In Acute Carbon Monoxide Poisoning Using Chemical Exchange Saturation Transfer

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Background and aims: This study adopted the Glutamate Chemical Exchange Saturation Transfer (GluCEST) imaging technique to quantitatively analyze the cranial glutamate, and discussed the value of the GluCEST in identifying the pathogenesis of encephalopathy after CO poisoning.

Methods: The routine MRI and functional MRI scans of two cohorts of subjects (CO group, n=29; Control group, n=16) were performed. Between-group comparisons were conducted for GluCEST% in regions of interest (ROI), including the basal ganglia, thalamus, frontal lobe, occipital lobe, genu of the corpus callosum, cingulate gyrus and cuneus. Moreover, age-stratified subgroup analysis was devised, and correlational analysis was performed for the GluCEST% with coma days, Simple Mental State Examination Scale (MMSE) score, Hamilton Anxiety Scale score, and blood COHb% in each ROI.
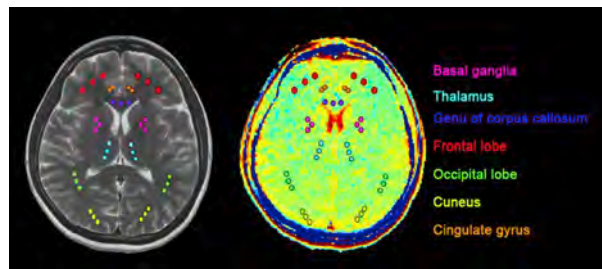
Figure 1. ROIs on T2WI and GluCEST: basal ganglia (purple), thalamus (light blue), genu of the corpus callosum (dark blue), frontal lobe (red), occipital lobe (green), cuneus (yellow), cingulate gyrus (orange).

Results: As compared to the healthy control, CO group led to significantly increasing GluCEST% in the basal ganglia, occipital lobe, genu of the corpus callosum, cingulate gyrus and cuneus (p<0.05). In subgroup analysis for age, adult patients had higher GluCEST% in the basal ganglia, thalamus, occipital lobe, cingulate gyrus and cuneus, compared with healthy adults (p<0.05). Additionally, the correlational analysis in CO-poisoned patients revealed statistical association between the GluCEST% and MMSE in the thalamus and genu of the corpus callosum.
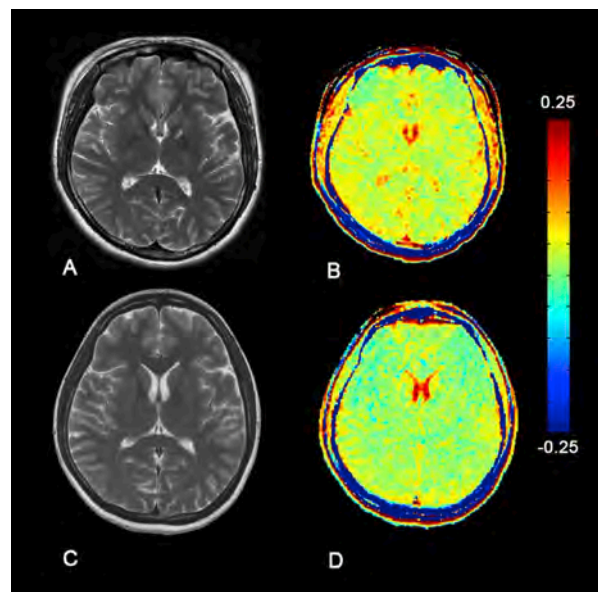
Figure 2. A–B. Abnormal T2WI images of patient, mainly manifested in the bilateral globus pallidus and the cerebral white matter region. C-D. T2WI and GluCEST images of the healthy adult.

Conclusion: The GluCEST technique is superior to routine MRI that can identify cerebral biochemical changes earlier after acute CO poisoning, which is significant for our understanding on the role of neurotransmitters in the pathological basis of this disease. Between adults and children, the cerebral injuries after CO poisoning might vary.

Disclosure: Nothing to disclose.

EPO-188

Functional Brain Network Topology Changes In Acute Carbon Monoxide Poisoning

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Background and aims: Carbon monoxide (CO) poisoning can cause damages to the important organs resulting in hypoxic injury and leading to death. A well understanding of the mechanism of action of CO poisoning for cerebral injury facilitates us to comprehensively study the occurrence and development of CO poisoning.

Methods: This study performed resting-state functional magnetic resonance imaging (fMRI) to construct a whole-brain functional network using the graph theory in 27 pairs of acute CO-poisoned patients and healthy people. Comparative analysis was devised for the topological properties (including global, node and edge measures) of the brain functional network between the two groups. Correlation of the whole-brain network with cognitive function was also analyzed.

Results: At a global level, patients after CO poisoning had significantly lower clustering coefficient, small-worldness and local efficiency as compared to the healthy control, indicative of a randomization shift of their brain functional networks. At a regional level, abnormal nodes (increase/decrease in nodal centrality) and edges (increase/decrease in functional connectivity strength) were noted and involved in the auditory network (AUD), visual network (VIS), salience network (SN) and default mode network (DMN) of their brain. Significant associations of the altered network measures with the coma degree and cognitive function in the acute phase after CO poisoning were also displayed.
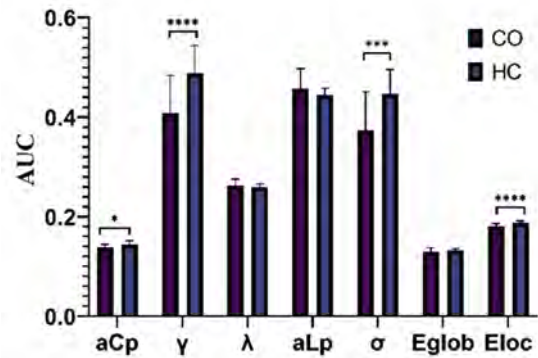
The differences in global measures of the networks between CO and HC. Significant effects after correction for multiple comparisons (pFDR<0.05, **for p<0.0021; *** for p<0.0002, **** for p<0.0001).

Conclusion: To conclude, there are specific changes in the topological organization of the whole-brain functional network in the acute phase after CO poisoning. The findings of the current study may provide a new thought into the mechanism of action of CO poisoning for nerve injury.

Disclosure: Nothing to disclose.
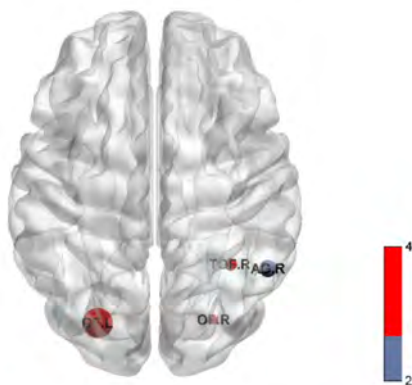
Figure 1. Differences between CO group and HC group at the node level. Red sphere represents (CO>HC, p<0.05 FDR corrected): Blue sphere (CO<HC, p<0.05 FDR corrected); The sizes of the significant nodes reflect the effect sizes of group differences.

Neuroimmunology 1

EPO-189

Theoretical nuclear physics study of the modulation of Gamma-Delta T cells in pathophysiology of autoimmunity in the CNS

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Background and aims: There are several subtypes of Gamma-Delta T cells. Failures in thymic control may be associated with autoimmune disorders that affect the central nervous system.

Methods: This study was elaborated based on computational simulations that analyzed (a) Gamma delta T cells in innate and adaptive immunity; (b) Induction of apoptosis of myelin basic protein (73–86) peptide specific T Cells by Gamma delta lymphocytes. Computational simulations and analyzes of this scientific work were elaborated with the use of software: ACD/ChemSketch, Swiss-PdbViewer, ABCpred, BepiPred-2.0, ElliPro, DEseq, GOseq, FunRich, Cytoscape, BiNGO, PepSurf, AxonDeepSeg, AxonSeg, Computer-assisted Evaluation of Myelin formation (CEM), PyMol, ICM-Browser, Visual Molecular Dynamics (VMD), Cell Illus-trator, C-ImmSim, Simmune, GENESIS, NEURON, NeuronStudio and ChemDraw. Computational design at the Density Functional Theory level, docking studies, computed Infrared-active modes, Highest Occupied Molecular Orbital (HOMO) - Lowest Unoccupied Molecular Orbital (LUMO) gaps, Ultraviolet–visible absorbance spectroscopy and molecular dynamics methods were applied in the computational analysis.

Results: This work suggests that naïve and central memory T$\gamma\delta$ cells express CCR7 receptor, which is a receptor for the chemokines CCL19 and CCL21. This study suggests that conformational changes in granzyme and perforin may disrupt $\gamma\delta$ T cell thymic regulation. This study suggests that conformational changes in the p85 subunit of PI3K and Grb2-Vav1 complex may disrupt the production of sTRAIL. This work suggests that the deficiency of IL-23 or IL-23R expression on $\gamma\delta$ T cells may influence immune responses.

Conclusion: Understanding the immunological mechanisms should help developing new therapeutic tools to treat disorders that involve autoimmunity in the central nervous system.

Disclosure: Nothing to disclose

EPO-190

Quantum Mechanics Methods for Dimethyl Fumarate, Monomethyl Fumarate and Cannabidiol in Neurons and Microglia

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Background and aims: Current studies suggest that dimethyl fumarate, monomethyl fumarate and cannabidiol have neuroprotective and anti-inflammatory effects. This study aims to develop a computational model using quantum mechanics for dimethyl fumarate, monomethyl fumarate and cannabidiol in neurons and microglia.

Methods: The molecular docking of dimethyl fumarate, monomethyl fumarate and cannabidiol were conducted with the tool AutoDock Vina (version 1.1.2), as implemented in the MolAr (Molecular Architecture) software. The loop regions were rebuilt using the Modeller. Key docking complexes were evaluated by molecular dynamics (MD) simulation using the GROMOS54A7 all-atom force field and performed using GROMACS 5.1 software. Using deterministic model based on Dirac notation, stochastic model using the stochastic differential equation with Poisson point process and Jackknife-Monte-Carlo Approach, a computational model was developed. Other software used in this work to neuroimmunology analysis were: ACD/ChemSketch, ABCpred, BepiPred-2.0, AxonDeepSeg, Computer-assisted Evaluation of Myelin formation, Visual Molecular Dynamics, C-ImmSim and Simmune.

Results: This work suggests that dimethyl fumarate (DMF) has a possible action through the nuclear factor-erythroid 2 related factor 2 (Nrf2) activation pathway in the CNS. DMF and monomethyl fumarate also activates the carboxylic acid receptor, which would be able to inhibit the expression of pro-inflammatory molecules through the inhibition of NF-kB in microglia. Cannabidiol can generate reduction of proinflammatory cytokines such as IL-17A, IFN-γ, TNF-α and increase of anti-inflammatory cytokines such as IL-4, IL-10 and TGF-β.

Conclusion: Understanding mechanisms and properties of dimethyl fumarate, monomethyl fumarate and cannabidiol should help developing therapeutic tools to treat diseases with problems related to neurons and microglia.

Disclosure: Nothing to disclose.

EPO-191

Neuronal intermediate filament autoimmunity as an unusual complication of immune checkpoint inhibitors

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Background and aims: Our aim is to report a case of immune checkpoint inhibitors related adverse effect (iRAE) who had neurological symptoms associated with serum and CSF neuronal intermediate filament immunoglobulins (NIF-IgG).

Methods: A 67-year-old woman was admitted to our Unit with subacute III cranial nerve palsy. She was receiving avelumab as immunotherapy for Merkel cell carcinoma. Brain MRI and immunological studies in serum and CSF were performed.

Results: On MRI, T2/FLAIR hyperintensity and contrast enhancement of the left III cranial nerve were observed and CSF analysis demonstrated slight increased cell number and protein concentration. Standard Western blot and fixed cell-bases assays excluded the presence of antibodies to intracellular and surface antigens, but home-made immunohistochemistry on rat brain sections showed a "neurofilament-like" pattern. NIF-IgG were thus tested and resulted positive in both serum and CSF, confirming the diagnosis of NIF-IgG autoimmunity. Avelumab was discontinued and treatment with steroids and intravenous immunoglobulins was administered with partial improvement.
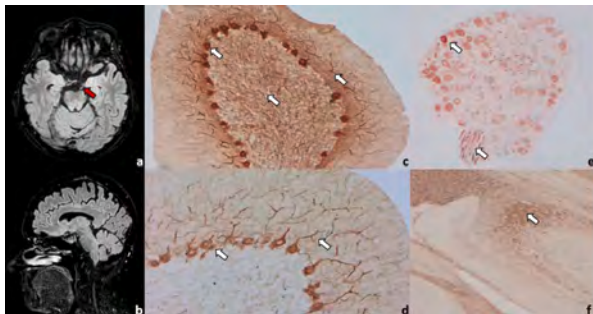
Brain MRI showing T2 hyperintensity of the left oculomotor nerve (red arrow), with contrast enhancement (not shown) (a) in absence of cerebellum or brainstem lesions (b). In-house immunohistochemistry on rat brain and cerebellum reveals a "neurofilament-l

Conclusion: This case expands the spectrum of NIF-IgG autoimmunity and adds avelumab as a potential trigger of this condition. Tissue-based assays should be performed in patients presenting with immune-related adverse effects of immune-checkpoint inhibitors to detect novel reactivities, which retain clinical relevance.

Disclosure: A.M has received royalties for the commercialization of septin-5 and MAP1B, has patents for neural IgGs as biomarkers for diagnosis and treatment of autoimmune neurological disorders, has received support from Euroimmun.

EPO-192

Multiple Sclerosis (MS) in elderly patients: a growing challenge

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Background and aims: The therapeutic advances in MS and the improvement in life expectancy explain an increase in the prevalence of older than 60 years old MS patients. We aim to describe demographic and clinical characteristics of patients over 60 years old with MS followed up in a neuroimmunology unit (NIU) of a tertiary hospital.

Methods: Observational cross-sectional study of a cohort of patients, over 60 years old, obtained from the registry of MS patients followed up at NIU. Demographic and clinical variables were obtained.

Results: Of 790 patients with MS, 150 (18.9%) were older than 60 years (66±5.8). 69.3% women, age at diagnosis 46±10.1 years [m(SD)]. The time of evolution was 21±8.15 years [m(SD)]. EDSS was [median,IQR] 4(2–6) . 95/150 (63.3%) RRMS, 42/150 (28%) SPMS and 13/150 (8.7%) PPMS. EDSS according to phenotype [median.IQR]: RRMS 2.5 (1.5–4), SPMS 6.5 (4–7), PPMS 6 (6–7); The number of relapses during the evolution was 4.2 (SD3.1). 87/150 (58%) continued disease modifying treatment (DMT). The relapses-free time (months) was 157±132 [m(SD)]; no difference was found between groups with or without DMT [m(SD)]: 166±82 vs.150±165] or EDSS (median 4 in both groups,p>0.05).

Conclusion: Patients over 60 years old are a large group of MS patients, with frequent RRMS phenotype persistence and late onset. There is not difference in relapse-free time between patients with and without DMT, perhaps in relation to immunosenescence and evolution of MS.

Disclosure: The authors have no conflicts of interest to declare.

EPO-193

Serum neurofilament light levels in relation to the Brain-Age Paradigm in normal ageing

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Background and aims: Serum neurofilament light (sNfL) is an easy accessible biomarker that increases upon neuro-axonal injury and neurodegeneration. Previous studies have shown that sNfL levels rise in normal ageing, which was further correlated to brain volume changes. The Brain-Age paradigm is a machine learning approach which predicts brain-age from neuroimaging data. We assessed whether brain-predicted age differences (brain-PAD) correlated with sNfL levels in a community-dwelling cohort.

Methods: We included 328 neurologically normal individuals participating in a community-dwelling cohort study free of a history of previous stroke or dementia. There were 193 females. Age ranged from 38 to 85 years, with a median of 68.11 (IQR: 55.90–73.18) years. Brain-PAD was measured using neuroimaging data attained from T1-weighted MRI, and sNfL was quantified by a single molecule array (Simoa) assay.

Results: sNfL correlated with chronological aage (r=0.73, p<0.001) and brain-predicted age (r=0.65, p<0.001). However, sNfL was unrelated to brain-PAD (r=0.038, p=0.50). Further analyses revealed no differences in brain-PAD comparing individuals within the lowest and the highest sNfL quartile (p=0.57), with a mean brain-PAD of 0.79±6.03 and 1.42±7.97 years respectively.

Conclusion: Although sNfL correlated with chronological and brain predicted age, no correlation was found regarding brain-PAD. This could be due to a lower brain-PAD variation in our community-dwelling cohort. Moreover, factors apart from neurodegeneration such as reduced protein turn-over in higher age may be associated with the age-related increase in sNfL, which may have hampered to find associations between sNfL and brain-PAD.

Disclosure: Nothing to disclose.

EPO-194

No association between naturally occurring plasma tau autoantibodies and risk of neurological disease

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Background and aims: The microtubule-associated protein tau has a well-established role in neurodegenerative diseases, including Alzheimer's disease (AD). Naturally occurring tau autoantibodies have been found in the plasma of AD patients and tau immunization strategies are being tested in clinical trials of neurodegenerative diseases. We aimed to assess if plasma tau autoimmunity was associated with a higher risk of neurological disease.

Methods: Using a miniaturized indirect ELISA (Enzyme-Linked Immunosorbent Assay) automated platform, we tested >20,000 plasma samples from a university hospital cohort for their reactivity against the microtubule-binding domain of tau protein. Using multivariate log-binomial regression models (including age, sex and disease), we estimated the risk ratios and 95% confidence intervals for the presence of plasma tau autoantibodies in 12 main groups of neurological disorders classified using ICD-10 (International Classification of Disease and Related Health Problems, 10th revision) codes. We also performed a targeted-screen in which plasma tau reactivity of 47 patients with AD was compared to 98 similarly aged controls.

Results: Using data from 21,995 patients, we found no association between plasma tau autoimmunity and neurological disease, including dementia, stroke or traumatic brain injury. A targeted screen, using samples of AD patients and non-neurodegeneration controls also did not show a significant difference in tau autoimmunity between the two groups.

Conclusion: Using data from >20,000 university hospital patients, we found no evidence that the presence of plasma autoantibodies directed against the microtubule-binding domain of tau protein is associated with AD or other neurological disorders.

EPO-195

Predictive value of anti-titin antibodies in myasthenia gravis patients with underlying thymus pathology

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Background and aims: Myasthenia gravis (MG) is frequently associated with thymus pathology, ranging from hyperplasia to malignancy. Anti-titin antibodies are predictive of thymoma in early onset generalized MG series. Our aim is to assess the value of anti-titin antibodies in predicting underlying thymus histopathology in the population of patients followed in the outpatient clinic of a tertiary referral hospital.

Methods: Retrospective analysis through an institutional registry of all MG patients followed between 2000 and 2021. The histological pattern of thymectomy samples was collected from clinical registries.

Results: A total of 230 patients were identified, with a mean age of onset of symptoms of 42.00 years (IQR 27.0-65.0). Of the 132 that tested for anti-titin antibodies, 32 cases (13.9%) were positive. In total, 85 (37.0%) patients underwent thymectomy: 36 cases had thymus hyperplasia (15.7%) and 30 had thymoma (13.0%). Older age of symptom onset (>50 years) was associated with thymoma, while thymus hyperplasia was more present in patients with onset <50 years (p<0.001). Anti-titin positivity was significantly associated with older age of symptom onset (p<0.001) (table 1.). There was a tendency towards anti-titin positive patients having more thymoma while anti-titin negative displayed more hyperplasia (p=0.01). A subanalysis accounting for age of onset showed that anti-titin positivity also correlated with thymoma in <50 years (p=0.028).

	Anti-titin negative N=100 (43.5%)	Anti-titin positive N=32 (13.9%)	p
Demographic data			
Female sex	66 (50.0)	18 (13.6)	0.40
Age, median (IQR)	39.5 (25.5-61.5)	63.0 (44.5-70.5)	<0.01
Diagnostic data			
Positive EMG	69 (52.3)	23 (17.4)	0.48
Positive anti-AchR	66 (50.0)	26 (19.7)	0.26
Thymectomy	39 (29.5)	12 (9.1)	1.00
Thymoma	9 (6.8)	10 (7.6)	0.01
Thymus hyperplasia	17 (12.9)	2 (1.5)	

From the total sample, 98 (42.6%) patients were not tested for anti-titin.
IGQ – Interquartile range; EMG – Electromyography; AchR – Acetylcholine receptor

Table 1. – Comparison myasthenia gravis patients based on anti-titin positivity

Conclusion: The presence of anti-titin antibodies appears to correlate with the presence of underlying thymoma, even when accounting for age of symptom onset. Larger series are needed to approve this association and the utility of anti-titin as a suitable biomarker.

Disclosure: The authors have nothing to disclose.

EPO-196

Impact of relapsing-remitting multiple sclerosis on sleep quality and quality of life

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Background and aims: Multiple sclerosis is a neurological disorder characterized by demyelinating lesions of the central nervous system, which causes a wide range of neurological deficits. It is the most common neurological cause of invalidity in young adults, with an impact on mobility, cognition, and sleep quality. Our aim was to assess the impact of severity of multiple sclerosis on sleep quality and subsequently on life quality.

Methods: We conducted a cross-sectional study on 30 patients with relapsing-remitting multiple sclerosis. Sleep quality was assessed using Pittsburgh Sleep Quality Index (PSQI), and quality of life using the Short Form (36) Health Survey (SF-36).

Results: Demographic characteristics of patients can be seen in (Table 1.). 20 (67%) patients had impaired sleep quality (PSQI score>5), while 10 (33%) patients had good sleep quality. Quality of life subscores on the SF-36 survey can be seen in Table 2. There was a significant negative correlation between sleep quality and quality of life, especially regarding mental health subscores, as seen in Table 3.

		N	%/Median	IQR
Sex	**Male**	11	36,66%	
	Female	19	63,33%	
Age (in years)		30	45	24-64
Age at first onset of simptoms (in years)		30	32	12-51
Age at diagnosis of MS (in years)		30	35	18-57
Number of relapses in last year		30	1	0-1
EDSS		30	4	2-6

IQR – interquartile range

Table 1. Patients' demographic characteristics

		Median	*IQR*
Physical health	**Physical functioning**	45	10-73
	Role limitations (physical)	13	0-75
	Bodily pain	40	0-90
	General health perceptions	51	10-92
Mental health	**Energy/vitality**	50	30-61
	Social functioning	50	25-66
	Role limitations (emotional)	33	0-100
	Mental health	58	46-72
	Physical health	42	29-52
	Mental health	42	25-72

IQR-interquartile range

Table 2. Average SF-36 scores

		Spearman Rho correlation coefficient (correlation with PDSQI)	P*
Physical health	Physical functioning	-0,275	0,14
	Role limitations (physical)	-0,178	0,35
	Bodily pain	-0,457	0,01
	General health perceptions	-0,354	0,06
Mental health	Energy/vitality	-0,661	<0,001
	Social functioning	-0,618	<0,001
	Role limitations (emotional)	-0,465	<0,01
	Mental health	-0,490	0,006
	Physical health	-0,560	0,001
	Mental health	-0,709	<0,001

*Spearman's correlation

Table 3. Correlation between PDSQI and SF-36 scores

Conclusion: Multiple sclerosis has a large impact on the quality of sleep, with 67% of examinees with inadequate sleep quality. These patients also have impaired quality of life, especially regarding mental health and social functions. Measures aiming at the improvement of sleep quality should be recommended to patients with MS.

Disclosure: Authors have nothing to disclose.

EPO-197

Retinal degeneration in Myelin Oligodendrocyte Glycoprotein-associated disease: a single centre italian study

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Background and aims: Data about Optical Coherence Tomography (OCT) features in patients with Myelin Oligodendrocyte Glycoprotein-antibody associated disease (MOG-AD) are still lacking. We investigated MOG-ab titres and OCT features in a cohort of MOG-AD patients.

Methods: We obtained OCT scans from MOG-AD patients referring to IRCCS Mondino Foundation(Pavia). Patients were divided into groups, according to MOG-ab titres at disease onset: low-titre-LT ($\leq$1:640) and high-titre– HT ($\geq$1:1,280). We collected clinical characteristics at disease onset and compared retinal nerve fiber layer (RNFL) and ganglion cell layer (GCL) thicknesses among the two groups.

Results: Our cohort was made up of 8 patients (male/female: 1/7). Mean age was 39 years (SD 11.7). At disease onset, myelitis occurred in 2 patients while 6/8 patients experienced optic neuritis (ON). Four/8 patients showed high MOG-ab titres at disease onset, belonging to the HT group. OCT scans were obtained at a mean time of 4 years (SD 3.7) from disease onset. Considering 6 eyes with history of ON, mean GCL thickness was lower in the HT (77 µm, SD 9.7) than in the LT (82.7 µm, SD 1). Among 8 unaffected eyes, RNFL thickness was similar between groups (96 µm - SD 7.3 - in LT versus 97 µm – SD 15.6 - in HT), while GCL thickness was lower in HT group (79 µm, SD 10.5) than LT group (84 µm, SD 4.9).

Conclusion: Even in patients without history of optic neuritis, MOG-ab titres at disease onset could be related to retinal damage, reflecting a subclinical retinal degeneration. Moreover, GCL parameter could be considered more reliable than RNFL in assessing retinal damage.

Disclosure: Nothing to disclose.

EPO-198

Comparison of fixed and live cell based assay for the serological diagnosis of Myasthenia Gravis

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Background and aims: The study aim was to analyse the performance of live and fixed cell-based assay (CBA) in the serological diagnosis of myasthenia gravis (MG).

Methods: MG serum samples pre-selected according to radioimmunoassay (RIA) results and stored at -20°C until use were tested with live CBA (L-CBA) employing HEK293 cells transfected with adult/foetal AChR or MuSK and the commercial fixed CBA (F-CBA) (Euroimmun, Lubeck). Two blinded independent raters assessed the assays. The results of F-CBA and L-CBA were compared with McNemar's test. Interrater agreement was evaluated with Cohen's kappa.

Results: 86 samples from MG patients were tested, including 21 AChR-RIA-positive, 21 MuSK-RIA-positive and 44 RIA-negative samples. L-CBA was positive in all RIA-positive cases, while F-CBA was positive in all RIA-positive sera but one MuSK-RIA-positive sample. Of the 44 RIA-negative sera, 14 (31.8%) were positive on L-CBA (9 for AChR antibodies - Abs, 5 for MuSK Abs) and 9 (20.5%) resulted positive on F-CBA (8 for AChR Abs, 1 for MuSK Abs). All F-CBA positive samples were also positive on L-CBA. Although both assays were effective in detecting Abs in RIA-negative MG patients, L-CBA was significantly more sensitive than F-CBA (p=0.0313). Interrater agreement was 98.9% for L-CBA (Cohen's kappa: 0.975, 95% C.I.=0.926–1.000) and 97.5% for F-CBA (Cohen's kappa: 0.955, 95% C.I.=0.893–1.000).

Conclusion: L-CBA was more sensitive than F-CBA in the detection of both AChR and MuSK Abs. Interrater agreement was excellent for both assays. While F-CBA may be a valuable alternative to RIA, L-CBA could be reserved to the diagnostic workup of RIA and F-CBA negative samples.

Disclosure: Nothing to disclose.

EPO-199

Abstract withdrawn

Neuro-oncology 1

EPO-200

Genome-driven medicine for patients with recurrent glioma enrolled in early phase trials

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Background and aims: Recent studies showed that patients with glioma can safely participate in early phase clinical trials; however, clinical benefits in this population were limited. We aimed to evaluate the benefit of molecular profiling to guide enrolment in early phase trials for patients with recurrent glioma.

Methods: Records of patients enrolled in early phase trials from 2008 to 2018 were reviewed for clinico-pathological characteristics, toxicity, response, progression-free survival and overall survival (OS). The primary objective was to evaluate response rates in molecularly-oriented versus non-molecularly-oriented patients.

Results: 88 patients were enrolled, of whom 45 (51.1%) patients were molecularly-oriented. Targets included IDH1/2 (n=15), BRAF (n=11), and FGFR1 (n=3) mutations, FGFR2-3 fusions (n=9), and mismatch repair deficiency (n=7). Among patients with high-grade glioma (n=74), the rate of stable disease ≥6 months and partial or complete response was 25.7% in molecularly-oriented versus 5.1% in non-molecularly-oriented patients (p=0.02). Upon multivariable adjustment, baseline steroid use ≥20 mg prednisone equivalent per day was associated with shorter OS (OR 3.15 [95% CI 1.62–6.13], p=0.0008), while molecular enrichment strategy was associated with longer OS (OR 0.40 [95% CI 0.22–0.73], p=0.003). Nine (10.2%) patients experienced grade 3–4 toxicity and no dose limiting toxicity (DLT) occurred in both cohorts.

Conclusion: The use of molecular profiling to guide enrolment in early phase trials is feasible and might provide benefits to selected patients with glioma. Further studies are warranted to confirm these results.

Disclosure: Nothing to disclose.

EPO-201

Reactive lymphoid follicular hyperplasia mimicking subdural hematoma

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Background and aims: Reactive lymphoid follicular hyperplasia is a benign lymphoid follicles proliferation. It can be present in the central nervous system (CNS), being part of the differential diagnosis of meningiomas or CNS lymphoma. It is also known as pseudolymphoma. Histologically it may present characteristics of Castleman Disease, such as vascular proliferation and vessel wall hyalinisation.

Methods: We describe the case of a 48 years old woman, with left hemicranial headache for five days. She had a history of left orbital, mucosal associated lymphoid tissue lymphoma, treated with radiotherapy (36Gy, 20 fractions) one year before. On brain-CT, a subdural right frontal hyperdense collection was observed. The following MRI confirmed the presence of this lesion, which was isointense in T1, slightly hyperintense in FLAIR and with uniform contrast uptake. The frontal polar pachymeninges were contrast enhanced, a finding compatible with lymphoproliferative origin. Lumbar puncture was innocent, without neoplastic cells. Surgical removal was performed, with the intraoperative pathology examination being suggestive of low grade non-Hodgkin lymphoma. Slides revision showed clonality absence and the presence of reactive lymphoid follicular hyperplasia with "Castleman-like" features, without HHV-8 expression. On bone marrow examination, no evidence of lymphoma invasion was documented and systemic staging was normal. Thus, the dural lesion was considered to be an inflammatory pseudotumor. 14 months after surgery, the patient shows no evidence of relapse.

Results: N/A

Conclusion: Reactive follicular hyperplasia and more malignant conditions, such as dural lymphomas, may be similar on imaging techniques to subdural hematomas. These etiologies should be considered to its different therapeutic and prognostic implications.

Disclosure: Nothing to disclose.

EPO-202

The result of surgical treatment of patients with mr-signs of spontaneous regression of vestibular schwannoma

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Background and aims: Vestibular schwannomas are the most frequent among all neoplasms of the cerebellar angle. Spontaneous regression is confirmed if the tumor has decreased in size by 2 mm or more between the first and last MRI images in at least one of the presented diameters. However, surgical treatment is the preferred tactic of choice.

Methods: A clinical study of 27 patients with vestibular schwannomas was conducted in the period 2016–2021. The studied patients were aged from 23 to 67 years. All patients had a histologically confirmed diagnosis of schwannomas. We used the described Lahlou G.et al. (2019) MR-signs of spontaneous regression: scalloped edges of the tumor and filling of the internal auditory canal (IAM) with cerebrospinal fluid. These signs were applied to all the studied patients before surgery and within 2 years from the moment of surgical treatment.

Results: Among the studied patients, 26% of patients (n=7) had one of two MR signs of spontaneous regression in the preoperative period. Among all patients - in the postoperative period, a recurrence of the formation was observed in 6 patients. Of all cases of relapses – in 67% of cases, these were patients with a preoperative picture of spontaneously regressing vestibular schwannoma (50% of them with a relapse in the first 3 months after surgery, 17% with a relapse in the first 6 months after surgical treatment) (p<0,05).

Conclusion: The detection of MR signs of spontaneous regression of vestibular schwannoma is an important prognostic factor at the preoperative stage.

Disclosure: Nothing to disclose.

EPO-203

Assessment of the probability of recurrence of craniopharyngiomas in adults after surgery using MR classification

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Background and aims: Craniopharyngiomas are benign epithelial tumors that develop from the remnants of the cells of the Ratke pocket connecting the primary oral tube cavity with the pituitary gland in the embryonic period. Among all intracranial formations in adults, craniopharyngiomas account for 2–5%. According to statistics, craniopharyngiomas are epithelial tumors, but despite their histologically benign nature, with complete removal, they recur in 30% of cases within 10 years after surgery.

Methods: A clinical study of 20 patients with craniopharyngiomas was conducted. The studied patients were aged from 19 to 71 years. All patients had a histologically confirmed diagnosis of craniopharyngioma. The classification of Prieto R., Pascual J.M. (2008) was used as an MR classification. All the studied patients underwent surgical treatment using transsphenoidal endoscopic approach. The assessment was carried out in the preoperative period and 3–6 months after surgical treatment.

Results: Recurrence of the formation in 10% with total removal of the tumor (CTR). Continued growth occurred during the first 3 months after surgical treatment after subtotal removal (SGR) (15%). Recurrence of the formation occurred in patients with adhesion of craniopharyngioma to the ependymal lining of the bottom of the 3rd ventricle, with adhesion according to the of fusion and replacement, with serious and severe adhesion (p<0.05).

Conclusion: The severity and strength of adhesion of craniopharyngioma are significant MR signs of recurrence of craniopharyngioma in the postoperative period.

Disclosure: Nothing to disclose.

EPO-204

Does glioblastoma recurrence affect anxiety level? A six-month longitudinal study

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Background and aims: Glioblastoma is associated with a limited survival, underlying the need for greater attention on health-related quality of life (QoL) and mood disorders. In this study, we prospectively assessed anxiety levels in a cohort of patients during the adjuvant phase of temozolomide (TMZ) (after radiotherapy).

Methods: We prospectively collected data from patients with newly diagnosed glioblastoma after standard TMZ chemoradiotherapy. Anxiety was assessed using the State part of the State-Trait Anxiety Inventory, QoL with the Cancer Quality of Life Questionnaire 30 and Brain Cancer Module-20 (BN-20) and depressive symptoms using the Hospital Anxiety and Depression Scale. Patients completed the questionnaires at the beginning of adjuvant TMZ, then 3 and 5 months later.

Results: 45 patients were included (mean age 57 ± 12 years, 24% female; median Karnofsky performance status 90%). At baseline, 39% of patients reported a pathological level of anxiety ($>44/60$) versus 15% in the general population. Anxiety was positively correlated with female sex and the presence of a caregiver, but not with age, marital status, education level, tumour localization, or presence of depressive symptoms. On follow-up, the anxiety, depression and BN-20 scores were remarkably stable, even in the 19 patients who experienced recurrence.

Conclusion: During the maintenance TMZ chemotherapy, the prevalence of anxiety in glioblastoma patients is high, being more frequent in women and in patients with a caregiver. Recurrence did not significantly worsened anxiety in this series.

Disclosure: Nothing to disclose.

EPO-205

In vivo 2-hydroxyglutarate monitoring with edited MR spectroscopy for the follow-up of IDH mutant diffuse gliomas

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Background and aims: D-2-hydroxyglutarate (2HG) characterizes IDH-mutant gliomas and can be detected and quantified with edited MRS (MEGA-PRESS). Here, we investigated the clinical, radiological, and molecular parameters affecting 2HG detection.

Methods: MEGA-PRESS data were acquired in 71 patients with glioma (24 untreated, 47 treated) on a 3 T system. Eighteen patients were followed during cytotoxic (n=12) or targeted (n=6) therapy. 2HG was measured in tumor samples using gas chromatography coupled to mass spectrometry (GCMS).

Results: MEGA-PRESS detected 2HG with a sensitivity of 95% in untreated patients and 62% in treated patients. Sensitivity depended on tumor volume (>27 cm^3; p=0.02), voxel coverage ($>75\%$; p=0.002) and expansive presentation (defined by equal size of T1 and FLAIR abnormalities, p=0.04). 2HG levels were positively correlated with IDH-mutant allelic fraction (p=0.03) and total choline levels (p<0.001) and were higher in IDH2-mutant compared to IDH1R132H-mutant and non-R132H IDH1-mutant patients (p=0.002). In patients receiving IDH inhibitors, 2HG levels decreased within a few days, demonstrating the on-target effect of the drug, but 2HG level decrease did not predict tumor response. Patients receiving cytotoxic treatments showed a slower decrease in 2HG levels, consistent with tumor response and occurring before any tumor volume change on conventional MRI. At progression, 1p19q codeleted gliomas, but not the non-codeleted, showed detectable in vivo 2HG levels, pointing out to different modes of progression characterizing these two entities.

Conclusion: Megapress edited MRS allows in vivo monitoring of 2-hydroxyglutarate, confirming efficacy of IDH inhibition and showing different patterns of tumor progression in astrocytomas compared to oligodendrogliomas.

Disclosure: Nothing to disclose.

EPO-206

Primary Diffuse Leptomeningeal Gliomatosis Mimicking tuberculous pachymeningitis

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Background and aims: Primary diffuse leptomeningeal gliomatosis (PDLG) is a rare neoplastic disease, characterized by an insidious clinical symptomatology and non-specific imaging which often leads to misdiagnosis.

Methods: We report the case of a patient with a clinico-radiological presentation initially suggestive of tuberculous pachymeningitis: a 10-year-old child who presented headache, vomiting, and diplopia with esotropia of the left eye which spontaneously regressed in 15 days. Five months later, he rapidly developed neck pain and stiffness, paraplegia with urinary incontinence, and decreased visual acuity without fever. Magnetic resonance imaging (MRI) showed diffuse meningeal thickening and several non-contrasting supratentorial and subtentorial hypersignals. Cerebrospinal fluid (CSF) analysis showed, protein 37g/l, glucose 0.21g/l, with normal cellularity. Tuberculostatic drugs combined with corticosteroid therapy was initiated. However, the weakness continued to worsen reaching the upper limbs, with blindness, and seizures. A biopsy of the spinal meninges was performed, revealing the diagnosis of a PDLG, which justified palliative chemotherapy.

Magnetic resonance imaging of spinal cord (parasagittal T1 with gadolinium): meningeal thickening of spinal cord with gadolinium enhancement.

Magnetic resonance imaging of spinal cord (parasagittal T2): meningeal thickening of spinal cord with cervical spinal hypersignal .

(a) Hematoxylineosin stain, (b) Positive staining of tumour cells with OLIG 2 antibody, (c) Diffuse inmunostaining for glial fibrillary acid protein (GFAP).

Results: Less than 100 cases of PDLG have been reported in the literature. This rare neoplastic disease, with a poor prognosis, is often diagnosed lately or in post-mortem. It can affect both children and adults. Generally, the non-specific clinical, biological and radiological presentation can be confounded with other differential diagnoses, especially tuberculous meningitis and pachymeningitis.

Conclusion: Our case illustrates the difficulty in making the diagnosis, and the importance of the meningeal biopsy which represents the key investigation to provide histological confirmation and to guide the therapeutic management.

Disclosure: to consider the diagnosis of the Primary Diffuse Leptomeningeal Gliomatosis in the presence of pachymeningitis.

EPO-207

Multiple myeloma presenting with autoimmune myaesthenic syndrome as an initial symptom- A case report

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Background and aims: Multiple myeloma (MM) is the most frequent malignant plasma cell disorder that is characterized by skeletal lesions, anemia, hypercalcemia and renal failure. The most commonly seen neurological complications in MM are peripherally neuropathy, radiculopathy, spinal-cord compression, leptomeningeal myelomatosis, stroke and drug-related neurotoxicity. Very rarely, maysethenia gravis (MG) may precede symptoms of MM as an autoimmune neurological complication.

Methods: A 58 year old male patient presented to our clinic with acute diplopia, right-sided ptosis and headache. He underwent neurological and physical examinations, Nerve conduction studies (NCS), repetitive nerve stimulation (RNS), cerebrospinal fluid (CSF) studies, MG antibody tests, tumor markers, 24 hour urine proteins test, test for M-protein and imaging studies of the brain and lungs.

Results: Brain imaging studies showed no significant abnormalities. Neurological examination revealed only unilateral ptosis at first examination followed by slightly pronounced dysphonia, generalized weakness and dysphagia a month later. NCS and CSF studies were normal. RNS performed on the nasalis, trapezius and abductor digiti minimi muscles showed a decrement of $>10\%$, but he was seronegative for tested MG-antibodies. He had elevated protein levels in his 24 hour urine test, as well as abnormal results in renal function tests. Lung imaging studies revealed a nodular lesion, which on histological examination confirmed the diagnosis of multiple myeloma.

Conclusion: We report a rare case presenting with autoimmune myasthenic syndrome as an initial symptom of multiple myeloma. Prognosis depends on the speed of disease progression, the stage of haemopathy and the extent of neuro-muscular damage.

Disclosure: Nothing to disclose.

EPO-208

A Case Report of Turcot Syndrome with high microsatellite instability (MSI)

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Background and aims: Lynch Syndrome highly predisposes patients to develop colorectal and endometrial cancer, and increases the risk to develop multiple other cancer types including primary brain tumor and skin cancer. It is caused by germline mutations in DNA mismatch repair (MMR) genes resulting in an accumulation of mutations in microsatellites called MSI. Turcot syndrome is the association of primary brain tumor with colorectal cancer and can genotypically be either secondary to MMR gene defects or APC gene mutations.

Methods: A 36 years old male patient developed adenocarcinoma of the sigmoid colon. He received extended left hemicolectomy and chemotherapy, showing no colorectal tumor recurrence since then. However at the age of 40, he was diagnosed with an anaplastic astrocytoma grade III. He received neurosurgical subtotal resection, and standard radiochemotherapy showing stable disease until now. At the age of 41 the patient also developed melanoma, which was successfully removed in total.

Results: MSI screening of the resected colon sample showed a MSI high (MSI-h) tumor suspicious for Lynch syndrome. A genetic testing for germline mutations in the Turcot Syndrome associated genes has been performed. Immune checkpoint inhibitor (ICI) therapy is planned.

Conclusion: Different studies demonstrated that several cancers with MMR deficiencies are sensitive to ICIs. However, not many studies have been done on ICI use in MSI-h brain tumors, but there have been some case reports of MSI-h brain tumors that benefited from it. Therefore, the possibility of hereditary germline mutations should be considered in young brain tumor patients with a cancer history.

Disclosure: Nothing to disclose.

EPO-209

Abstract withdrawn

EPO-210

Reduction of monocular visual acuity – pituitary apoplexy

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Background and aims: Pituitary apoplexy is an uncommon pathology, which usually manifests with thunderclap headache, visual changes, and symptoms of hypopituitarism. Thunderclap headache is the most frequent presentation form, followed by visual changes. This triad usually develops within 24–72 hours, but less frequently it can have a subacute presentation.

Methods: A 32-year-old hypertensive male presented with 1,5-month evolution of insidious and slowly progressive visual change, corresponding to a scotoma in the lateral portion of the right eye visual field. He denied pain or dyschromatopsia. The onset of the clinical picture was accompanied by a mild occipital headache, admitted in the context of hypertensive crisis, for which he was medicated, with complete headache remission. The ophthalmology examination documented significant reduction of the right eye visual acuity. The neurological examination revealed no other abnormalities. Head CT showed a sellar and suprasellar mass, causing superior deviation of chiasm and stretching the optic nerves. Brain MRI also revealed T2 hyperintensity of chiasm's right portion, with extension to the adjacent ipsilateral optic nerve. Laboratory testing disclosed hypothyroidism and hyperprolactinemia. He was diagnosed with pituitary apoplexy and underwent lesion excision by endoscopic endonasal transsphenoidal approach, with complete recovery of the visual deficit.

MRI (sagittal T1) evidencing a mass that causes superior deviation of chiasm and stretches the optic nerves

Results: N/A

Conclusion: We present a case of atypical manifestation of pituitary apoplexy, given the insidious onset and slowly progressive evolution of monocular impairment. We intend do evidence that, being a neurological emergency, the diagnosis requires rapid recognition of symptoms and a high level of suspicion, especially in the presence of predisposing factors such as hypertension.

Disclosure: Nothing to disclose.

Head CT showing a sellar and suprasellar mass with heterogeneous densities, including areas of spontaneous hyperintensity

EPO-211

The wide prognostic spectrum of melanotic intracranial lesions: the particular case of a trigeminal melanotic schwannoma

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Background and aims: Peripheral nerve tumors are histologically heterogeneous and range from benign to highly malignant lesions. They can develop sporadically or be a part of several genetic syndromes.

Methods: Case report

Results: A 42-year-old male, with unremarkable previous medical history, was referred to a Neurosurgery Outpatient Clinic, due to a year-long decrease of right facial sensitivity. Upon neurological examination, facial hypoesthesia in the first and second divisions (V1 and V2) of the right trigeminal nerve was noticed. A brain MRI evidenced a space occupying lesion in the right cavernous sinus with hyperintense T1 and hypointense T2/FLAIR signal, maintaining signal with fat suppression, suggesting a melanin-rich lesion. A six-month later repetition showed lesion growth towards Meckel's cavum and the path of the right trigeminal nerve. A pigmented lesion was surgically removed, and the patient was further referred for stereotaxic radiotherapy. Neuropathological examination revealed a tumor with mixed of epithelioid and spindled cells, with great nuclear anaplasia, but without necrosis, mitotic activity or psammoma bodies. Immunohistochemistry was reactive for vimentin, S100, HMB-45 and Melan-A. A diagnosis of melanotic schwannoma (MSch) was proposed.

Conclusion: Intracranial MSch are a rare variant of schwannoma, composed of Schwann cells with melanocytic differentiation. They may carry worse prognosis than classical schwannomas, with higher recurrence and metastatic rates. Although not always an easy diagnostic, histomorphology and immunohistochemistry profile can allow this differentiation and distinction from highly aggressive lesions such as metastatic melanoma by showing positivity for both Schwann cell and melanocytic markers.

Disclosure: Nothing to disclose.

EPO-212

Frontal meningioma after cerebellar medulloblastoma: radiotherapy effect, genetic susceptibility or combination of both?

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Background and aims: Radiotherapy has the risk of developing secondary tumors several years after treatment, being meningiomas the most frequent reported. This risk is higher in patients with cancer susceptibility. Medulloblastomas comprise an heterogeneous group of embryonal tumors, which can be framed in a tumoral susceptibility syndrome.

Methods: A 26-years-old man, who was operated and received radiotherapy due to a typical cerebellar medulloblastoma at 19-years-old, presented headache and behavioral disruption. At 19, he was diagnosed of dyshidrosis. At 23, a supernumerary tooth was removed. At 24, a metacarpal enchondroma was detected. He has prominent frontal bossing and hyperthelorism. In the maternal side, there're several relatives with cancer. Uncle: gastric tumor at 55. Other uncle: esophageal tumor (non age reported). Aunt: breast tumor at 30. There isn't syndromic/genetic diagnosis.
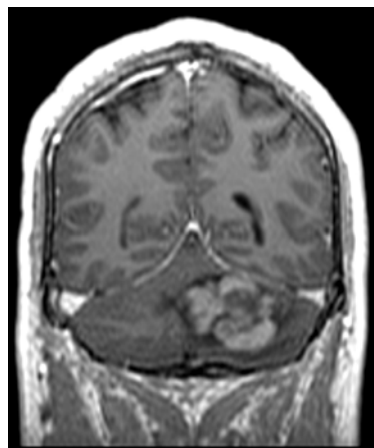
Typical cerebellar medulloblastoma

Perintense bone marrow lesion with cortical insuflation of the distal 2/3 of the 5th metacarpal in STIR sequence, showing guminous images inside. Enchondroma as final diagnosis

Results: Urgent brain CT: left frontal bulk with vasogenic edema. Brain MRI: extraaxial solid mass, T2-hyperintense with hypointese areas related with hematic focus and homogeneous contrast enhancement. Histological diagnosis: atypical meningioma, meningothelial subtype. Genetic panel: none pathogenic variants.
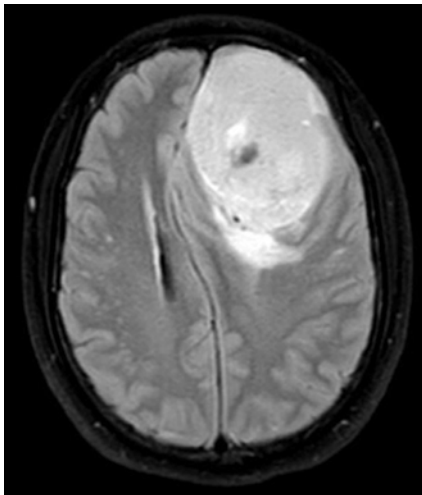
Hyperintense left frontal extraaxial mass T2-ponderated, with hypointense areas related with hematic focus and perilesional vasogenic edema. Meningioma as final diagnosis

Conclusion: Because of personal and family history, there're two main explanations for development of tumors histologically different: A radiotherapy effect or an underlying susceptibility. Gorlin-Goltz syndrome has a great clinical variability and 20-30% of patients don't have a family history. It's diagnosis can be clinical. Radiotherapy suppose a synergistic factor for develop a secondary tumor with a latency period about 3-10 years. Radiation induced meningiomas are atypical, aggressive, with faster growth and recurrence. We remark the need to perform a close follow-up to early recognition of secondary malignancies.
Disclosure: Nothing to disclose.

EPO-213

The spread of pituitary adenoma according to hardy and knosp as a recurrence factor in the postoperative period

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Background and aims: According to statistics, the frequency of recurrence of adenoma after transsphenoidal endoscopic removal is 25.8%. Surgical treatment of patients with pituitary adenomas is a serious problem of modern neurosurgery both due to the significant number of patients and due to the fact that the involvement of the most important anatomical structures in the pathological process causes the complexity of radical resection of the tumor with a minimum number of complications.
Methods: A clinical study of 280 patients with pituitary adenomas was conducted. The studied patients were aged from 24 to 72 years. All patients had a histologically confirmed diagnosis of pituitary adenomas. The classifications of Hardy and Vezin (HaVC – for patients with intra-and suprasellar spread) and Knosp (KS – for patients with parasellar invasion) was used as an MR classification. All the studied patients underwent surgical treatment using transsphenoidal endoscopic approach. The assessment was carried out before surgery and 6–12 months after surgical treatment.
Results: The recurrence rate is 7.14% after total removal of pituitary adenoma (CTR). Tumor recurrence occurred in patients with grade III-IV KS and grade IV HaVC (p<0.05). Subtotal removal (SGR) was in 2,9% of the subjects. Continued growth was observed during the first 1–3 months after subtotal removal.
Conclusion: Invasion III-IV by KS and the spread of Grade IV HaCV of pituitary adenoma are reliable prognostic factors of recurrence of the formation after 6-12 months, even in the case of total removal of the formation.
Disclosure: Nothing to disclose.

Neuro-ophthalmology/neuro-otology

EPO-214

Ocular contrapulsion followed by ipsipulsion in Wallenberg syndrome: the first case report in literature

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Background and aims: Wallenberg syndrome is a retro-olivar lesion in which disruption of fibers at the level of the lateral medulla leads to reduced excitation and inhibition of contralateral burst neurons, causing left hypermetric saccades and saccadic ipsipulsion.

Methods: Case report with information collected at the ischemic stroke unit of Santa Casa de Montes Claros, obtained by medical record review, interview with the patient during the ward consultation, and bibliographic review.

Results: A 51 year-old man started 5 days before admission with sudden presentation of permanent rotatory dizziness with unsteady gait and numbness in the left hemibody. On neurological examination, left palate paresis, incoordination on left side, horizontal jerk nystagmus with left fast fase and saccadic contrapulsion in ocular exam. CT brain showed left cerebellar hypodensity. Magnetic resonance imaging (MRI) showed diffusion restriction of dorsolateral left medulla and cerebellar suggestive of acute ischemic vascular insult. After 7 days of symptoms he reported intermittent and frequent hiccups treated with chlorpromazine. The ocular exam at this time reveled saccadic lateropulsion ipsilateral to lesion (ipsipulsion). This semiologic feature had not been decribed in literature until now.
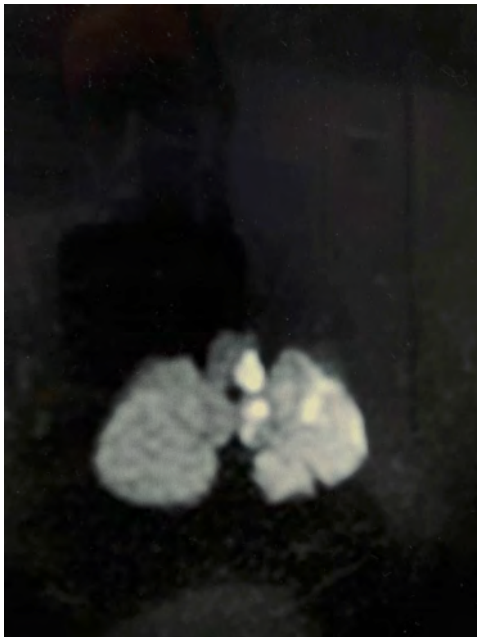
Conclusion: The presence of ocular ipsilusion is a forgotten feature in lateral medullary syndrome and the ocular contrapulsion is very rare in this setting. The initial presence of ocular contrapulsion followed by ipsipulsion had not seen until now in case reports. The exact mechanism is not understood.

Disclosure: Finally, this feature is important to help the professionals to think about lateral medulla topography and related circuits.

EPO-215

Slow stepping rate in the Unterberger test in Persistent Postural-Perceptual Dizziness (PPPD)

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Background and aims: PPPD incorporates features of phobic postural vertigo, space-motion discomfort, visual vertigo, and chronic subjective dizziness. History taking can be challenging in many cases and, therefore, positive signs might be necessary to establish the diagnosis. Here we followed the hypothesis that PPPD patients exhibit a marked slowness in their stepping rate during the conventional Unterberger test.

Methods: The Unterberger test was carried out in PPPD patients, in organic vestibular patients with various etiologies and in healthy volunteers. The number of steps was recorded for 30 seconds and multiplied by a factor of 2 to get the stepping rate per minute for each subject. ANOVA with post-hoc pairwise comparisons as well as ROC analyses were performed using the R 4.1.2.

Results: 23 PPPD patients (mean age: 49.7), 33 dizzy patients with various organic etiologies (mean age: 59.8) and 37 controls (mean age: 45.2) were analyzed. The mean stepping rate was 88.13±22.6 in PPPD, 124.79 ± 21.7 in organic patients and 122.27 22.0 in controls. Differences were highly significant ($p<0.001$) in comparisons of PPPD with controls and PPPD with organic patients, but not when comparing organic patients to controls. ROC curves revealed an optimal cut-off of 108 steps/min for both PPPD vs. controls (sensitivity 91%, specificity 78%) and PPPD vs. organic patients (sensitivity 91%, specificity 82%).

Conclusion: A stepping rate less than 108 steps/min, as obtained by counting steps during the Unterberger test, is a positive clinical sign with a high diagnostic value in PPPD.

Disclosure: Nothing to disclose.

EPO-216

The nosological entities of CRION and RION in the advent of Myelin Oligodendrocyte Antibody disease (MOGAD)

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Background and aims: The clinical and serological characteristics of chronic relapsing inflammatory optic neuropathy(CRION) and relapsing inflammatory optic neuritis(RION) are controversial.

Methods: Retrospective descriptive analysis of a cohort of 13 consecutive patients followed from 2000–2021 with atypical and recurrent ON, excluding patients with multiple sclerosis and anti-AQP4 positivity.

Results: Of 13 patients, 7 were male (54%). Median age of symptoms: 40 (29–47), one pediatric onset. Classification: 3 atypical isolated ON, one MOG-Ab positive. 9 CRION, 4 MOG-Ab positive. 1 RION, seronegative. On the first relapse, the left eye (OS) was affected in 7 patients, 2 had bilateral ON. 10 relapsing patients, 7 had a second relapse within 6 months of disease onset; in 6 ON affected the same eye. 3 patients had more than 6 relapses; all MOG-Ab positive. The corticosteroid(CE) response was excellent, 4 needed plasmapheresis in at least one relapse (3 MOG-Ab negative); 9 were CE-dependent. Nadir of visual acuity (VA) on relapses was ≤20/200 in 9 patients. 3 patients have final VA of 20/200; 2 CRION MOG-Ab positive, 1 RION. 92,30% patients had pathological optical coherence tomography. Oligoclonal IgG bands were negative in all. 9 patients received chronic immunosuppressive (IS) therapy, 8 with azathioprine. 4 needed escalation.

Conclusion: Atypical relapsing ON should be tested for MOG-Ab. MOG-Ab positivity was associated with a more relapsing course, variable response to IS therapy but similar response to CE, with a not so benign course, differing from prior reports, probably because of longer follow up. IS treatment should be given to minimize risk of relapses and to spare corticosteroids.

Disclosure: Nothing to disclose.

EPO-217

Emotional features and quality of life in patients with persistent postural-perceptual dizziness and vestibular migraine

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Background and aims: Psychiatric comorbidity, mainly anxiety and somatoform disorders are common in patients with vestibular migraine (VM). and patients with neurotic temperament or preexisting anxiety disorders appear to be at higher risk for developing persistent postural-perceptual dizziness (PPPD).

Methods: 30 patients with VM, and 30 patients with PPPD were given the Big Five Inventory (BFI) of personality traits, Beck depression and anxiety scales, the Somatic Symptom Scale-8 (SSS-8), the Short Form (36) Health Survey (SF 36) and Dizziness Handicap Inventory (DHI). Thirty healthy volunteers constituted the control group.

Results: Anxiety, depression and SSS-8 scores of the PPPD patients ($p<0.001$ for all) and anxiety (p: 0.026) and SSS-8 ($p<0.001$) scores of the VM patients were significantly high in comparison with the healthy controls. Neuroticism ($p<0.001$) was the significant trait for both patient groups. All sub-scores of the DHI and SF-36 were significantly affected ($p<0.001$).Comparison of the VM and PPPD patients revealed increased anxiety (p: 0.009) and SSS-8 (p. 0.005) scores in PPPD. Though the physical sub-scores of the DHI was not different between groups (p: 0.54), functional (p: 0.022) and emotional (p: 0001) scores were high in PPPD patients. Vitality (p: 0.002), emotional (p: 0.045) and social role functioning (p: 0.006) scores of the SF-36 were significantly worse in the same group.

Conclusion: PPPD patients had high levels of anxiety and somatic symptom burden. Though the physical handicap due to dizziness was similar with the VM patients they had more functional and emotional impairment reducing similar aspects of their quality of life.

Disclosure: Nothing to disclose.

EPO-218

Oscillopsia in patients with cerebellar ataxia and its relation to dynamic visual acuity

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Background and aims: Oscillopsia significantly affects the quality of life in patients with vestibulopathy. Recently, high prevalence of DVA impairment has been described in patients with cerebellar ataxia, where DVA impairment was related to the vestibular dysfunction. Our aim was to assess subjective severity of oscillopsia in CA and to evaluate its relation to the DVA and vestibular impairment.

Methods: We examined 32 patients with CA – 20 without vestibulopathy (CA-NV) and 12 with vestibulopathy (CA-V) and two control groups: 13 patients with bilateral vestibulopathy (BV) and 21 age matched healthy controls (HC). The subjects were examined by means of clinical DVA test, VOR was assessed by videoHIT. Subjective oscillopsia was assessed by our newly prepared and administered Oscillopsia severity scale. Relationship between OSC and DVA impairment in CA patients was examined by Pearson's product-moment correlations.

Results: Oscillopsia occurred in 56% of CA (58,3% of CA-V and 55% of CA-NV) compared to 76,9% BV and 0% HC. The oscillopsia severity score correlated significantly with DVA impairment during DVA test at 1 and 2 Hz (r=0,44 [0,23–0,61] and 0,56 [0,37–0,70] respectively in the full sample, and 0,57 [0,26–0,77] and 0,45 [0,11–0,70] respectively in ataxia group). CA-V patients reported similar severity of oscillopsia as patients with BV.

Conclusion: Oscillopsia might be an important cause of disability in CA patients. DVA and oscillopsia evaluation should be a part of clinical evaluation as this information can help to target vestibular and oculomotor rehabilitation.

Disclosure: Authors of this publication are member of the European Reference Network for Rare Neurological Diseases. The research was supported by Charles University Grant Agency, Project No. 608218; MH CZ – DRO, Motol University Hospital, Prague, Czech Republic Project No. 00064203; Institutional Support of Excellence 2. LF UK Grant No. 6990332.

EPO-219

Oculomotor features in CANVAS

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Background and aims: CANVAS (Cerebellar Ataxia, Neuropathy and Vestibular Areflexia Syndrome) is a late-onset, slowly progressive, autosomal-recessive disorder due to a biallelic intronic expansion in the RFC1 gene. Vestibular areflexia caused by vestibular ganglia degeneration is considered as a distinctive feature. Objective of this exploratory study is the assessment of the oculomotor system in a cohort of CANVAS patients.

Methods: Seventeen genetically-confirmed CANVAS patients were assessed by bedside oculomotor examination, including a "reading test" (with slowly sinusoidal head movements), and by video-oculography (EyeSeeCam), to explore lateral vestibulo-ocular reflex, smooth pursuit, optokinetic nystagmus, gaze holding and saccadic system.

Results: The patients were six males and 11 females (mean age: 66.9; range: 52–85; mean disease duration: 11 years; range: 1-33). The "reading test" was altered in 6/10 subjects (60%). The video-oculographic data were as follows: horizontal vestibulo-ocular reflex (VOR) impairment at video head-impulse test (vHIT) in 13/17 (77%), smooth pursuit impairment in 14/17 (82%); altered/absent optokinetic nystagmus (OKN) in 9/15 (60%); downbeat nystagmus (DBN) in 6/17 (35%), gaze-evoked nystagmus in 2/17 (12%), and mild-to-moderate saccadic dysmetria in 6/15 (40%). In 1 subject no clear oculomotor abnormality was found.

Conclusion: In CANVAS, characteristic oculomotor abnormalities consist of a varying combination of vestibulo-ocular hypo-/a-reflexia, marked reduction of smooth pursuit gain, reduction/lack of the OKN, DBN. These changes indicate a wider involvement of the vestibulocerebellum system, including flocculus and vestibular nuclei (beyond vestibular ganglia). The 'reading test' can be a simple test to identify vestibulo-ocular abnormalities at bedside.

Disclosure: Nothing to disclose.

EPO-220

The Spectrum of Bilateral Optic Neuropathy: a case series

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Background and aims: Bilateral optic neuropathies are uncommon presentations with a wide range of underlying aetiologies. The differential diagnosis includes autoimmune, infectious, toxic, and genetic causes. We aimed to review cases of bilateral optic neuropathy attending a neurology centre and describe the underlying clinical characteristics, diagnoses and investigations performed in this cohort.

Methods: Patients presenting to St Vincent's University hospital, a tertiary referral centre in Dublin, Ireland, between January 2011 and August 2021 with sequential or simultaneous bilateral optic neuropathy were included. Hospital coding information was searched for Optic Neuritis, Optic Neuritis with demyelination and Other Optic Neuropathies.

Results: 33 patients with bilateral optic neuropathy were identified. The majority of patients were male (64%). The mean age at onset was 35 (range 8–63). The most common diagnoses included myelin oligodendrocyte glycoprotein antibody disease (MOGAD) (n=6) and multiple sclerosis (n=6), followed by neuromyelitis optica (n=3) and neurosyphilis (n=3). Other aetiologies included systemic sarcoidosis with neurological involvement, Leber's herediatary optic neuropathy, nutritional deficiency and chronic relapsing inflammatory optic neuropathy (CRION). In six patients (18%) no diagnosis was reached despite extensive investigations. MRI Brain was performed in 97% of patients and was abnormal in 37%. MRI orbit was performed in 73% of patients with optic nerve abnormalities detected in 75%. CSF sampling was performed in 78% of patients and abnormal in 46%.

Conclusion: Bilateral optic neuropathy is an uncommon clinical presentation with a diverse range of aetiologies. Our cohort revealed a male preponderance with inflammatory causes predominating. However, almost one fifth of cases remained idiopathic.

Disclosure: Nothing to disclose.

EPO-221

Cavernous sinus infiltration presenting with bilateral neuromyotonia and aberrant regeneration

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Background and aims: Oculomotor nerve palsies can complicate with abnormal tonic muscle spasms (neuromyotonia, NM) or paradoxical co-contraction of muscles, upon aberrant regeneration (AR). Both are associated with compressive etiologies, although usually present isolated.

Methods: We report a case of a left sixth (6NP) and right third nerve palsy (3NP) with simultaneous NMT and AR.

Results: A 58-year-old female with a refractory nasopharynx undifferentiated carcinoma treated with radiation and chemotherapy, presented with a 2-month history of binocular horizontal diplopia. On exam there was partial left abduction deficit, consistent with a left 6NP, in possible association with tumor extension to the cavum and/or cavernous sinus. At 1-month reassessment, 6NP resolved, but there was now right upper lid ptosis, pupil dilation, and limitation of supraduction, adduction and infraduction of the right eye, consistent with right 3NP. Mass expansion with infiltration of the right cavernous sinus, was assumed and confirmed on MRI. Importantly, after sustained leftward gaze, there was transient restriction of abduction of the right eye and adduction of the left eye, consistent with right medial rectus and left lateral rectus NM. The patient was started on carbamazepine 100mg twice daily with fully resolved NM after 2-months. On follow-up, upon downgaze, there was now reproducible right upper lid retraction, consistent with right third nerve AR.

Conclusion: Simultaneous bilateral NMT followed by AR is undoubtedly rare. Such co-occurrence suggests the presence of a probable shared pathomechanism (i.e., chronic compression and/or infiltration) between NM and AR, leading to abnormal excitation and maladaptation of the ocular motor nerve complex.

Disclosure: Nothing to disclose.

EPO-222

Characterization of patients with Central Retinal Artery Occlusion – Time is vision?

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Background and aims: Central Retinal Artery Occlusion (CRAO) is a rare form of IS that manifests as a sudden, painless monocular visual loss. The most frequent etiologies are carotid atherosclerotic disease, cardiogenic emboli and small-vessel disease. Current therapeutic strategies are slender and have unknown efficacy. We aim to characterize these patients their approaches in the Emergency Department (ER).

Methods: Analysis of patients observed in the ER with CRAO between 2017–2021.

Results: 29 patients with CRAO were included, 72% males, with an average age of 69 (±12). About 90% of patients had at least one known vascular risk factor, the most frequent hypertension (88%), followed by hypercholesterolemia (79%), diabetes (27%) and smoking (27%). About 28% (n=8) had a previous history of TIA or IS and 14% (n=4) had atrial fibrillation. A carotid artery screening was performed in 79% (n=23) of patients; 30% of these (n=7) had an ipsilateral carotid stenosis >50%, 57% of which (n=4) were treated (by stenting or endarterectomy). The average duration of symptoms until medical evaluation was 8.6h (±6.3), 34% of patients (n=10) having been observed within 4.5 h of symptom onset. Of these, only 20% (n=2) underwent thrombolytic treatment. 93% of patients (n=27) did acute-phase hyperbaric oxygen therapy, with a median of 5 sessions (2–6.5).

Conclusion: Despite being a form of IS, CRAO is not approached as such in the ER. There is a need to establish an organized system of urgent care, in partnership with Ophthalmology and Hyperbaric Medicine, to improve the management and outcome of these patients.

Disclosure: Nothing to disclose.

EPO-223

Video Head Impulse Test and Supression-Video Head Impulse Test in Vestibular Migraine

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Background and aims: We evaluated the vestibulo-ocular reflex (VOR) in patients with Vestibular Migraine (VM), in order to find out if their VOR differs from that of healthy controls (HCs) and if there is a relation between any VOR impairment and their vertigo frequency or motion sickness (MS).

Methods: We studied 56 VM patients and 53 HCs with video Head Impulse Test (HIMP) and Supression Head Impulse Test (SHIMP). We examined VM patients in an inter-ictal period and asked them about monthly vertigo frequency and MS history.

Results: There were no differences in mean HIMP or SHIMP gain between VM patients and HCs. In VM group, there were patients with low HIMP gain in individual semicircular canals (SCCs) but not in SHIMP gain. The number of VM patients with overt saccades in lateral SCCs in HIMP were higher in VM than HCs. (p<0.001) VOR gain of the lateral SCCs in HIMP were lower in patients with MS than patients without MS in VM. (p=0.012) In VM group, vertigo frequency did not differ between patients with low or normal VOR gain in HIMP. VOR gain of lateral SCCs were lower in SHIMP than HIMP in both groups.(p<0.001).

Conclusion: As a group our VM patients had normal mean VOR gain, but 30% of them had lower than normal HIMP gain from one or more individual SCCs. Difference between VOR gain of HIMP and SHIMP is attributed to VOR supression at the onset of head impulses in the SHIMP test and our results showed that it is intact in VM.

Disclosure: We report no dislosure relevant to the study.

EPO-224

Anxiety and psychosocial impairment in patients with central vestibular disorders

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Background and aims: There is increasing evidence of a close interrelation between vestibular and emotional brain networks that is not yet sufficiently understood. A recent study in patients with bilateral peripheral vestibulopathy (BVP) showed relatively low anxiety levels related to vertigo/dizziness compared to those in episodic vertigo, e.g. vestibular migraine (VM) or functional vertigo, despite their severe functional impairment [1]. These results led to the hypothesis that an intact peripheral vestibular system is a prerequisite for the development of vertigo-related anxiety (VRA). Our aim was to evaluate VRA and psychosocial impairment in patients with central vestibular disorders. The question was whether types of central vestibular dysfunction influence VRA.

Methods: Retrospectively 278 patients with pure central vestibular disorders (cerebellar oculomotor disorder/COD, n=65; cerebellar ataxia/CA, n=59; VM, n=154) were identified, who presented to our tertiary vertigo centre. 64 patients with served as a peripheral vestibular control group. All patients received neuro-otological examinations including detailed vestibular testing. The Vertigo Handicap Questionnaire (VHQ) was used to assess the effects of vertigo on quality of life in two subscales (anxiety/ psychosocial activity limitation).

Results: Central vestibular syndromes were associated with higher VHQ anxiety subscores (CA 2.42, p=0.036; VM 2.50, p=0.002) compared to BVP (2.07), although their psychosocial activity limitation did not differ significantly, despite in CA (p =0.011). No significant difference was found between BVP and OCD.
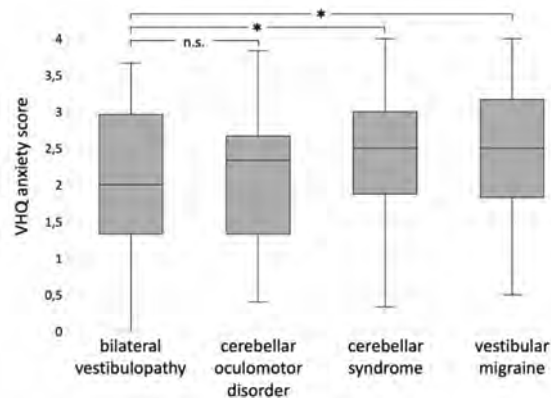
VHQ anxiety subscores.
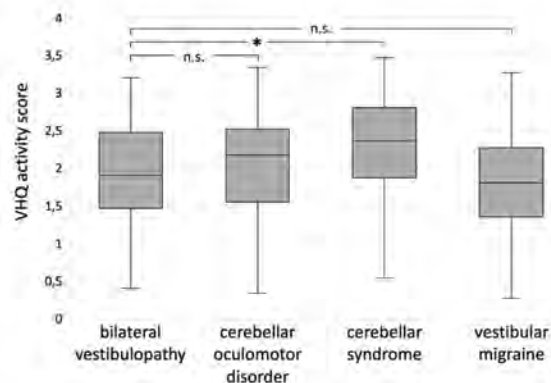
VHQ psychosocial activity limitation subscores.

Conclusion: Our data support the hypothesis that an intact peripheral vestibular system, as it is the case in patients with central vestibular disorders, is required for the development of VRA and psychological distress.

Disclosure: None. (1.) Decker et al., J Neurol 2019;

EPO-225

iPhone Exophthalmometry: A Novel Approach to Measure Eyeball Protrusion

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Background and aims: Accurate and reproducible measures of abnormal eyeball protrusion are important for the diagnosis of exophthalmos and following patients with Grave's orbitopathy and retroorbital masses like meningioma. The current clinical gold standard is the Hertel exophthalmometer, which is prone to reading errors and rather inconvenient to use.

Methods: 16 healthy volunteers and 23 patients with exophthalmos of different etiology were examined twice within an interval of minimum 2 weeks or after exophthalmos-changing treatment by 3 operators using an iPhone11 TrueDepth camera, a high-resolution 3D-face-scanner (Artec Space Spider), and a Hertel-exophthalmometer as reference. The obtained 3D-images from the scanners were further processed and analyzed using a custom exophthalmos analysis algorithm to determine the distance between the pupillary plane and the lateral orbital rim.

Results: Good accuracy and precision of the eyeball protrusion measurements using the 3D scanners on healthy individuals and patients, compared to the Hertel exophthalmometer, with interclass correlation coefficients (ICC) of 0.965 for the high-resolution scanner and 0.963 for the smartphone. We observed a high inter-rater agreement for both the high-resolution scanner (ICC of 0.998) and the smartphone (ICC of 0.983) as well as high test-retest reliability (ICC for Artec 0.967 and ICC for iPhone 0.935).

Conclusion: The results suggest high precision and accuracy, as well as a high inter-operator reliability and test-retest reliability for the novel scanning methods. Smartphone exophthalmometry makes measurement and follow-up of eyeball protrusion quick, easy and objective. Our mobile medical application holds promising potential to replace the traditional Hertel exophthalmometer in the future.

Disclosure: Nothing to disclose.

EPO-226

Worldwide survey on the treatment of peripheral vestibular disorders

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Background and aims: For the therapy of vestibular disorders, there are basically four treatment options: physiotherapy, pharmacotherapy, surgery and psychotherapy. The aim of this world wide survey was to evaluate the currently used treatment options of the six most frequent peripheral vestibular disorders: BPPV, acute unilateral vestibulopathy (AUVP), Menière's disease (MD), bilateral vestibulopathy (BVP), vestibular paroxysmia (VP) and superior canal deshiscence syndrome (SCDS).

Methods: A web-based standardized survey questionnaire on the treatment of the six most frequent peripheral vestibular disorders was used to collect data. 234 replies from five continents, 47 countries, 162 cities and 188 centers were received.

Results: As % from all 234 replies; multiple answers possible: BPPV: posterior canal: 71% Epley, 40% Sémont, and 12% others. Horizontal canal BPPV canalithiasis: 58%% roll-maneuver, 33% Gufoni. Horizontal canal cupulolithiasis: 35% Gufoni, 27% roll maneuver. AUVP: 79% pharmacotherapy, namely 47% glucocorticoids, 39% antiemetics, and 24% betahistine; 67% physiotherapy. MD: 85% pharmacotherapy, namely 65% betahistine, 21% diuretics, 14% gentamicin; 37% surgery. VP: 65% pharmacotherapy, namely 57% anticonvulsants. BVP: 77% physiotherapy. SCDS: 50% Surgery, namely 19% canal plugging, 12% capping, and 8% resurfacing.

Conclusion: In this world wide survey with 234 replies from 188 centers widely heterogeneous applied treatment options were reported for the six most frequent peripheral vestibular disorders. For example, medication use is often not supported by evidence. Namely in AUVP, MD and VP well designed controlled trials are needed with clinically meaningfull endpoints are needed.

Disclosure: M. Strupp is Joint Chief Editor of the Journal of Neurology, Editor in Chief of Frontiers of Neuro-otology and Section Editor of F1000. He has received speaker's honoraria from Abbott, Auris Medical, Biogen, Eisai, Grünenthal, GSK, Henning Pharma, Interacoustics, J&J, MSD, NeuroUpdate, Otometrics, Pierre-Fabre, TEVA, UCB, and Viatris. He receives support for clinical studies from Decibel, U.S.A., Cure within Reach, U.S.A. and Heel, Germany. He distributes "M-glasses" and "Positional vertigo App". He acts as a consultant for Abbott, AurisMedical, Heel, IntraBio and Sensorion.

Sleep-wake disorders & Autonomic nervous system diseases 1

EPO-227
Skin sympathetic responses in synucleinopathies

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Background and aims: Multiple system atrophy (MSA) is one of neurodegenerative diseases belonging to the group of synucleinopathies. A core symptom of MSA is an autonomic failure: urinary dysfunction and/or orthostatic hypotension. Autonomic failure may also be present in another common synucleinopathy, Parkinson's disease (PD). Similar clinical presentations of these two diseases require new approaches to differential diagnosis.

Methods: The studied cohort comprised 24 patients (17 females, 7 males, mean age 62.9 ± 7.0 yrs). Patients with MSA were divided into parkinsonian (MSA-P, n=8) and cerebellar (MSA-C, n=7) subgroups. The group of PD patients (n=9) was comparable by gender and age with the MSA group. To assess autonomic failure we used skin sympathetic responses (SSR) and orthostatic systolic BP (SBP) drop test.

Results: We found an increased SSR latency in the MSA group (p<0.01). There was no significant difference between groups in response amplitudes. A statistically significant correlation was found between the SBP drop in the orthostatic test and the latency (r=0.56, p<0.05).

Parameters	PD	MSA	
		MSA-P	MSA-C
Response threshold, mV	7.0 ± 0.7	6.3 ± 0.9	5.9 ± 0.9
Latency, s	$1.3\pm0.2^*$	$2.0\pm0.1^*$	$1.7\pm0.1^*$
Amplitude A1, mV	0.5 ± 0.2	0.5 ± 0.2	0.4 ± 0.2
Amplitude A2, mV	2.3 ± 0.9	0.6 ± 0.3	1.3 ± 0.7
SBP drop, mm Hg	$20\pm8.06^*$	$31.8\pm14.2^*$	$31.7\pm6.1^*$

(*p<0.05)

Table 1. Skin sympathetic responses and orthostatic test in PD and MSA groups
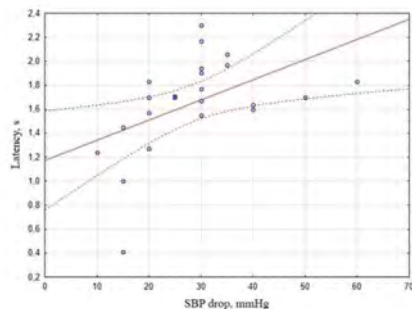
Figure 1. Relationship between SBP drop in orthostatic test and latency in SSR

Conclusion: The mechanisms of autonomic dysfunction in PD and MSA are thought to be similar and caused by alpha-synuclein accumulation. However, there is a difference between these diseases concerning the involvement of different parts of the autonomic nervous system. SSR indicates the degree of autonomic dysfunction, but their role in topical diagnosis is limited. Our results showed that SSR could be a promising tool to differentiate MSA and PD cases.

Disclosure: Authors declares nothing to disclose.

EPO-228
REM sleep and muscle atonia in brainstem stroke: a quantitative polysomnographic study

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Background and aims: Important brainstem regions are involved in the regulation of rapid eye movement(REM) sleep. We hypothesized, that brainstem stroke is associated with dysregulated REM sleep and related muscle activity(ma).

Methods: We compared quantitative/qualitative polysomnography features of REM sleep and ma(any, phasic, tonic) between 15 patients with brainstem stroke and 16 patients with lacunar/non-brainstem stroke. Further, in the brainstem group, we performed an MRI-based lesion overlap analysis. We compared both stroke groups with patients with Parkinson's disease and polysomnography-confirmed REM sleep behavior disorder (PDRBD group, n=7).

Results: In the brainstem group, the mean ratio of ma to REM sleep epoch was significantly lower than in the lacunar group ("any" ma 0.09 ± 0.12 vs. 0.15 ± 0.17, p-value<0.0001; phasic ma 0.08 ± 0.12 vs. 0.14 ± 0.16, p-value<0.0001). MRI-based lesion analysis indicated an area of maximum overlap in the medioventral pontine region for patients with reduced phasic ma index. For both stroke groups, mean values of ma were significantly lower than in the PDRBD group ("any" activity 0.51 ± 0.26, phasic ma 0.42 ± 0.21,p<0.0001 for both stroke groups). For the tonic ma in the mentalis muscle, no significant differences were found between the three groups. In the brainstem group, contrary to the lacunar group, "any" ma index during REM sleep was significantly reduced after the third REM sleep phase.

Conclusion: This study reports on the impact of brainstem stroke on REM atonia features in a human cohort. Our findings highlight the important role of the human brainstem, in particular the medioventral pontine regions, in the regulation of phasic ma during REM sleep and the ultradian distribution of REM-related ma.

Disclosure: The authors have nothing to disclose.

EPO-229

A Turkish validity and reliability study of the Swiss Narcolepsy Scale

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Background and aims: The Swiss narcolepsy scale (SNS) was shown in three independent populations to have a high sensitivity and specificity for the diagnosis of narcolepsy with cataplexy (NT1). Here we aimed to investigate the Turkish validity and reliability of the SNS.
Methods: The Turkish SNS (SNS-TR) was tested in five different cities in Turkey. The power curve of a sample size of 25 per group showed a power of 90% with a difference of 5. The SNS-TR was administered to all participants once and repeated one month later by the same researcher to avoid bias in the interviews.
Results: 78 participants were involved; 26 patients (33.3%) had idiopathic hypersomnia, 21 (26.9%) had NT1, 6 (7.6%) had NT2; and 25 (32.1%) were healthy controls. The construct validity analysis showed that all five questions were above the critical value, and highly significantly valid. All patients with NT1 but two had a negative SNS-TR score. None of the other participants had an SNS-TR score <0 points. The sensitivity and specificity of the SNS-TR were 90.5% and 100%, respectively, for diagnosing NT1. The Cronbach's alpha analysis showed a high level of internal consistency. The ICCs demonstrated almost perfect agreement for the validity and reliability between two evaluations with 1-month intervals.
Conclusion: As there are only limited numbers of specialized sleep centres for narcolepsy in Turkey, the SNS, will be useful to screen patients with excessive daytime sleepiness and decide who should be referred to a specialised sleep centre for further assessments with the suspicion of narcolepsy.
Disclosure: Nothing to disclose.

EPO-230

Cardiovascular autonomic function in chronic insomnia assessed by cardiovascular reflexes

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Background and aims: The cardiovascular autonomic nervous system is closely linked to sleep and circadian physiology. The purpose was to evaluate cardiovascular autonomic functions during wakefulness in de novo patients with chronic insomnia (CI) compared to healthy controls (HC).
Methods: De novo patients with CI and HC underwent cardiovascular function tests including head-up tilt test, Valsalva Maneuver, deep breathing, hand grip, and cold face.
Results: 18 de novo patients with CI and 13 HC were included. The systolic blood pressure (SBP) values at 10 min head-up tilt test were significantly higher in patients with CI than in controls (p<0.031), while heart rate (HR) values at 10 min head-up tilt test were significantly lower in patients than in controls (p<0.034). Furthermore, at Valsalva Maneuver, the Valsalva Ratio values (VR) were significantly lower in patients with CI compared to controls (p<0.046), although without reaching pathological values.
Conclusion: Although these values are not suggestive of hypertension, the data emerged suggest the presence of a systolic pre-hypertension that is known to increase the risk of cardiovascular diseases. The VR is an index of parasympathetic function representing the vagal component of the baroreflex. It was reduced in our sample, so we can speculate that the predisposition to hypertension in CI may be favored by a blunted parasympathetic response to changes in blood pressure. These findings support the hypothesis of autonomic nervous system involvement during wakefulness and consequently an enhanced cardiovascular risk in patients with CI.
Disclosure: I have no conflicts of interest to disclose.

EPO-231

SPHYNCS: Longterm monitoring with Fitbit in patients with narcolepsy and its borderland

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Background and aims: The multicenter Swiss Primary Hypersomnolence and Narcolepsy Cohort Study (SPHYNCS) aims to identify novel biomarkers for narcolepsy and its borderland (NBL). Ambulatory monitoring in narcolepsy and NBL is limited in clinical routine to actigraphy over 1–2 weeks. Fitbit devices have been shown to monitor one-year circadian rhythm parameters. This study aims to identify new digital biomarkers of narcolepsy and NBL using a Fitbit device over months.

Methods: Of the 72 subjects so far enrolled in the SPHYNCS study, 60 participants agreed to wear a Fitbit device. We performed a long-term analysis on the total time the device was worn. Next, we selected the two weeks in which the Fitbit was worn most consistently for each patient. 37 participants were included in the two-week analysis.

Results: The 60 participants (13 males, 47 females) with an average age of 29 years (range 17–56) received the Fitbit. We have collected overall 31 years of Fitbit data, with a patients' compliance of 65%. According to diagnosis, there was a significant difference in compliance (75%: controls; 62% NBL; 38%: narcolepsy). In the preliminary two-week analysis, sleep efficiency and duration were similar among the groups (p-value 0.35 and 0.57, respectively).

Conclusion: Preliminary results of this ongoing study suggest that using a Fitbit in narcolepsy and NBL for an extended period exhibits significant individual differences. Differences shown in sleep parameters need to be correlated with daily activity measures. This demonstrates the necessity to monitor adherence and support patients, for example, with technical help to improve compliance.

Disclosure: The study is supported by the Swiss National Fonds (320030_185362).

EPO-232

Antiepileptic drugs and polysomnographically recorded periodic limb movements in sleep in epilepsy

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Background and aims: The adequate management of epilepsy requires 24h seizure-control by taking antiepileptic drugs (AED). The connection between epilepsy and sleep and effects of AEDs taken by a patient with epilepsy (PWE) may impact sleep and sleep-related phenomena. Periodic limb movements in sleep (PLMS) are a sleep-related arguably abnormal phenomenon, frequently observed in PWE and may impact seizure control. We aimed to assess the differences in objective PLMS data between patients that take AEDs and those who do not.

Methods: We assessed PWE referred to a specialized sleep center, where they underwent polysomnographic study (PSG) with full electroencephalography. PWE were interviewed and based on their history they were classified into those currently receiving AED therapy (AED group, AEG), and those who were not receiving AEDs for recent months (no AED group, NAEG). Limb movements (LM) in sleep were measured according to PSG scoring rules and divided into limb movements index (LMI) and PLMS index (PLMI). Mann-Whitney U test was used.

Results: Our study involved 88 patients with epilepsy (mean age 35.0 (SD-13.3); F-50.0%). The AEG patients comprised 65.9% (58) of the study population, and 34.1% (30) were from the NAEG. The following distribution was noted for AEG and NAEG respectively: LMI-10.4/h (SD-9.5) vs 16.5/h (SD-17.4), PLMI-3.6/h (SD-6.8) vs 9.0 (SD-16.5), with significant differences (p<0.05).

Conclusion: Our data suggest that PWE who were not taking AEDs at the time of assessment had higher indices of LMs and PLMS compared to patients on AED therapy. AEDs may play inhibitory role for PLMS.

Disclosure: Nothing to disclose.

EPO-233

Spectral analysis in a large sample of Disorders of Arousal episodes in adulthood

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Background and aims: Disorders of Arousal (DoA) are NREM parasomnias characterized by incomplete awakenings from NREM sleep. During DoA episodes, an admixture of both deep sleep and wake EEG activity has been observed. A few EEG studies detected changes in EEG activity in the seconds preceding DoA episodes. The objectives of this work were to characterize the topography of EEG spectral changes prior to DoA episodes and to compare the EEG activity preceding episodes of different behavioural complexity.

Methods: We collected 103 consecutive video-polysomnographic recordings of 53 DoA adult patients. We classified DoA episodes according to three different motor patterns of increasing complexity. For each episode we compared a 5-seconds window prior to the motor onset ("pre-event") and a time frame of 60 seconds from 2 to 3 minutes before the episodes ("baseline"). Subsequently, a between-group comparison was performed for the pre-event of simpler versus the more complex episodes.

Results: Spectral analysis over 325 DoA episodes showed an absolute significant increase prior to DoA episodes in all frequency bands excluding sigma, which showed a decrease. In normalized maps, the increase was relatively higher over the central/anterior areas for both slow and fast frequency bands. No significant differences were detected from the comparison between simpler and more complex episodes.

Conclusion: These results show that deep sleep and wake-like EEG rhythms coexist over overlapping areas before DoA episodes, suggesting an alteration of local sleep mechanisms. A similar EEG activation preceded episodes of different complexity, suggesting that a common mechanism possibly leads to their occurrence.

Disclosure: Nothing to disclose.

EPO-234

The role of sleep disorders in the development of cognitive deficit in patients with chronic cerebral ischemia

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Background and aims: The study of disturbances in nocturnal sleep as a risk factor for the development of cognitive deficit in patients with chronic cerebral ischemia (CCI) opens up new diagnostic possibilities and creates the basis for effective therapeutic strategies development. It is important to investigate the state of cognitive functions and the structure of nocturnal sleep in patients with CCI.

Methods: We examined 43 patients aged 53.8±6.2 years with CCI. The severity of cognitive impairment (CI) was assessed using the Minimental scale examination (MMSE), and the structure of nocturnal sleep was studied using polysomnography data.

Results: Using the MMSE scale, 1 group was allocated with score of 27.4±1.6 points, which corresponds to mild CI, and group 2 with score of 24.3±1.6 points, which corresponds to moderate CI. It was shown that in patients with moderate CI, in contrast to patients with mild CI, the time to fall asleep statistically significantly increased [Figure 1]; in the structure of night sleep, there was an increase in the representation of surface stages of slow-wave sleep against the background of a decrease in delta sleep, as well as a decrease in the representation of the phase of rapid sleep, which indicated the suppression of the regulatory somnogenic mechanisms of the brain.
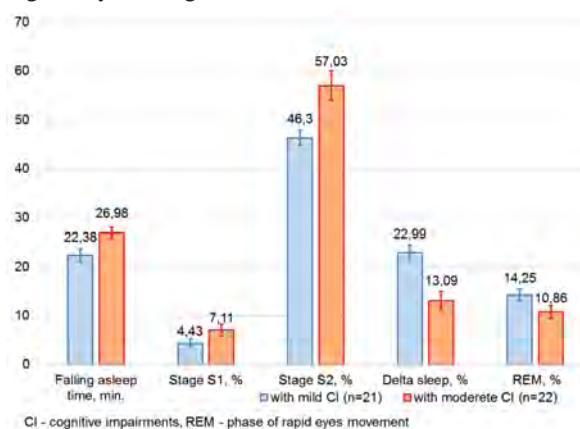
Figure 1. Polysmnography indicators in patients depending on level of cognitive impairment

Conclusion: Sleep disturbance in patients with CCI can lead to the progression of CI, which must be taken into account when choosing a treatment regimen.

Disclosure: Nothing to disclose.

EPO-235

Sleep inertia in hypersomnias of central origin: importance of depression and sleep architecture

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Background and aims: Sleep inertia (SI) is defined as difficulty becoming fully awake after sleep. Sleep Inertia Questionnaire (SIQ) has been validated in mood disorders, and utilized also in hypersomnolence disorders. Our aim is to assess SI in patients affected by narcolepsy type 1 (NT1), narcolepsy type 2 (NT2) and idiopathic hypersomnia (IH) and to find correlations with depression and polysomnographic (PSG) parameters.

Methods: Patients with NT1, NT2 and IH underwent to nocturnal PSG recording, 5 naps Multi-sleep latency test (MSLT), Epworth Sleepiness Scale (ESS), SIQ and Beck Depression Inventory (BDI-II). SIQ total score and four SIQ subdomains (physiological, SIQ-P cognitive, SIQ-C, emotional, SIQ-E and responses to SI, SIQ-R) were assessed.

Results: 26 patients (15 females, 11 males, mean age 37.96 ± 15.06 years) with diagnosis of NT1 (n=10), NT2 (n=8), IH (n=8). Mean SIQ total score was higher in IH (63.3 ± 14.8). Strong positive correlation was observed between SIQ (total score and all SIQ subdomains) and BDI-II ($p < 0.01$). REM latency showed strong positive correlations with SIQ and SIQ-R ($p < 0.01$) and a positive correlation with SIQ-E ($p < 0.05$). SIQ was positively associated with stage N2 ($p < 0.05$). SIQ-R negatively correlated with stage N3 ($p < 0.05$), whereas was positively associated with sleep onset latency at MSLT($p < 0.05$). Finally, SIQ-P negatively correlated with REM sleep ($p < 0.05$).

Conclusion: SI assessed by SIQ is a common symptom reported by patients with NT1, NT2 and IH. Depression can get worse physiological, cognitive, emotional factors of SIQ as well as responses to SI. Some PSG parameters seem to be associated with sleep inertia.

Disclosure: I have no disclosure.

EPO-236

Cardiovascular autonomic modulation is diferentially altered in multiple sclerosis.

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Background and aims: This study evaluates cardiovascular autonomic dysfunction (CAD) in multiple sclerosis (MS) and explores if CAD is related to clinical outcomes and fatigue severity.

Methods: A total of 53 MS patients (30 relapsing-remitting, RRMS; 23 progressive, PMS) and 30 healthy controls were evaluated (Table 1). TaskForce® Monitor was used to assess impedance cardiography parameters, heart rate (HRV) and blood pressure (BPV) variability during head-up tilt test (HUTT). Expiration/inspiration (E/I) ratio was assessed in response to a deep breathing test. Fatigue severity was evaluated using Chalder Fatigue Scale (CFQ).

	MS	HCs	P
Number of subjects (n)	53	30	
Sex (Male/Female)	10/43	7/21	0.519
Age, years	45.8±10.9	40.8±11.6	0.058
Disease duration (years)[range]	9.7±6.6 [0.5-28]	n.a.	
Mean EDSS score (range)	3.6±1.9 [0.5-7]	n.a.	
MS variant n (%)			
RRMS	30 (57%)		
SPMS	16 (30%)		
PPMS	7 (13%)		
Type of DMD n (%)			
Interferon-beta	8 (15%)		
Glatiramer acetate	4 (8%)		
Dimethyl fumarate	2 (4%)		
Natalizumab	1 (2%)		
CFQ value			
Total	17.8±4.8		
Physical	11.5±3.8		
Mental	5.8±2.2		

MS, multiple sclerosis; HCs, healthy controls; RRMS, relapsing-remitting multiple sclerosis; SPMS, secondary progressive multiple sclerosis, PPMS, primary progressive multiple sclerosis; DMD, disease modifying drugs; EDSS, Expanded Disability Status Scale; CFQ, Chalder Fatigue Scale.

Table 1. Demographic and clinical data of the study participants

Results: Compared to controls, PMS patients were characterized by increased sympathetic–parasympathetic ratio at rest ($p < 0.01$), decreased resting values of parasympathetic parameters (high-frequency HRV, $p < 0.05$; E/I ratio, $p < 0.001$) and index of contractility ($p < 0.05$), whereas RRMS patients showed reduced E/I ratio ($p < 0.01$). Compared to RRMS group, PMS patients had higher sympathovagal ratio and lower cardiac inotropy parameters ($p < 0.05$). No intergroup differences were observed for cardiovascular and autonomic function test parameters after HUTT (Table 2). PMS and low CFQ physical score were identified as independent predictors of sympathetic hyper-reactivity as measured with HRV. Greater disability and male sex were predictors of diastolic BP increase and reduced cardiac inotropy parameters, older age was predictor of decreased vagal tone (E/I ratio, high-frequency HRV) (Table 3).

Group	RRMS	PMS	HCs	RRMS	PMS	HCs
		Baseline			Delta (change baseline-tilt)	
Cardiac data						
HR [1/min]	64.7±7.3	69.1±5.4	66.5±9.4	14.0±8.5	12.6±7.8	15.1±8.0
sBP [mmHg]	110.4±10.6	115.8±11.9	112.2±12.1	12.8±13.5	10.5±14.9	12.1±10.0
dBP [mmHg]	70.1±8.1*	76.1±7.7*	73.1±9.0	17.7±9.6	13.0±10.2	15.1±8.4
mBP [mmHg]	87.2±8.6	92.6±9.5	90.3±9.8	15.6±10.8	11.9±13.0	13.6±8.9
SI [ml/m²]	57.0±14.3*	47.1±11.7*	55.6±12.7	-15.9±9.8	-16.9±9.7	-14.8±10.1
CI [l/min/m²]	3.7±1.0	3.3±0.8	3.7±0.9	-0.49±0.6	-0.74±0.7	-0.33±0.7
HI [1/s²]	0.4±0.1*	0.3±0.1*	0.4±0.1	-0.14±0.1	-0.14±0.1	-0.13±0.1
IC [1000/s]	71.7±18.9*	54.5±24.7**	71.6±21.5*	-21.4±15.0	-22.2±15.8	-19.1±15.7
TPRI [dyn*s*m²/cm⁵]	2036.5±785.4	2366.2±677.7	2018.7±838.3	655.6±529.4	885.8±741.4	596.6±702.7
LVWI (mmHg*L/(min*m²))	4.2±1.0	4.0±1.2	4.4±0.9	0.1±0.8	-0.4±1.1	0.2±0.9
LVET [ms]	323.0±9.7	315.6±13.2	318.9±13.1	-37.5±16.4	-31.7±15.6	-38.0±17.0
TFC [1/Ω]	28.6±5.8*	27.4±4.5*	33.0±9.7*	-2.5±1.0	-2.3±2.1	-2.8±0.9
TAC [ml/mmHg]	2.6±0.6	2.3±0.6	2.6±0.7	-0.4±0.6	-0.6±0.6	-0.5±0.1
Heart rate variability (HRV)						
LFnu-RRI [ms²]	59.1±15.7*	67.5±14.7*	56.1±12.2*	12.8±16.5	11.1±12.3	16.2±15.7
HFnu-RRI [ms²]	41.0±15.7*	32.7±14.6*	44.0±12.2*	-13.0±16.3	-12.7±10.8	-16.1±15.7
PSD-RRI [ms²]	2055.1±1761	1300.1±1538.1	1725.7±1361.1	-1159.3±1346.9	-757.8±1821.5	-519.1±977.2
LF/HF-RRI [1]	2.0±1.4*	3.0±1.9***	1.6±1.0**	1.9±2.5	2.9±3.3	2.2±2.4
LF/HF [1]	1.4±0.8*	1.9±1.4***	1.2±0.7**	1.2±1.4	2.0±2.5	1.4±1.4
Systolic and diastolic pressure variability (BPV)						
LFnu-dBP [%]	44.4±10.7	44.0±14.8	46.3±11.8	5.5±6.9	7.0±11.2	6.1±11.7
HFnu-dBP [%]	10.6±4.7	7.9±3.9*	10.9±4.5*	0.3±2.4	1.5±2.4	0.6±3.2
PSD-dBP [mmHg²]	8.9±4.6	8.1±5.6	8.0±5.6	-2.1±1.7	-1.7±1.9	-1.7±2.7
LF/HF-dBP	5.0±2.4	6.8±4.4*	5.0±2.3*	0.4±1.8	-0.1±2.3	0.7±2.5
LFnu-sBP [%]	41.5±10.2	44.0±13.9*	40.4±11.4*	8.6±11.8	10.7±14.6	7.7±11.0
HFnu-sBP [%]	11.7±5.8	11.8±8.4	12.2±5.6	4.0±5.4	3.9±7.0	2.3±4.0
PSD-sBP [mmHg²]	13.4±7.5	15.1±12.2	13.0±10.6	-3.5±2.9	-2.9±5.7	-4.1±4.9
LF/HF-sBP [1]	4.4±2.0	5.0±2.8	4.2±1.7	-0.1±1.8	-0.1±1.8	0.2±1.7
E/I ratio	1.2±0.0*	1.1±0.0**	1.3±0.0**			

MS, multiple sclerosis; PMS, progressive MS; RRMS, relapsing-remitting MS; HC, healthy controls; HR, heart rate; sBP, systolic blood pressure; dBP, diastolic blood pressure; mBP mean blood pressure; SI, stroke index; CI, cardiac index; HI, heather index; IC, index of contractility; TPRI, total peripheral resistance index; LVWI, left ventricular work index; LVET, left ventricular ejection time; TFC, thoracic fluid content; TAC, total arterial compliance; LFnu-RRI, low-frequency R-R interval in normalized units; HFnu-RRI, high frequency R-R interval in normalized units; LF-RRI, low-frequency R-R interval; HF-RRI, high-frequency R-R interval; PSD-RRI, power spectral density R-R interval; LF/HF, ratio between low and high band for heart rate and blood pressure variability; LF/HF-RRI, ratio between low and high band for heart rate variability; LFnu-dBP, low frequency of diastolic blood pressure variability in normalized units; HFnu-dBP, high frequency of diastolic blood pressure variability in normalized units; LF-dBP, low frequency of diastolic blood pressure variability; HF-dBP, high frequency of diastolic blood pressure variability; PSD-dBP, power spectral density of diastolic blood pressure variability; LF/HF-dBP, ratio between low and high band for diastolic, blood pressure variability; LFnu-sBP, low frequency of systolic blood pressure variability in normalized units; HFnu-sBP, high frequency of systolic blood pressure variability in normalized units; LF-sBP, low frequency of systolic blood pressure variability; HF-sBP, high frequency of systolic blood pressure variability; PSD-sBP, power spectral density of systolic blood pressure variability; LF/HF-sBP, ratio between low and high band for systolic blood pressure variability; E/I ratio, expiration/inspiration ratio; nu, normalized values; statistically significant differences are indicated with * $p < 0.05$, ** $p < 0.01$ (PMS vs HCs or RRMS vs HCs) and $p < 0.05$, $p < 0.01$ (PMS vs RRMS).

Table 2. Mean ± standard deviation of resting and during tilt test cardiac autonomic measures for patients with RRMS, PMS and healthy controls.

Dependent variables	Independent variables	BETA (β)	SE	t	p-value
dBP R=0.55; R²=0.30 F(2,51)= 10,83; p<0.001	EDSS	0.33	0.13	2.59	0.013
	Sex	0.31	0.13	2.45	0.018
SI R=0,48; R²=0.23 F(1.52)=15.73; p<0.001	EDSS	-0.55	0.19	-2.90	0.006
HI R=0.48; R²=0.23 F(4.42)=3.18; p<0.022	EDSS	-0.47	0.20	-2.38	0.022
	Sex	-0.29	0.14	-2.02	0.049
IC R= 0.52; R²= 0.24 F(2.51)=9.52; p<0.001	EDSS	-0.45	0.19	-2.40	0.021
	Sex	-0.27	0.13	-2.00	0.052
LFnu-RRI R=0.36; R²=0.117 F(1.52)=8.05; p<0.006	Age	0.37	0.13	2.88	0.006
LF/HF-RRI R=0.46; R²=0.18 F(2.51)=6.90; p<0.022	CFQ physical	-0.338	0.05	-2.672	0.010
	Variant	0.389	0.426	3.081	0.003
HFnu-RRI R= 0.36; R²=0.132 F(1.51)=7.49 p<0.008	Age	-0.36	0.13	-2.74	0.008
LF/HF R=0 .34 R²= 0.12 F(1.51)=3.43 p<0.039	Variant	0.28	0.13	2.13	0.038
E/I R=0.36 R²=0.13 F(1.51)=7.49 p<0.008	Age	-0.36	0.13	-2.74	0.009

dBP, diastolic blood pressure; SI, stroke index; HI, heather index; IC, index of contractility; LFnu-RRI, low-frequency R-R interval in normalized units; HFnu-RRI, high frequency R-R interval in normalized units; LF/HF, ratio between low and high band for heart rate and blood pressure variability; LF/HF-RRI, ratio between low and high band for heart rate variability; CFQ, Chalder Fatigue Scale; BETA (β), standardized beta coefficient; t-values; SE, standard error; R, squared; Statistically significant differences are indicated with * p < 0.05.

Table 3. Multivariate analysis e prediction of frequency domain and cardiac variables by clinical features.

Conclusion: Cardiovascular autonomic modulation is altered in MS and highly dependent on disease variant, disability level, fatigue severity and patients' demographics.
Disclosure: Nothing to disclose.

EPO-237

Applicability of the Sustained Attention to Response Task (SART) in clinical practice

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Background and aims: Evaluation of disorders of hypersomnolence should include assessment of disturbed vigilance, which can be quantified using the computerized, short and objective Sustained Attention to Response Task (SART), assessed five times over the course of the day. Here we describe our experience with the SART in a tertiary referral center.

Methods: We analyzed clinical data of 317 patients with hypersomnolence complaints, diagnosed with narcolepsy type 1 (NT1; n=102), narcolepsy type 2 (NT2; n=21), idiopathic hypersomnia (IH; n=46), obstructive sleep apnea syndrome (OSAS; n=28) and complaints of EDS without explanatory diagnosis (CEDS; n=120). Multiple sleep latency test (MSTL), polysomnography (PSG), Epworth Sleepiness Scale (ESS), Hospital Anxiety and Depression Scale (HADS) and SART outcomes (reaction time, total errors, commission and omission errors) were compared between diagnostic groups and with each other, corrected for age.

Figure 2: Differences SART outcomes between diagnostic sample patient groups: narcolepsy type 1 (NT1, n=89), narcolepsy type 2 (NT2, n=11), idiopathic hypersomnia (IH, n=39), OSAS (n=27), CEDS (n=120). Boxplots represent median, IQR, minimum and maximum.. * p<.05; ** p<.005; differences that remain significant after correction for age are colored red.

Figure 1: Representation of our routine diagnostic work-up in a clinical setting. During the night a polysomnography (PSG; black) is performed, followed by the Epworth Sleepiness Scale (ESS; dark grey) and five sessions of the Sustained Attention to Response Task (SART; light grey) and the Multiple Sleep Latency Test (MSLT; white).

Results: SART-outcomes did not correlate with the MSLT, PSG or HADS. Higher ESS-scores were associated with longer reaction times and more commission errors (p<0.01). Reaction times were significantly longer in the morning with more omission errors (p<0.05). OSAS patients has slower reaction times than the NT1, IH and CEDS groups (median 428 ms, p<0.05).

Figure 3: Differences in Sustained Attention to Response Task outcomes between sessions. Median and IQR are shown. * p<.05; ** p<.005. Reaction time differed significantly between all sessions.
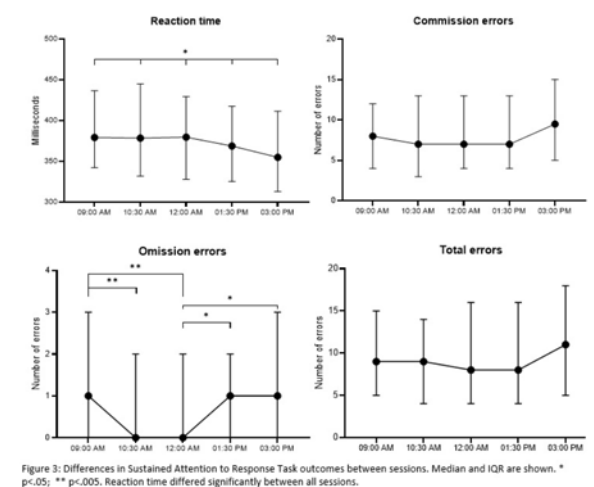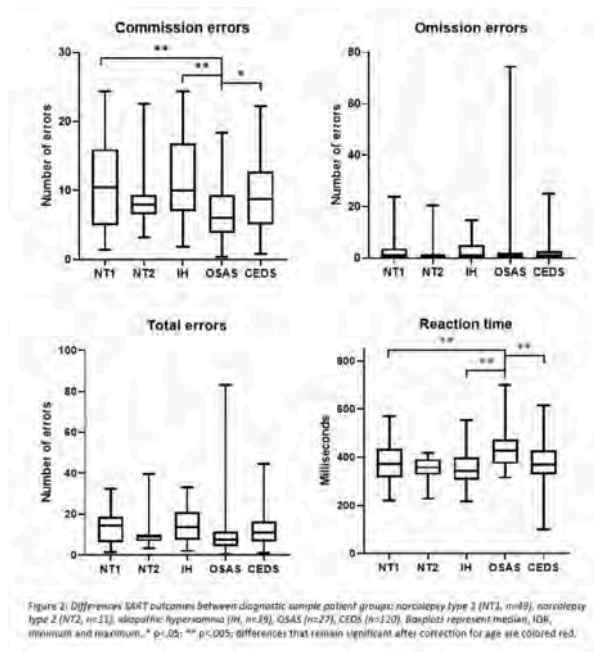
Conclusion: The SART quantifies disturbed vigilance, which is a different dimension of disorders of hypersomnolence than measured by the MSLT or PSG. It does not differentiate between sleep disorders and is not affected by symptoms of anxiety or depression. In the clinical practice for the diagnosis and clinical monitoring of hypersomnolence patients, multiple testing times during the day are advised, for example before each MSLT nap opportunity.

Disclosure: There are no known conflicts of interest associated with this publication and no financial disclosures to be made.

EPO-238

Investigation of sleep-related respiratory disorders in the young stroke patients

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Background and aims: Many cases of stroke have also sleep-related breathing disorders (SRBD) most of which being obstructive sleep apnea syndrome (OSAS).

Methods: 60 patients with history of stroke under age of 55 were included in our study. Demographic characteristics (age at stroke, sex, body-mass index) of the patients Etiology of stroke was evaluated according to the Trial of Org 10712 in Acute Stroke (TOAST) classification. National Institute of Health Stroke Scale (NIHSS) and Modified Rankin Scale (MRS) were used to evaluate functionality. The patients were done polysomnography (PSG) investigation.

Results: Based on PSG investigation 7 with normal , 10 with primary snoring, 14 with mild , 11 with moderate , and 18 with severe OSAS were detected. No significant correlation was found between severity of disease and NIHSS, MRS or TOAST classification. Large artery atherosclerosis in the etiology, facial paralysis and dysarthria in the neurological examination, and brain stem involvement in the stroke location were observed to accumulate in the group of severe OSAS. When the anterior system, posterior system, and association of both were compared for vessel location, no significant difference was found in regard to circulatory systems.

Conclusion: It is considered that SRBD included in stroke etiology has also role in etiology of the cases under 55 years old, and it should be taken into consideration as much as other risk factors. Importance of this topic was intended to be emphasized in the literature for the first time.

Disclosure: There is no conflict of interest regarding this abstract.

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Sunday, June 26 2022
Ageing and dementia 2

EPO-239

Perspectives and satisfaction with telemedicine for neurodegenerative diseases in the Aegean during COVID-19: pilot study

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Background and aims: Patients of remote areas with neurodegenerative disorders (ND) have limited access to specialized healthcare, due to travel restrictions, long waiting times and financial difficulties. Although during COVID-19 pandemic telemedicine use rose sharply, patients' views remain unclear. Our aim was to investigate, for the first time, the perspectives and satisfaction of ND patients, care-givers and healthcare professionals in Aegean islands of Greece with telemedicine services.

Methods: Data were derived from the newly designed "University Unit of Memory, Dementia and Parkinson's disease through the National Greek Telemedicine Network", during 03/2021–12/2021. Telemedicine (video-based) visits were conducted by specialized neurologists, psychiatrists and neuropsychologists. Satisfaction questionnaires [10 questions from 0 (not at all) to 4 (extremely)] on convenience, effectiveness, accessibility, and open-ended questions (comments for improvement) were anonymously filled.
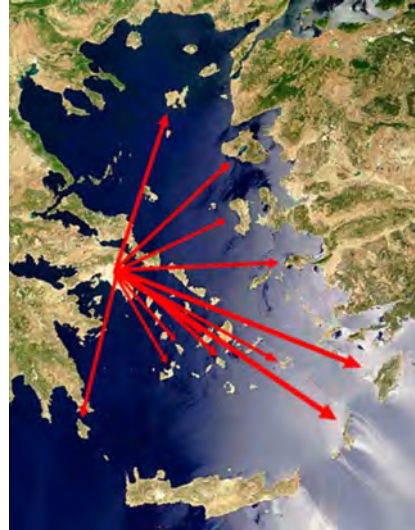
Schematic demonstration of the Aegean Islands covered by the Outpatient Telemedicine Unit in Greece for patients with neurodegenerative disorders.

Results: Of total 46 telemedicine examinations (30 first,16 follow-up visits;10 (33%) males, 20 (67%) females, age: 67±12.5 years), we received 27 questionnaires (11 ND patients, 5 care-givers, 11 healthcare professionals). Average general satisfaction was 3.73 for patients, 3.60 for care-givers, 3.36 for healthcare professionals. Totally, most participants mentioned increased accessibility to specialized healthcare (3.67±0.56), comfort (3.59±0.69), reduced transportations (3.52±0.94) and cost (3.81±0.62), adequate follow-up (3.22±0.85), reliable medical assessment (3.37±0.63), information delivery (3.41±0.84), health improvement (3.19±0.88), and future selection of telemedicine (3.67±0.56). Commonest remarks were the need for more frequent visits, available specialties and the dissemination of the information.
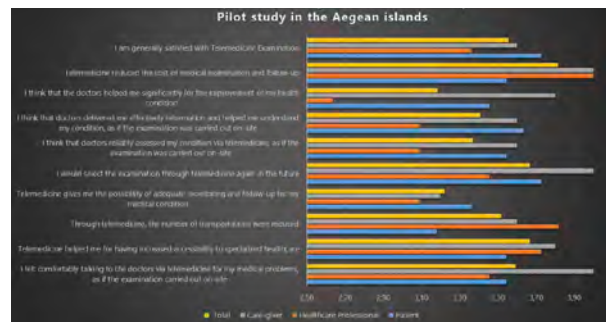
"University Unit of Memory, Dementia and Parkinson's disease through the National Greek Telemedicine Network": Satisfaction Rates of Patients, Care-givers and Healthcare Professionals.

Conclusion: The results of this pilot study show that most ND patients, care-givers and healthcare professionals are satisfied with telemedicine in the Aegean, highlighting its significance for equal specialized healthcare particularly in remote areas.

Disclosure: This pilot activity is part of the Project SI4CARE, co-financed by the EU via Interreg ADRION Program. It doesn't reflect the official opinion of the EU. Responsibility for the information and views expressed lies entirely with the authors.

EPO-240

Use of telemedicine and digital technology for the elderly with dementia in Adrion Region: Results from SI4CARE Project

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Background and aims: COVID-19 pandemic has highlighted the need of telemedicine and digital technologies, especially for the vulnerable elderly population with chronic conditions including dementia, in order to improve their accessibility to healthcare services and facilitate their living. As a part of the European SI4CARE Project, the aim of this study was to investigate the extent to which telemedicine and new technologies are currently used for the elderly with dementia in the Adrion Region.

Methods: Data were collected through e-questionnaires regarding the use of telemedicine and digital technologies for the elderly with dementia, which were anonymously administered during 02/2021–05/2021 to elderly and healthcare stakeholder providers (hospitals, dementia associations, institutions, policy makers) in Italy (Calabria), Croatia, Bosnia & Herzegovina, Greece and Serbia. Rating was from not at all to extremely.

Results: The number of the interviewees was 495 elderly people and 183 stakeholders. The majority of all stakeholders (46–100%) and elderly (60–100%) indicated that it was not at all easy for an elderly person with dementia

to be examined via telemedicine, especially in Serbia and Italy. Most participants revealed that digital technologies were not at all being used to facilitate the living of the elderly with dementia in all countries.
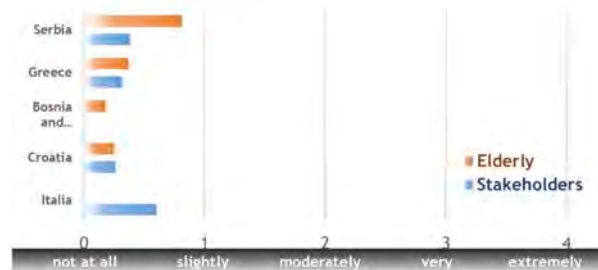
How easy it is for an elderly person with dementia to be examined through telemedicine? Results from SI4CARE Project in Adrion Region.

To what extent are new technologies being used to facilitate the living of people with dementia? Results from SI4CARE Project in Adrion Region.

Conclusion: Telemedicine and digital technologies have not been adequately incorporated in healthcare services for the elderly with dementia in the Adrion Region. Major attempts are needed for their successful integration especially in remote areas, in order to facilitate daily living and improve the accessibility to healthcare services of these patients.

Disclosure: This work was elaborated with the contribution of the partnership of the Project SI4CARE, co-financed by the EU via Interreg ADRION Program. This content does not reflect the official opinion of the EU. Responsibility for the information and views expressed therein lies entirely with the authors.

EPO-241

Pathological Aβ42/Aβ40 predicts brain damage load in Alzheimer's Disease

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Background and aims: According to the NIA-AA research framework biomarker-based classification system, in Alzheimer's disease(AD)exposure of neurons to amyloid β(Aβ)facilitates the spread of pathologic tau;recent studies also suggested a role of Aβ oligomers(AβOs)in membrane repair mechanisms, which could eventually lead to tau hyperphosphorylation.Previous studies demonstrated that the combination of abnormally low CSF Aβ42 and abnormally high p-tau levels predicts the presence of pathologic neuritic plaques in the brain, measured by means of p-tau/Aβ42 ratio.

Methods: The study included 157 patients from the memory clinic of Policlinico Tor Vergata, classified according to the ATN system and further stratified according to Aβ42/Aβ40 ratio.An over cut-off p-tau/Aβ42 ratio was used as indirect marker identifying AD anatomo-pathologic changes.

Results: Patients with A+T- presented different frequencies of over cut-off values of p-tau/Aβ42 depending on values of Aβ42/Aβ40. 89.6% of patient with pathological β42/Aβ40 presented over cut-off values, while only 32.6% of patients with normal Aβ42/Aβ40 did (p<0.001).The Spearman's correlation analysis highlighted a strong inverse correlation between p-tau/Aβ42 and Aβ42/Aβ40 in the same group(rho=-0.647, p<0.001). All A+T+ subject presented both pathological Aβ42/Aβ40 and over cut-off p-tau/Aβ42.

Conclusion: Over cut-off p-tau/Aβ42 occurs both in A+T- and A+T+ patients, suggesting that AD-related brain damage and subsequent cognitive decline might be present regardless of CSF evidence of tauopathy; pathological tau-related changes could remain below threshold as long as Aβ-mediated compensatory mechanisms of repair withstand.The inverse correlation described in the A+T- group suggests a crucial role of AβOs in determining brain damage load, and hints that Aβ42/Aβ40 predicts anatomo-pathological findings better than low CSF Aβ42 alone.

Disclosure: No potential competing interest was reported by the authors.

EPO-242

1H-Magnetic Resonance Spectroscopy in Older People with Delirium

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Background and aims: Delirium is an acute disorder of consciousness that affects up to 35% of hospitalised older people and is associated with significant morbidity, including an ≥8-fold increased risk of dementia. The mechanism underlying this is unknown. Because glutamate excitotoxicity is associated with brain injury, we used 1H-Magnetic Resonance Spectroscopy (MRS) to measure brain glutamate concentrations in older adults with delirium.

Methods: Medical inpatients aged 65+ with and without delirium were recruited. Delirium was confirmed according to DSM-5 criteria. Physical illness severity was assessed using APACHE-II, pre-admission frailty with CFS and pre-admission cognitive decline with IQCODE. MRS was acquired from parietal white matter.

Results: MRS data were obtained from 13 delirium patients and 12 controls. There was no significant difference between groups in age (82 vs. 79; p=0.152), IQCODE (4 vs. 3, p=0.095) or APACHE-II (8 vs 6.5, p=0.068); however, delirium patients were slightly frailer (CFS 5 vs. 4.5, p=0.049). MRS demonstrated no difference in combined glutamate + glutamine (Glx) concentration (p=0.516). However, when patients with known neurodegenerative disease or severe atrophy were excluded, Glx concentration was elevated in the delirium group (Glx/tCr 1.75 vs. 1.51, p=0.024). Exploratory analysis suggested this was due to a difference in glutamate (p=0.046) rather than glutamine (p=0.297) concentration.

Conclusion: This study suggests that brain glutamate concentrations might be elevated in delirium and supports further investigation of glutamate excitotoxicity as a potentially modifiable contributor to delirium severity and post-delirium cognitive decline.

Disclosure: Nothing to disclose.

EPO-243

Utility of asymmetric temporal lobe atrophy on the diagnosis of Frontotemporal Lobar Degeneration

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Background and aims: Patients with Frontotemporal Lobar Degeneration (FTLD) have considerable variations in brain atrophy patterns. However, dominant left-temporal lobe atrophy has been classically associated with semantic dementia (SD), while right-temporal atrophy is considered a marker of right-temporal-variants (rtvFTD) (Erkoyun et al, 2020). The aim of this study was to describe the clinical and genetic profile of FTLD patients with asymmetric temporal atrophy at disease onset.

Methods: We retrospectively reviewed 60 CT and/or MRI of FTLD patients, performed at early disease stage. Patients with predominant-frontal or symmetric-temporal atrophy were excluded. In those with asymmetric temporal atrophy, 19 had left-predominance (LeftTLA) and 8 had right-predominance (RightTLA). Each patient clinical and genetic data was analyzed.

Results: Patients with LeftTLA had a mean age of 67±9.4 years, male predominance (n=13, 68.4%) and mean age at onset of 65.0±9.2 years. RightTLA patients were older (69±9 years), had no gender dominance and lower mean age at onset (63.4±6.4 years). Considering clinical variants in LeftTLA patients, 16 were behavioral-variants (bvFTD) (84.2%) and 3 progressive non-fluent aphasias (PNFA) (15.8%). Five RightTLA patients were bvFTD (62.5%) and 3 rtvFTD (37.5%). Four LeftTLA patients were genetic forms (21%), namely, 3 with c9orf72 mutation (15.8%) and 1 progranulinopathy (5.3%). Two genetic forms were identified in RightTLA group (25%): 1 c9orf72 mutation and 1 progranulinopathy.

Conclusion: Structural imaging at disease onset, specifically temporal atrophy pattern, does not seem to be a robust phenotype marker. Thus, clinical criteria and functional imaging are of utmost importance. There was a significant prevalence of genetic forms in both atrophy groups.

Disclosure: Nothing to disclose.

EPO-244

Neurophysiological correlates of motor and cognitive dysfunction in prodromal and overt dementia with Lewy bodies

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Background and aims: The neurophysiological correlates of cognitive and motor symptoms in prodromal and overt dementia with Lewy bodies (DLB) are still to be elucidated. The objective of the present study was to evaluate if cognitive and motor features of patients with prodromal and overt DLB are associated with the impairment of specific neurotransmitter circuits, evaluated in vivo with transcranial magnetic stimulation (TMS).

Methods: 51 patients with DLB (25 prodromal; 26 with dementia) underwent neuropsychological and clinical evaluation, with 25 patients having at least one follow-up evaluation. All patients were assessed with TMS at baseline, with protocols assessing cholinergic circuits (short latency afferent inhibition – SAI), GABAergic circuits (short interval intracortical inhibition – SICI) and glutamatergic circuits (intracortical facilitation – ICF).

Results: Compared to HC, SICI, ICF and SAI resulted significantly impaired in both prodromal and overt DLB, with the latter showing a reduced SICI and SAI also compared to prodromal DLB. There was a significant correlation between motor deficits, evaluated with the UPDRS-III, and the impairment of GABAergic (SICI) (r=0.729, p<0.001) and glutamatergic (ICF) (r-0.608, p<0.001) circuits; global cognition, evaluated with the MMSE, correlated with the impairment of cholinergic (SAI) circuits (r=-0.738, p<0.001). Worsening of cognitive functions at follow-up was associated with reduced cholinergic functions at baseline (R2=0.53, p<0.001).

Conclusion: These results suggest that motor and cognitive dysfunctions in prodromal and overt DLB depend on specific and independent neurotransmitter circuits.

Disclosure: Alberto Benussi is listed as an inventor on issued and pending patents on the use of non-invasive brain stimulation for the differential diagnosis of dementia and to increase cognitive functions in patients with neurodegenerative disorders. Andrea Pilotto is consultant and served on the scientific advisory board of Z-cube (Technology Division of Zambon Pharma), received speaker honoraria from Biomarin and Zambon Pharmaceuticals. Alessandro Padovani is consultant and served on the scientific advisory board of GE Healthcare, Eli-Lilly, and Actelion Ltd Pharmaceuticals; and received speaker honoraria from Nutricia, PIAM, Lansgstone Technology, GE Healthcare, Lilly, UCB Pharma, and Chiesi Pharmaceuticals. All other authors report no disclosures.

Conclusion: We present a patient with an early onset of possible behavioral variant FTD, appearance of fasciculations three years later and a mutation of clinical interest and autosomal dominant inheritance in FUS gene, which had not been previously described.

Disclosure: Nothing to disclose.

EPO-245

Behavioural variant frontotemporal dementia associated to fus gene variant of clinical interest

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Background and aims: Frontotemporal dementia (FTD) is a heterogeneous clinical syndrome characterized by progressive abnormalities of personality, behaviour, and/or language. Underlying neuropathology allows a subclassification of frontotemporal lobar degeneration according to the major protein identified forming cellular inclusions. FUS protein accumulations has been identified in 5% of patients. Mutations in FUS gene have been described as the major cause of familiar amyotrophic lateral sclerosis, but reports of FTD associated to FUS gene mutations are rare.

Methods: Clinical case description of a 48 years old male with no family history of neurological diseases and possible behavioural variant frontotemporal dementia associated to FUS gene mutation.

Results: At the age of 45, he started behavioral disturbances consisting on apathy, emotional lability and irritability. Progressively, others related to food and understanding and verbal expression difficulties. In last Neurology visit, her wife described small movements of patient's muscles as 'small worms under his skin'. Neuropsychological evaluation showed fronto-temporal disfunction. Laboratory blood tests were normal. Initial brain MRI did not show any abnormalities. CSF biomarkers and amyloid-PET CT were negative for amyloid pathology. Brain FDG-PET CT showed hypometabolism in frontal lobe and anterior temporal pole, predominantly on the right side. Genetic tests were positive for a variant of clinical interest in FUS gene: NM_004960.3:c.681_686del, NP_004951.1:p.G230_G231del, rs746532502. Heterocygosis, autosomal dominant inheritance.

PET-CT FDG, axial

EPO-246

Motor worsening in the Alzheimer's disease continuum in Down's syndrome

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Background and aims: Down syndrome (DS) is a genetically determined form of Alzheimer's disease (AD). In addition to cognitive and behavioral impairment, AD is associated with motor worsening. Late-onset myoclonic epilepsy (LOMEDS) is a frequent condition in the context of AD in DS and it seems that can accelerate motor decline. There is a need to systematize the neurological physical examination in patients with AD in DS.

Methods: A cross-sectional study conducted in adult population with DS from October 2020 to December 2021. All subjects were assessed by neurologists and neuropsychologists and were categorized according to intellectual disability and cognitive status (asymptomatic – aDS-, prodromal –pAD- and dementia AD –dAD-). The presence of comorbidities and active pharmacological treatment was recorded and physical examination including assessment with motor Scales for Outcomes in Parkinson's disease (SCOPA) and Tinetti scales was performed for all of them.

Results: 244 subjects with age 44.6 years (±10.7), 51.6% women (table 1). Motor impairment measured by Tinetti and SCOPA scales was significantly greater in the group of symptomatic subjects (pAD and dAD) compared to aDS (p<0.001, figures 1 and 2). Regression coefficients (RC) in multivariate analysis revealed that LOMEDS (RC 6.65 and -6.48), treatment with antipsychotics (RC 1.52) and cognitive status (RC 1.52 and -1,43) had the greatest impact on SCOPA and Tinetti scores, respectively (p<0.01).

	Asymptomatic (n = 153)	Symptomatic (n = 91)
Age, years	39.2 (9.02)	53.6 (6.5)
Sex		
Men	77 (50.3)	41 (45.1)
Women	76 (49.7)	50 (54.9)
Level of intellectual disability		
Mild	29 (19)	7 (7.69)
Moderate	69 (45.1)	43 (47.3)
Severe	55 (35.9)	41 (45.1)
Cognitive category		
Prodromal AD	NA	30 (33)
AD dementia	NA	61 (67)
Epilepsy	8 (5.23)	28 (30.8)
LOMEDS	0	25 (27.5)
APS	24 (15.7)	34 (37.4)
ASD	15 (9.8)	28 (30.8)
AD	37 (24.2)	34 (37.4)
BZD	12 (7.84)	10 (11)
ACEI	0	44 (48.4)
SCOPA motor	1.03 (1.86)	6.16 (7.67)
Tinetti	27.5 (1.37)	22.2 (7.5)

Table 1: Summary Summary of demographic and clinical characteristic of the sample. Asymptomatic = Down syndrome without Alzheimer's disease. Symptomatic = Down syndrome with prodromal or Alzheimer's disease dementia. ADD: antidepressants. BZD: benzodiazepines.
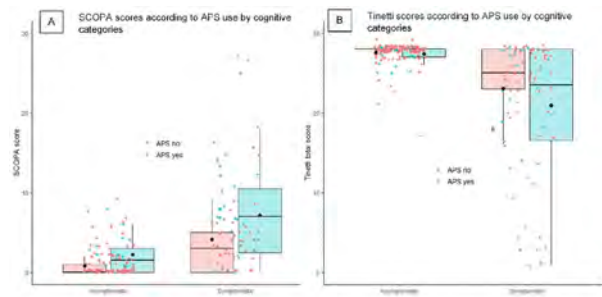
Figure 1: Boxplot with SCOPA (1.A) and Tinetti scores (1.B) by cognitive categories in relation to antipsychotic drug use (APS). A higher SCOPA scale score and a lower Tinetti scale score imply greater motor impairment.

Figure 2: Boxplot with SCOPA (2.A) and Tinetti scores (2.B) by cognitive categories in relation to late-onset myoclonic epilepsy in Down syndrome (LOMEDS). A higher SCOPA scale score and a lower Tinetti scale score imply greater motor impairment.

Conclusion: A systematic physical examination can identify motor impairment related not only to symptomatic DS, but also linked to the use of antipsychotics and condition of epilepsy, both of them very frequent in AD in DS.

Disclosure: There are no relevant financial or non-financial competing interests to report.

EPO-247

A MATTER OF VISION: HEIDENHAIN VARIANT OF SPORADIC CREUTZTFEULDT JAKOB DISEASE

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Background and aims: Creutzfeldt-Jakob disease (CJD) is a rapidly progressive neurodegenerative disease with heterogeneous clinical presentations. One rare and peculiar presentation is the Heidenhain variant, characterized by isolated visual symptoms.

Methods: We describe a patient with sporadic CJD that presented with a syndrome of posterior cortical atrophy (PCA).

Results: A 64-year-old woman with unremarkable medical history presented to the hospital with a three-month history of visual disorientation, imbalance, and reduced awareness of stimuli on her left side. Neurological examination revealed simultanagnosia, oculomotor apraxia and optic ataxia, comprising a Balint's syndrome, visual agnosia, ideomotor apraxia and severe left hemi-neglect (video available). Neuropsychological assessment revealed multidomain cognitive impairment with marked posterior deficit with relative preservation of memory. Blood analysis were unremarkable, including, autoimmune encephalitis and anti-neuronal antibodies. Electroencephalogram showed posterior brief periodic sharp complexes (Figure 1). Cerebrospinal fluid (CSF) study revealed elevated protein levels without pleocytosis, high levels of tau protein with normal phospho-tau and positive CSF 14-3-3 protein. DWI brain-MRI showed bilateral ribbon-shaped hyperintense signal in the occipital lobes and hyperintensity in both pulvinar and dorsomedial thalamic nuclei (Figure 2). The diagnosis of probable sporadic CJD was made, based on clinical aspects presence of typical EEG, typical brain MRI and positive CSF 14-3-3.
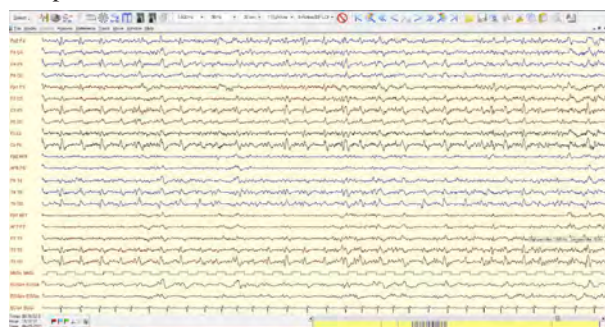
Figure 1: Electroencephalogram showing diffuse slow wave activity and posterior brief periodic sharp complexes.
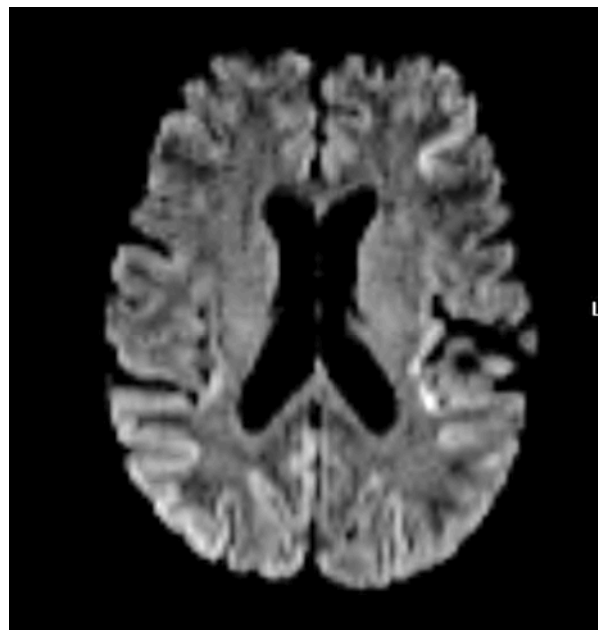
Figure 2: DWI brain-MRI showing bilateral ribbon-shaped hyperintense signal in the occipital lobes

Conclusion: This is a clinical presentation of Creutzfeldt-Jakob disease that could be mistaken with PCA. In this case, the rapidly progressive evolution and the extensive complementary data pointed towards the Heidenhain variant of Creutzfeuldt-Jakob disease. Early recognition of this syndrome allowed the appropriated care and support to the patient and family.

Disclosure: The author declares that she has no relevant or material financial interests that relate to the research described in this abstract.

EPO-248

Functional connectivity rearrangements propagating from disease epicenters in frontotemporal lobar degeneration variants

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Background and aims: Stepwise functional connectivity (SFC) is a graph-theory-based neuroimaging method, which detects whole-brain functional couplings of a selected region of interest, at increasing link-step distances. This study assessed SFC rearrangements in frontotemporal lobar degeneration (FTLD) presentations.

Methods: Patients with behavioral variant of frontotemporal dementia (bvFTD, n=64), non-fluent (nfvPPA, n=34) or semantic variant of primary progressive aphasia (svPPA, n=36) and 94 healthy controls underwent 3T MRI. The peaks of atrophy of each variant (identified in an independent cohort of path-proven cases) were used as seed regions for the subsequent SFC analyses. Correlations between SFC architecture in controls and atrophy patterns in FTLD patients were tested.

Results: Selected seeds were the left insula for bvFTD, left supplementary motor area for nfvPPA, and left inferior temporal gyrus (ITG) for svPPA. Compared with controls, bvFTD and nfvPPA patients showed widespread decreased SFC in bilateral cortical regions with direct/intermediate connections, and increased SFC either in circumscribed regions close to the respective seed region or in more distant cortical and posterior cerebellar areas. Across all link-steps, svPPA showed SFC decrease mostly localized in the temporal lobes, with only modest SFC increase in the lingual gyrus and cerebellar regions at intermediate link-steps. Average functional link-step distance from the left ITG was found to correlate with grey matter volume in svPPA (r=0.29, p=0.03).

Conclusion: This was the first study exploring SFC in FTLD, opening promising perspectives to understand the physiopathological underpinnings of these presentations and model disease evolution.

Disclosure: Supported by Italian Ministry of Health (GR-2011-02351217); European Research Council (StG-2016_714388_NeuroTRACK); US National Institutes of Health (R01-DC010367, R01-DC12519, R01-DC14942, R01-NS89757, R21-NS94684)

EPO-249

Investigating neuroprotective effects of semaglutide in early Alzheimer's disease: trial designs for evoke and evoke+

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Background and aims: Alzheimer's disease (AD) is a complex disorder and its pathophysiology involves neuroinflammation and microvascular alterations. AD patients often have cerebrovascular small vessel disease (CSVD) co-pathology, which can be associated with increased rates of cognitive decline. Patients with established CSVD co-pathology are often excluded from AD trials. Data suggest that glucagon-like peptide-1 receptor agonists (GLP-1RAs) may have neuroprotective and anti-neuroinflammatory effects (Fig. 1). Two phase 3 trials are now recruiting AD patients and will assess the efficacy and tolerability of the GLP-1RA semaglutide in patients with early AD. In one of these trials, AD patients with CSVD co-pathology can be included.
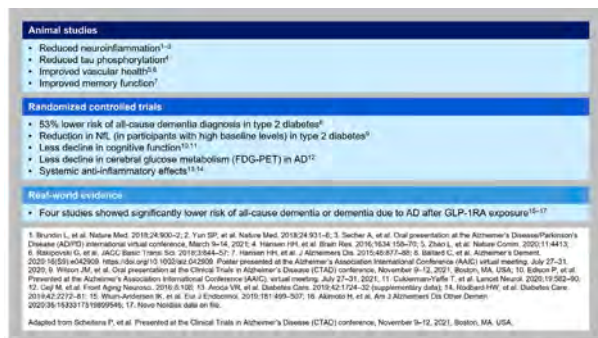
Figure 1. Summary of data supporting GLP-1 RAs as treatment for AD

Methods: The evoke (NCT04777396) and evoke+ (NCT04777409) trials are two large international, randomised, double-blind, placebo-controlled trials (Fig. 2). Each trial includes 1,840 amyloid-positive patients with mild cognitive impairment (MCI) or mild dementia. In evoke+ ≥20% of participants will have CSVD (age-related white matter changes >2 and/or >1 lacunar infarct). Patients will be randomised 1:1 to once-daily oral semaglutide 14 mg or placebo, added to standard of care, for 104 weeks plus a 52-week extension. The primary endpoint is change in the Clinical Dementia Rating Scale – Sum of Boxes. Confirmatory secondary endpoints include the time to

progression to dementia among patients with MCI at baseline. An exploratory substudy will investigate neurodegenerative and neuroinflammatory biomarkers in cerebrospinal fluid (Fig. 3).
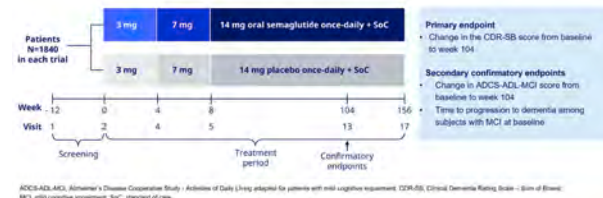
Figure 2. Study design of the evoke and evoke+ studies

Figure 3. Study design of the biomarker analyses

Results: Expected in 2025.

Conclusion: The evoke and evoke+ trials will investigate the neuroprotective effects of semaglutide in early AD with and without CSVD.

Disclosure: NT: UK lead and co-chair, evoke Global Expert Panel JC: consultant: AB Science, Acadia, Alkahest, AlphaCognition, ALZPath, Annovis, AriBio, Artery, Avanir, Biogen, Biosplice, Cassava, Cerevel, Clinilabs ,Cortexyme, Diadem, EIP Pharma, Eisai, GatehouseBio, GemVax, Genentech,Green Valley, Grifols, Janssen, Karuna, Lexeo, Lilly, Lundbeck, LSP, Merck, NervGen, Novo Nordisk, Oligomerix, Otsuka, PharmacotrophiX, PRODEO, Prothena, ReMYND, Renew, Resverlogix, Roche, Signant Health, Suven, Unlearn AI, Vaxxinity, VigilNeuro, Zai Laboratories; various shareholdings HF: evoke steering committee (payments by Novo Nordisk to UCSD); grants: AC Immune, Biohaven Pharmaceuticals, Annovis, Vivoryon (Probiodrug), LuMind (funding through UCSD); consultant: Roche/Genentech, Janssen, Tau Consortium, Samus Therapeutics, Arkuda Therapeutics, Biosplice, Axon Neurosciences SG, PJ, PP: employees and shareholders,Novo Nordisk FKK: evoke steering committee; various activities: Novo Nordisk, Amgen, AstraZeneca, Bayer, BI, Carmot Therapeutics, Eli Lilly, Gubra, Lupin, MedImmune, MSD/Merck, Mundipharma, Norgine, Novo Nordisk, Pharmacosmos, Sanofi, ShouTi, Zealand Pharma, Zucara; minority shareholder, Antag Therapeutics Aps LLR: employee, Novo Nordisk MS: none HS: funding paid to institution: Academy of Finland, EU Research Programs, Nutricia AA: various activities: AbbVie, Acadia, Allergan, Alzheimer's Association, Axovant, AZ Therapies, Biogen, Eisai, Grifols, Harvard Medical School Graduate Continuing Education, JOMDD, Lundbeck, Merck, Roche/Genentech, Novo Nordisk, Qynapse, Sunovion, Suven, Synexus.

EPO-250

Effects of ENT1 inhibitor on cognitive deficits in sporadic Alzheimer's mice

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Background and aims: Alzheimer's disease (AD) is one of the most common neurodegenerative diseases in the elderly and there is no adequate medicine for the treatment. This study employs the intracerebroventricular (icv) injection of streptozotocin (STZ) and intrahippocampal (ih) injection of amyloid-beta to establish a reliable animal model of sporadic AD (sAD) and determine the efficacy of equilibrative nucleoside transporter (ENT)1 inhibitor on sAD treatment.

Methods: Mice received icv injection of STZ (3 mg/kg; the total injection volume is 1 μl) with ih microinjection of Aβ1-42 (1 μg/μl; the total volume is 1 μl) in consecutive 4 days. The expression of pathological hallmarks of amyloid-beta plaques and phosphorylated tau proteins, the indicator of apoptosis, the marker of broken DNA double-strand, the nitrite levels of oxidative stress, the cell number of cholinergic, the Morris water maze (MWM) and novel object recognition (NOR) task were evaluated after oral administration of the ENT1 inhibitor.

Results: Our results indicated that the ENT1 inhibitor blocked the increases of nitric oxide, caspase 3 and phosphorylated γ-H2AX, increased activities of nuclear DNA-dependent serine/threonine protein kinase (DNA-PKcs) through the non-homologous end joining (NHEJ) pathway to repair DNA double-strand breaks and alleviated cholinergic neuronal loss in sAD mice. The ENT1 inhibitor also improved the cognitive deficits in the MWM and NOR tasks.

Conclusion: Our result indicated that the ENT1 inhibitor could successfully reverse the pathogenesis of sAD, including oxidative stress, DNA double strand breaking, neuronal loss of cholinergic neurons, and cognitive deficits. The ENT1 inhibitor could be potential for sAD treatment.

Disclosure: Nothing to disclose.

Cerebrovascular diseases 2

EPO-251

Prognostic value of intracerebral hemorrhage spread and localizaton

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Background and aims: We aimed to determine the factors affecting the hematoma resorption rate besides evaluating the effect of risk factors, hematoma features, localization and spread of hematomas on the prognosis of intracerebral hemorrhages.

Methods: Data obtained from medical reports between 2015 and 2021, retrospectively. Hematoma volume and hematoma resorption rate were calculated at admission and on the seventh day. Functional status was evaluated by Modified Rankin Score, Functional Independence Scale, and Barthel Index on admission, the 1st and 3rd months.

Results: Total 179 (37.4%F/62.6%M) patients with a mean age of 62.90 ± 15.14 years were included. Hematoma localizations were: lobar (42.5%), cerebellar (8.4%), thalamic (21.2%), basal ganglia (24%) and brainstem (3.9%). In the first CT, the bleeding volume was 21.78 ± 29.77 cm^3. The resorption rate was 0.65 ± 0.91 (0–4.1)cm3/day. Poor prognosis indicators were old age and higher resorption rate measurements. Resorption rate measurements were higher in males, in patients with coronary artery disease and stroke histories,or with lobar and cerebellar hemorrhage. A significant and good correlation was found between hematoma resorption rate and volume measurement on the initial CT.

Conclusion: In our study, male gender, history of stroke and coronary artery disease, volume and localization of hematoma were detected as factors affecting the rate of resorption. Rate of resorption was higher in patients with lobar and cerebellar hematomas and with large hematoma volume. In intracerebral hemorrhages demographic, clinical and laboratory data, hematoma volume and localization are factors used in estimation of the prognosis. We suggest that measurement of hematoma resorption rate will contribute to these factors.

Disclosure: Nothing to disclose.

EPO-252

A new timeframe indicator for ischemic stroke treatment: the treatment to stroke unit admission time

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Background and aims: Optimal time intervals of acute ischemic stroke (AIS) treatment from symptom onset to intravenous thrombolysis (IVT) and/or mechanical thrombectomy (MT), are recommended by international guidelines. The admission to Stroke Unit (SU-A) is the next step in the correct management of AIS but the time interval between procedure termination and SU-A has never been evaluated. We aimed to investigate the time between end of MT and/or IVT and SU-A as a variable potentially impacting on clinical outcome of AIS patients.

Methods: We retrospectively reviewed the medical records of AIS patients receiving MT and/or IVT and subsequently admitted to our SU. We collected the time elapsed between the end of procedure and SU-A, neurological severity, and outcome. Primary outcome was functional independence at 90 days (mRS 0–2) and failure of early neurological improvement (fENI = 7days/discharge NIHSS $\geq$ baseline NIHSS).

Results: We included 103 patients. Patients with fENI had a significantly higher time from end of procedure to SU-A (19.28hrs vs 8.16hrs, p=0.044). At multivariate analysis, this time was statistically associated with fENI when corrected by onset-to-procedure time, age, sex and, baseline NIHSS (OR:1.035, p=0,013, CI 95%:1.007–1.063). End of procedure-to-SU-A time and door-to-SU-A time were not statistically different between patients with good and bad outcome at 3 months.
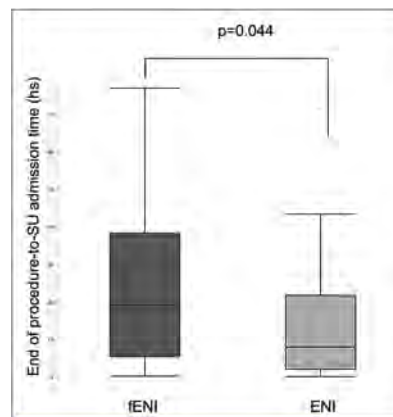
Median and IQR of End of procedure-to-SU admission time between patients with fENI and patients with ENI

Conclusion: Delay in SU-A of ischemic stroke patients treated with MT and/or IVT resulted in higher rate of fENI. The admission to dedicated SU of AIS patients receiving MT and/or IVT should not be withheld or delayed.
Disclosure: Nothing to disclose.

EPO-253

Emergent carotid stenting in mechanical thrombectomy for acute stroke: outcomes and complications

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Background and aims: Optimal management of steno-occlusive carotid lesions in patients with acute stroke undergoing mechanical thrombectomy (MT) is still under discussion. We aimed to describe outcomes and complications of emergent carotid stenting and associated antithrombotic therapies in this setting.
Methods: Retrospective observational study of patients with carotid steno-occlusive lesions treated with MT between January 2019 and December 2021. We compared clinical characteristics, antithrombotic treatments and outcomes (at discharge and after 3 months) focusing on stent occlusion, haemorrhagic transformation and modified Rankin scale (mRS) of patients with and without emergent stenting.
Results: 53 patients, 37 (69.8%) men, median age 68 (61–79) years were included. 34 (64%) were treated with emergent carotid stenting. We found no differences in basal characteristics between patients with and without stenting. Patients undergoing stenting had lower NIHSS scores on admission [median (IQR): 14 (7–20) vs 18 (14–23), p=0.033]. Atherothrombotic etiology and carotid dissection were more frequent in the stenting group (p=0.024). Intravenous thrombolysis rates were similar in both groups (50% vs 42.1%, p=0.581). Hemorrhagic transformation occurred in 17.6% and 15.8% patients respectively (p=1). Eighteen (53%) patients received tirofiban and 20 (59%) iv aspirin during stent placement; amongst them there were no differences in hemorrhagic transformation rates. Stent occlusion occurred in 4 (11.8%) patients. Dependency rates (mRS 3–6) were similar between patients with and without stenting at discharge and 3 months (58.8% vs 63.3% and 57.7% vs 76.9%, respectively).
Conclusion: Emergent carotid stenting during MT seems safe regardless of the use of intravenous thrombolysis and antithrombotic therapy.
Disclosure: Nothing to disclose.

EPO-254

The role of biochemical markers in the early diagnostics of ischemic stroke

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Background and aims: We aimed to evaluate serum levels of neuron-specific enolase (NSE), glial fibrillary acidic protein (GFAP) and NR2-antibodies for NMDA-receptor (NR2) in patients with acute ischemic stroke (IS), compared to chronic brain ischemia (CBI) and healthy controls.
Methods: 63 patients with IS, 11 patients with CBI and 20 controls were included. Serum biomarker levels were evaluated twice in IS group [point 1 (p1) in the first 72 hours and point 2 (p2) at 10–14 day of IS] and once for others. Patients with IS were clinically evaluated with stroke scales (NIHSS, Barthel, Rankin, Rivermead) in dynamics.
Results: In IS group NSE and GFAP levels at p1 were elevated, lowering significantly by p2 (p=0.003, p=0.034) while NR2 levels were within reference values both at p1 and p2, slightly rising with time. NSE and NR2 levels in CBI and control groups were significantly lower than in p1 of IS group (p=0.002 for NSE and 0.0002 for NR2), while GFAP levels were lower compared to p2 of IS group (p=0.0003). In patients with IS and severe neurological deficit (NIHSS >6) NSE and GFAP levels at p1 were significantly higher (p=0.041, p=0.021). We observed higher NSE p2 levels (p=0.019) in patients with unfavorable outcomes (Rankin >2). Correlations were found between biomarker levels and higher p1 NIHSS, lower p2 Barthel and higher p2 Rankin scores. ROC-analysis showed higher AUC score (0.741) for biomarker panel in comparison with separate markers.
Conclusion: This demonstrates potential benefit of NSE, GFAP and NR2 as diagnostic and prognostic biomarkers.
Disclosure: Nothing to disclose.

EPO-255

Reversible Cerebral Vasoconstriction Syndrome (RCVS) in a young hypertensive patient

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Background and aims: RCVS refers to a group of conditions that show reversible multifocal narrowing of the cerebral arteries, typically manifesting with thunderclap headache that can recur over a span of days to weeks. About one-third of patients may have blood pressure (BP) surges accompanying the headache attack. Clinical awareness of this entity is essential for timely intervention and prevention of ischaemic brain injury.

Methods: We report the case of a 39-year-old Afro-Caribbean woman who had presented with a 2-day history of recurrent thunderclap headache followed by sudden onset left-sided weakness and confusion. She was on treatment for hypertension and previously had pre-eclampsia during her pregnancy 15 years ago.

Results: Her presenting CT head scan revealed a right temporal haematoma. Cerebral angiogram showed mural irregularities mainly in distal segments of the anterior circulation. Her BP was particularly difficult to control requiring transfer to HDU. Within 72 hours of admission, she developed watershed ischaemic infarcts in left frontal and right parietal areas. Serial cranial imaging demonstrated resolution of arterial narrowing. Investigations with renal artery ultrasound and urine catecholamine screen did not detect abnormalities. She made a good clinical recovery.
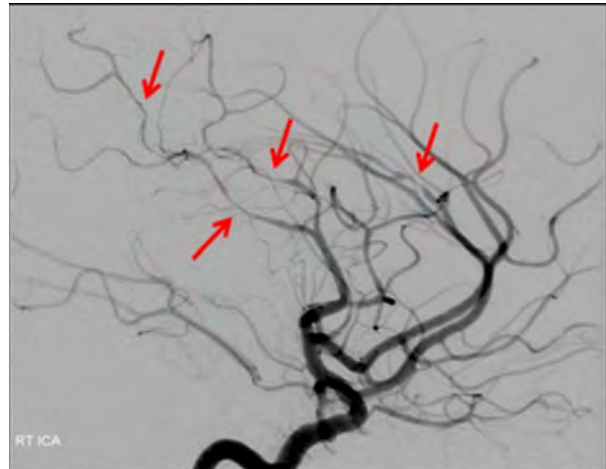
Cerebral Angiogram
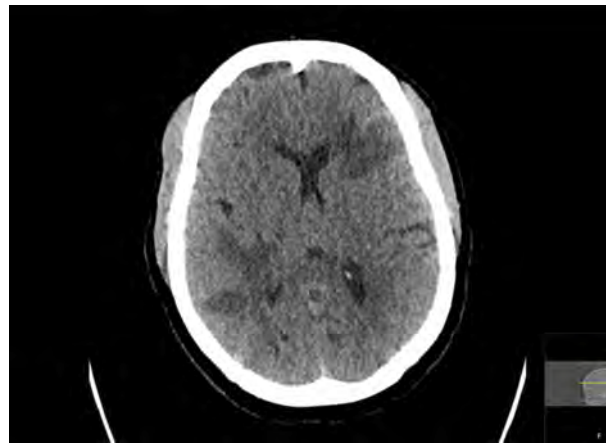
Follow-up CT Head scan: Watershed infarcts

Conclusion: High initial BP in RCVS may be caused by severe headache, predisposing condition, or associated vascular risks. In the setting of cerebral vasoconstriction, relatively mild hypotension can trigger ischaemia in watershed territory of cerebral arteries. On the other hand, uncontrolled hypertension may result in focal brain haemorrhage or ischaemia. Admission in a high dependency unit for neurological monitoring and BP management may benefit patients with RCVS.

Disclosure: Nothing to disclose.

Presentation CT Head scan: Right temporal haematoma

EPO-256

Impact of COVID-19 pandemic on stroke care in the Republic of Moldova

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Background and aims: The negative consequences of COVID-19 pandemic on healthcare systems have been reported globally. The objectives of this study were to measure the impact of the COVID-19 pandemic on the total numbers of stroke hospitalizations, intravenous thrombolysis (IVT) and thrombectomy (MT) procedures in the Republic of Moldova (RM).

Methods: We conducted a retrospective, cross-sectional study in country's main comprehensive stroke center. Diagnoses were selected according to ICD-10 codes from center's stroke database. A 4-month period containing the stroke hospitalization, IVT and MT rates immediately before first reported cases of SARS-COV-2 infections was compared to similar periods immediately after and at 1-year time point.

Results: There were 400 stroke admissions in the 4 months immediately before compared to 156 admissions during first pandemic months, representing a 61% (95% CI, $p<0.05$) decrease; respectively 174 admissions at 1-year time period showing a 56.5% (95% CI, $p<0.05$) decrease. There were 20 IVT therapies in the 4 months preceding compared to 29 procedures during first months, representing a surprising 45% (95% CI, $p>0.05$) increase; and 13 procedures at 1-year time period showing a 35% (95% CI, $p>0.05$) decline. Number of MT procedures decreased to 0 in first months and to 7 (95% CI, $p>0.05$) at 1-year time point. There was a 0.32% stroke rate across total COVID-19 hospitalizations during the whole analyzed pandemic period.

Conclusion: The COVID-19 pandemic has proven to have a considerate and persistent negative repercussion on stroke care in the Republic of Moldova. The severity of the impact was consistent with center's total processing capacity and COVID-19 inpatient volumes.

Disclosure: Nothing to disclose.

EPO-257

Abstract withdrawn.

EPO-258

Is the Cd/Zn molar ratio a potentially new diagnostic biomarker of carotid atherosclerosis in ischemic stroke patients?

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Background and aims: Cadmium is a nonessential metal with toxic, proinflammatory, proatherogenic effects. Oxidative stress, as well as inflammation, may thus likely be involved in the potentially adverse effects of Cd on the cardiovascular system and increased risk of ischemic stroke. This study aimed to examine the impact of the serum Cd/Zn molar ratio on the prevalence and severity of the carotid atherosclerotic process in patients with acute ischemic stroke (AIS) in northeastern Poland.

Methods: We enrolled 175 patients with AIS (mean age 67.41 ± 11.9 years, 51.4% men). The serum concentrations of mineral components (Cd, Zn) were determined by the atomic absorption spectrometry method. Clinical data were collected from medical records. The molar ratio of Cd/Zn was assessed.

Results: We observed a positive correlation between Cd/Zn molar ratio (the highest values in patients with 30-50% carotid stenosis, median: 0.00319) and the stage of carotid atherosclerosis assessed with carotid Doppler ultrasound or computed tomography angiography ($r=0.18, p=0.020$), HDL cholesterol ($r=0.18$, $p=0.017$) and fibrinogen values ($r=0.20$, $p=0.008$) in patients with AIS. Smokers compared to non-smokers had a statistically higher Cd/Zn molar ratio ($p<0.001$). In molar ratio there were no significant differences in sex ($p=0.466$), TOAST classification ($p=0.525$), administered treatment (intervention therapy compared to conservative) ($p=0.053$), types and locations of atherosclerotic lesions ($p=0.570$, $p=0.895$). There were no significant correlations with age, blood concentrations of CRP, TC, LDL, TG, homocysteine, uric acid, total antioxidant status.

Conclusion: These findings emphasize the potential of toxic trace elements to develop novel biomarkers for acute ischemic stroke patients with carotid atherosclerosis. Smoking has been implicated as a source of proatherogenic cadmium exposure.

Disclosure: Nothing to disclose.

EPO-259

Could median nerve somatosensory evoked potentials be helpful in extracranial internal carotid artery recanalization

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Background and aims: Favorable clinical outcome after extracranial internal carotid artery (eICA) recanalization therapy is reported between 30–62%. Median nerve somatosensory evoked potentials (SEP) amplitude is a direct marker of rolandic area neuronal activity and correlates well with cortical cerebral blood flow. Rolandic neurons survival is the main condition for the attainment or recovery of motor function. Evaluate the role of preoperative and intraoperative SEPs on functional outcome after urgent surgical eICA recanalization.

Methods: Prospective enrollment. Inclusion criteria: Acute ischemic stroke with eICA occlusion within 24 hours eligible for recanalization therapy. Pre-stroke performance modified Rankin score (mRS) ≤2.Parameters measured: Preoperative ipsilateral SEP amplitude (SEP-amp), side-to-side ratio (SEP-ratio) and significant intraoperative SEP amplitude decrease after carotic artery cross-clamp (SEP-CC). 3-month functional outcome according to mRS.

Results: Cohort: 33 patients, 30 males (90.1%), age of 70.4±8.9 years.Abnormal SEP-amp (<0.8uV) and SEP-ratio (<0.5) were in 6 (18.2%) and 4 (12.1%) respectively. Positive predictive value for unfavourable (mRS >2) outcome: 92.6% and 100%, false negatives: 9.1% and 3.1% respectively.Intraoperatively SEP-CC decreased in 6 (18.2%). SEP-CC recovered after intervention (blood pressure gain, shunt insertion) in 5 of them. 3-month outcome: favorable (mRS 0–2) in 28 (84.8%), (mRS 4–5) in 2 (6.1%), three (9.1%) died.

Conclusion: In urgent eICA recanalization SEP-ratio might be promising and reliable predictor of functional outcome after eICA recanalization.

Intraoperative SEP seems to be beneficial in the prevention of intraoperative ischemia development.

Functional outcome could be positively affected both by intraoperative and preoperative SEPs.
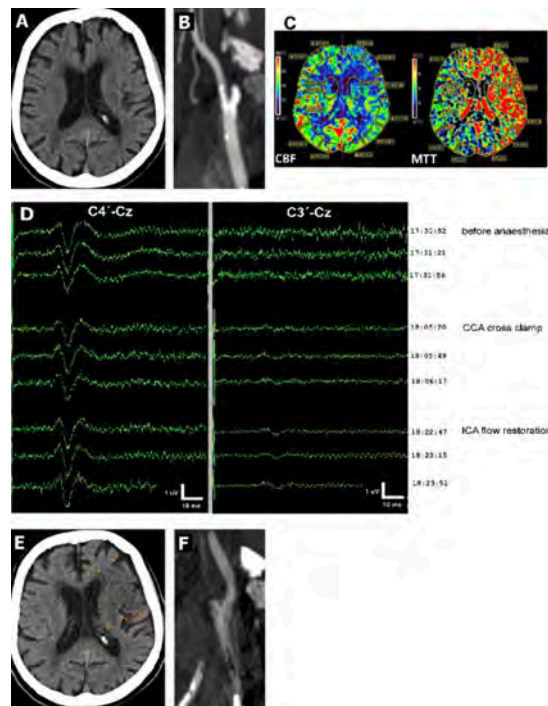
Fig 1. Preserved SEP-amp and SEP-ratio, NIHSS 19 before surgery. Right eICA occlusion (A, B), right MCA, ACA hypoperfusion with CBF decrease and MTT prolongation (C) and preserved SEPs on symptomatic side (D). 24 hours after surgery: nonenhanced brain sc..
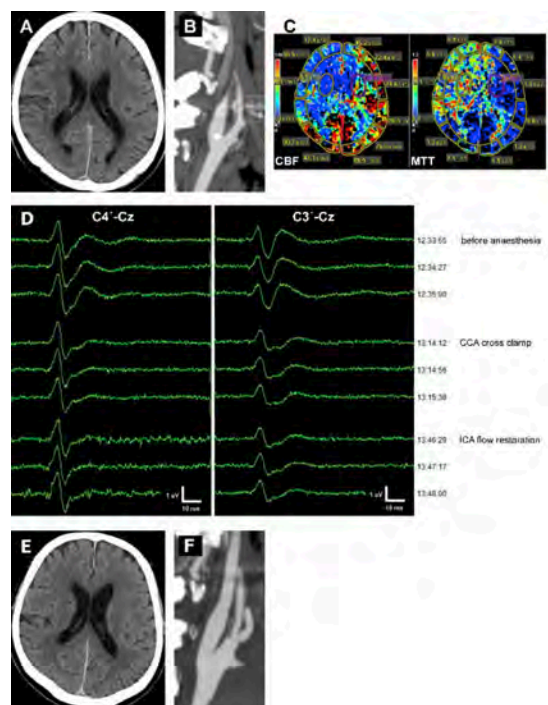
Fig. 2 Ipsilateral absent SEP-amp, abnormal SEP-artio, NIHSS 19 before surgery. Left eICA occlusion (A, B), left MCA, ACA hypoperfusion with CBF decrease and MTT prolongation (C) and severely decreased median nerve SEPs on symptomatic side (D) before.
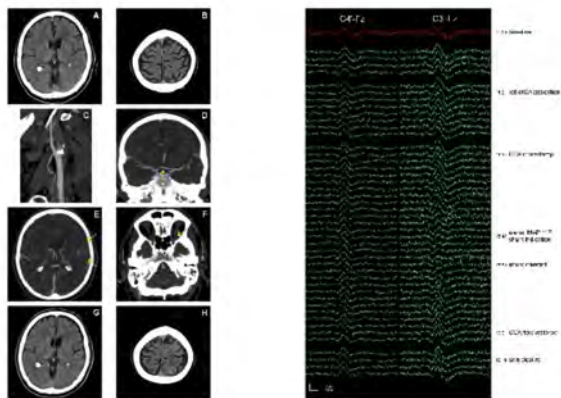
Fig. 3 The intraluminal shunt effect on SEP-CC amplitude recovery after cross-clamp drop. Right: SEP waterfall with ipsilateral N20/P25 amplitude drop after CCA-CC and recovery after intraluminal shunt insertion. Left: CT exams. Admission stroke protocol

Disclosure: Grant support: NV19-09-00199, NV19-04-00270.

EPO-260

Predictors Of Functional Outcome After Posterior Circulation Stroke

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Background and aims: It is not known whether specific symptoms or signs associated with the vertebrobasilar circulation (ataxia, diplopia, hemianopia, etc) particularly influence functional prognosis after a posterior circulation (PC) stroke. The aim of the present study was to investigate if specific neurologic symptoms or signs at admission are independent predictors of functional outcome 3 months after a PC stroke.

Methods: Retrospective cohort study with prospectively collected functional outcome of PC ischemic stroke patients admitted to the Stroke Unit of an university hospital and included in the PRECISE STROKE cohort between 2017 and 2020. We collected demographical, clinical and imaging characteristics as well as functional outcome 3 months after stroke using the modified Rankin scale (0–2: favorable vs 3–6: unfavorable). We performed a multiple logistic regression analysis.

Results: 159 patients were included in the analysis: 113 with favorable outcome and 46 with unfavorable outcome. Patients with unfavorable outcome were older (mean 73.7 years, p<0.01), had higher initial NIHSS scores (median 10, p<0.01) and had pc-ASPECTS≤7 more often (47.8%, p<0.01). The final multiple logistic regression model with 5 predictors revealed the following adjusted odds ratios: age (OR 1.08, p<0.01), admission NIHSS score (OR 1.12, p<0.01), pc-ASPECTS (≤7 vs >7) (OR 4.72, p<0.01), visual field defects (OR 2.71, p=0.05) and eye movements abnormalities (OR 0.34, p=0.07).

Conclusion: The independent predictors of functional outcome after PC stroke were age, NIHSS score and pc-ASPECTS. After adjusting for these variables no specific neurologic symptom or sign was shown to significantly impact daily activities at 3 months.

Disclosure: Nothing to disclose.

EPO-261

Undiagnosed major risk factors in patients with acute ischaemic stroke: clinical profile, stroke mechanisms and outcome

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Background and aims: There is scarce clinical information about the frequency, patient profile and stroke mechanisms in patients with acute ischaemic stroke (AIS) with previously undiagnosed major vascular risk factors (UMRF).

Methods: In a retrospective analysis from the ASTRAL-registry from 2003-2018, we analysed demographic, clinical, therapeutic and prognostic variables. Both univariate and multivariate logistic regression analysis were performed.

Results: After excluding 763 (14.9%) patients for lack of consent and 3 for missing information, we analysed 4,354 patients [median age 70 years (IQR 15.2), 44.7% female]. In the 1,125 (25.8%) UMRF patients, 30.3% (n=341) had no UMRF, and 67.7% (n=784) had at least one UMRF. The newly detected major risk factors were dyslipidaemia (61.4%), hypertension (23.7%), atrial fibrillation (10.2%), diabetes mellitus (5.2%), ejection fraction <35% (2.0%) and coronary disease (1.0%). Multivariate analysis (MVA) showed positive association with lower age, non-Caucasian ethnicity, PFO, contraceptive use (in patients <55 years old) and smoking (for patients ≥55 years old). We also found negative associations with antiplatelet use before event and higher BMI. Regarding stroke mechanisms, MVA showed a higher frequency of PFO related strokes and a lower frequency for large vessel, lacunar, cardiac or multiple coexisting causes. Functional outcome at 12 months and cerebrovascular recurrences were not different between groups.

Conclusion: In this large single centre AIS cohort, 67.7% of patients with UMRF were newly diagnosed with major vascular risk factors, the most common being dyslipidaemia, hypertension and atrial fibrillation. Patients of the UMRF group were younger and more often had PFOs, and both contraceptive and tobacco use.

Disclosure: Nothing to disclose.

EPO-262

WHAT'S BEST FOR WEBS?

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Background and aims: Carotid web (CaW) is an intimal version of fibromuscular dysplasia and an underrecognized cause of cryptogenic stroke in young patients. Aggressive therapy is required if CaW is detected given the high stroke recurrence rate in medically managed symptomatic patients. Herein, we report a case of CaW treated with carotid artery angioplasty and stenting (CAS), its intraprocedure complication and final outcome.

Methods: Case report and literature review.

Results: A 56-year-old black female, with personal history of smoking and a previous stroke of unknown etiology treated with ASA 100 mg/day in Cuba without sequelae, presented with sudden onset difficulty in speech and left-side weakness (NIHSS 20). Occlusion of right MCA-M1 segment and ipsilateral CaW were detected, she underwent iv thrombolysis plus mechanical thrombectomy (MT) with successful recanalization (TICI IIB), and was discharged with left hemiasomatognosia (NIHSS 1) a week after onset. Four months later, she underwent CAS for definitive treatment. During the placement of distal filter protection, acute occlusion of distal ICA occurred. Fortunately, MT could be performed immediately, followed by CAS achieving TICI III result. The patient was discharge with NIHSS 0 four days after, and continues asymptomatic without recurrence at 2-year follow-up.

Angiography showing Carotid Web (CaW) in the Right Internal Carotid Artery (ICA)

Conclusion: Although first described decades ago, optimal therapy for CaW is still unknown. CAS and carotid endarterectomy (CEA) are increasingly used for CaW given its definitive treatment, with similar results. Due to the possibility of clot presence and subsequent risk of embolization during procedure, CAS may offer an advantage over CEA due to the possibility of performing a MT if needed.

Disclosure: Nothing to disclose.

EPO-263

Infective endocarditis and neurological complications: a monocentric, retrospective observational study

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Background and aims: Infective endocarditis (IE) should be suspected in patients with cerebrovascular accident of undetermined source among the less frequent but most prominent causes. Symptomatic or asymptomatic neurological complications occur in a high percentage of patients with IE because of a septic embolization before or after the diagnosis.

Methods: Our monocentric, retrospective observational study recruited patients, without age limits, admitted to Alessandro Manzoni Hospital in Lecco between January 2012 and October 2019, diagnosed with infective endocarditis. We involved patients admitted in any department using Hospital Health Service digital system. We collect data about epidemiological features, vascular risk factors, treatment at home, neurological complications, bacterial identification and antimicrobial therapy, surgical treatment and outcome.

Results: We enrolled 311 patients, 104 women and 207 men. Excluding duplicates or patients with incorrect classification 239 people were included. 22 patients (9.2%) received the diagnosis of IE after admission for ischemic stroke. About half of the patients undergo cardiac surgery during hospitalization with less than 15% with a negative outcome.

Conclusion: In our work, we identified a substantial similarity of epidemiological data with those of the international studies, trying to collect information about management of antiplatelet or anticoagulant treatment, need and time of surgery, adequate antimicrobial therapy and risk of recurrence.

Disclosure: Nothing to disclose.

EPO-264

Evaluation of delayed activation of AMPA receptor in sub-acute phase against ischemic reperfusion injury in rats

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Background and aims: Ischemic stroke is the second most common cause of mortality worldwide and is described as a sudden neurological outbreak triggered by diminished perfusion through the blood vessels to the cerebral tissues. Recent studies showed that activation of (α-amino-3-hydroxy-5-methyl-4-isoxazolepropionic acid) AMPA receptors at late stage after ischemic stroke improved post stroke recovery in rats. Hence, the present study was designed to investigate the effect of delayed activation of AMPA receptors by aniracetam in sub-acute phase on post stroke recovery in animal model of stroke.

Methods: Focal cerebral ischemia was induced in rats by occlusion of the middle cerebral artery (MCAo) using the intraluminal technique. Reperfusion was allowed by removing occlusion after 90 minutes of ischemia period. Rats were administered aniracetam (50 mg/kg, i.p.) after 3 and 5 days of reperfusion till 7 days followed by assessing neurobehavioral parameters & TTC staining. The MCAo rats were injected with a solvent mixture without aniracetam (vehicle-treated group).

Results: Aniracetam treatment after 3 and 5 days of reperfusion till 7 days demonstrated significant protective effect against neurological destruction and reduced infarct size (p<0.001) which were assessed by TTC staining. Aniracetam treatment exhibited significant diminution in neurological deficit score, when compared with MCAo group. Additionally, aniracetam treated groups augmented the motor coordination and grip strength, when compared with rats in the MCAo group (p<0.001).

Conclusion: This study indicated that aniracetam reduced the post stoke neurological damage and augmented the recovery after ischemic stroke, suggesting the beneficial effect of delayed activation of AMPA receptors on post stroke recovery.

Disclosure: Nothing to disclose.

EPO-265

The day you will not remember – Transient Global Amnesia Retrospective Study

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Background and aims: Transient Global Amnesia (TGA) is a neurological condition in which patients present cognitive impairment limited to amnesia with duration <24hours. Hippocampal DWI lesions support the TGA diagnosis and appear to be time-dependent between symptom-onset and MRI imaging, more reliably seen in the subacute phase. Aims: To characterise patients with DWI hippocampal lesions versus patients with normal MRI concerning demographic factors, duration of episode, recurrence, precipitating factors, past medical history, imaging/electroencephalographic exams and time of MRI imaging.

Methods: Selection of patients with TGA diagnosis according to Hodges and Warlow Criteria admitted to the Neurology or Internal Medicine department between January 2012 and November 2021 and review of their charts. The statistical analysis was performed using IBM SPSS Statistics® 25 and Microsoft Office Excel®.

Results: 58 patients with TGA were identified with a mean age of 63.8±10.7y.o. 51 patients (94,8%) performed MRI. Eght patients presented DWI positive for hippocampal lesion (Group A) and 43 patients presented normal DWI (Group B). In Group A, MRI was performed in a meantime of 3.00 days versus 5.89 days in Group B (p-value=0.0074). Other results in Group A include: older age, more patients observed during the episode of amnesia (versus reporting), more frequent migraine history and shorter duration of TGA. These results did not reach statistical significance possibly due to the small sample size.

Conclusion: TGA remains a mysterious neurological condition. DWI hippocampal lesion patients' had a smaller time-gap between symptom-onset to MRI performing, highlighting the importance of timely subacute MRI imaging in this condition.

Disclosure: Nothing to disclose.

Cerebrovascular diseases 3

EPO-266

Neurological phenotypes and treatment outcomes in Eagle Syndrome: A Systematic Review

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Background and aims: Eagle syndrome is caused by elongated styloid processes or ossified stylohyoid ligaments affecting vascular and neuronal structures, including carotid arteries and cranial nerves. Pain, dysphagia, tinnitus, paraesthesia, and neurovascular events may be triggered by head movements or arise spontaneously. Patients may present with ipsilateral ischemic stroke, carotid artery dissection and jugular vein stenosis. Treatments include surgical and medical approaches. However, therapeutic recommendations are based on low-grade evidence, and a systematic review of neurological symptoms and outcomes of Eagle syndrome is lacking.

Methods: We are conducting a systematic review of patient-level data on adults with Eagle syndrome, following PRISMA guidelines, to examine neurological and non-neurological symptoms and signs before and after treatment for Eagle syndrome. The study protocol is registered with PROSPERO.

Results: We extract data on demographics, presenting symptoms, neurological deficits, radiological findings, and treatments, including outcome and complications from studies in multiple indexing databases published between 2001 and 2021. 1,964 records were screened after duplicate removal. 675 full-text studies are being assessed. Results will be presented at the conference.

Conclusion: Eagle syndrome is an underdiagnosed neurovascular condition with potentially serious complications, including ischemic stroke. We are synthesizing the published data on clinical presentations, outcomes, and treatment options to raise awareness in the neurological community of this treatable condition.

Disclosure: The authors declare no relevant conflicts of interest. No funding was obtained for this work. Elisabeth Waldemar Jakobsen is supported by a scholarship grant from the Lundbeck foundation unrelated to the present study.

EPO-267

Early Neurological Deterioration in Isolated Pontine Stroke: Clinical and Imaging Features

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Background and aims: Patients with isolated pontine ischemic stroke may face early neurological deterioration (END). We aimed to assess clinical and neuroimaging factors associated to END in pontine stroke.

Methods: We analysed 112 consecutive patients, admitted to our Stroke Center, with MRI/CT-defined isolated pontine infarction, without basilar artery occlusion. END was defined as persisting NIHSS increase ≥ 2 points, occurring <48h after admission. Lesion anatomy was classified by neuroimaging. Pontine warning syndrome (PWS) was defined as transient neurological symptoms, typical for posterior circulation, occurring 2–7 days before stroke onset.

Results: Among 112 patients with isolated pontine infarction, END was recorded in 36 (32.1%). Demographic data and stroke risk factors did not differ between END and clinically stable patients. While median baseline NIHSS was similar in both groups (3 vs. 4, p=0.25), median increase of 5 NIHSS points (range 1–12) was observed at discharge in END patients (p<0.001). PWS occurred in 14/36 (38.9%) subjects with END vs. 16/76 (21.1%) subjects without END (p=0.067). Significant chronic small vessel disease (MRI-based Fazekas score ≥ 2) occurred in 24/32 (75.0%) patients with END vs. 39/70 (55.7%) without END (p=0.08). Anteromedial lesion location was the most common (n=27 deep, n=38 superficial), followed by anterolateral (n=19), tegmental (n=16) and other (n=12). END was observed in 8/27 (29.6%) deep anteromedial, 18/38 (47.4%) superficial anteromedial, 4/19 (21.1%) anterolateral, 0/16 (0.0%) tegmental, 6/12 (50.0%) other (p=0.0061 overall).

Conclusion: Early neurological deterioration is common in pontine stroke patients. We described possible association with significant chronic small vessel disease, ventral stroke location and occurrence of pontine warning syndrome.

Disclosure: Nothing to disclose.

EPO-268

Anaemia in acute ischemic stroke patients submitted to thrombectomy is associated with worse clinical outcome

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Background and aims: Acute ischemic stroke (AIS) is caused by impairment of nutrients supply due to vessel occlusion. The oxygen-carrying capacity in the blood, related to the haemoglobin (Hb) level, might influence the outcome. We aim to find the impact of Hb on the outcome of AIS patients treated with endovascular thrombectomy (EVT).

Methods: We included adult patients with anterior circulation AIS, admitted to our comprehensive Stroke Centre, treated with EVT, with or without previous Intravenous thrombolysis (IVT), between January and December 2019. We excluded patients with active cancers, absent imaging at 24 hours, vitamin B12 deficiency, on dialysis, with chronic hepatic disease, autoimmune disease, or no follow-up data at 90 days. Demographic, clinical, laboratory and imagological data at admission and first 24 hours after treatment were retrospectively collected. Functional outcome was defined by the modified Rankin scale: 3–6 (dependent or dead) versus 0–2 (independent) at 90 days.

Results: We included 130 patients (76 EVT, 54 IVT+EVT) in the analysis, with a median age of 76 years old and 39.2% male. The median Hb was 13.6mg/dL at baseline and 12.5mg/dL after treatment. 22.7% had anaemia at baseline while 43.6% had anaemia after treatment, according to the World Health Organization criteria for males and females. In a multiple logistic regression model, anaemia after treatment was associated with worse functional outcome (p<0.05), and anaemia before and after treatment was associated with higher mortality (p<0.05), when adjusted for confounding factors.

Conclusion: Presence of anaemia on EVT-treated patients appear to be associated with worse clinical outcome.

Disclosure: Nothing to disclose.

EPO-269

Time of day affects endovascular therapy workflows and outcome in a nationwide stroke system

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Background and aims: In Austria, nationwide coverage of endovascular therapy (EVT) for large vessel occlusion stroke including mandatory electronic documentation was established in 2013. We investigated whether outcome and other treatment-related factors differ at particular times of day.

Methods: We analyzed data from the prospective nationwide Austrian stroke registry capturing all consecutive stroke patients treated with EVT between 2016–2020. Patients were trichotomized according to time of groin puncture into treatment within regular working hours (7:00–13:59), afternoon/evening (14:00-20:59) and night-time (21:00–06:59), additionally 12 treatment windows with similar patient size were analyzed. Outcome variables included workflow parameters, EVT success/complications and modified Rankin Scale (mRS) scores three months post-stroke.

Results: We included 2911 EVT patients (median age 74 years, 50.7% female). While NIHSS at admission, onset-to-door and groin-to-recanalization times were not different between groups, door-to-groin time was considerably longer outside of regular working hours, especially at night-time (93 vs. 75 minutes, p=0.003). No such differences were seen when comparing treatment at weekdays and weekend or regarding number of passes, recanalization success and treatment-related complications in different time windows. Patients treated within regular working hours had better outcome three months post-stroke (mRS 0–2: 42.7% compared to 35.8% treated in the afternoon/evening and 35.6% treated at night-time, p=0.004). The lowest rates of good functional outcome were found in the time window of 0:41–6:59 (32.4%), the highest rates at 7:00–9:30 (48.2%).

Conclusion: EVT workflows outside of regular working hours need to be improved in order to reach similar treatment speed and functional outcome as within regular working hours.

Disclosure: Nothing to disclose.

EPO-270

Prediction of acute symptomatic seizures in cerebral venous thrombosis

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Background and aims: Cerebral venous thrombosis (CVT) accounts for 0.5–1% of all strokes and 24–50% of patients develop acute symptomatic seizures (AS). We aimed to identify clinical and imaging predictors associated with a higher risk of acute seizures in a population of CVT patients.
Methods: We conducted a single-center, retrospective cohort study and included all patients with CVT admitted to our stroke unit between January 2011 and December 2021. We defined our primary outcome as AS and compared clinical and radiological characteristics in both groups using logistic binary regression.
Results: Of the 141 patients, 40 experienced AS (28.4%). We found a higher risk of AS in patients with focal neurological signs (OR 7.09, CI 95% 3.15–16.00, p<0.001), involvement of the superior longitudinal sinus (SLS) or cortical veins (OR 6.22, CI 95% 2.67–14.50, p<0.001; OR 2.97, CI 95% 1.30–6.77, p=0.01), presence of hemorrhagic lesions or edema (OR 3.06, CI 95% 1.43–6.51, p=0.004; OR 3.49, CI 95% 1.57–7.75, p=0.002) and with frontal or parietal lobe lesions (OR 5.48, CI 95% 3.00–13.08, p<0.001; OR 4.60, CI 95% 1.98–10.68, p<0.001).
Conclusion: AS occurred in 25% of our CVT patients. We identified the involvement of SLS or cortical veins, hemorrhagic lesions, edema, parietal or frontal lobe involvement, and focal neurological deficits upon presentation as independent predictors for AS. Our findings were concordant with previous studies, but further evidence is needed to determine which patients would potentially benefit from prophylactic anti-convulsive therapy and whether this would impact long-term outcomes.
Disclosure: The authors have nothing to disclose.

EPO-271

Mechanical Thrombectomy in acute ischemic stroke: predisposing factors for hemorrhagic transformation.

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Background and aims: The mechanical thrombectomy (MT) has been established as a standard treatment for acute large artery occlusion. One of the unwanted effects of this treatment method is hemorrhagic transformation (HT), so searching for factors increasing the risk of HT are very important. The aim of our study was to evaluate predisposing factors for hemorrhagic transformation (HT) in patients with acute ischemic stroke treated with mechanical thrombectomy (MT).
Methods: We retrospectively reviewed the records of patients with ischemic stroke treated with MT, referred to our neurology ward between (12.2017–12.2021). We enrolled 142 patients (71 females and 71 males). Variables included initial NIHSS, blood glucose (BG), lipid concentration, initial blood pressure, age, gender, BMI, IV tPA and TICI score. Outcome measures were HT on 24-hour post-procedure head CT and modified Rankin scale (mRS) upon discharge.
Results: Among 142 patients (66.2±24 years), 51 (35,7%) experienced HT after thrombectomy. Average admitting NIHSS was significantly higher in the HT group (15.6 vs 12.1, p=0.035). Treatment with IV tPA was statistically significantly associated with higher odds of HT (OR=2.40, 95% C.I. 1.068–5.405; p=0.033). Higher BG levels were also statistically significantly associated with higher odds of HT (OR=2.19, 95% C.I. 0.969–4.933; p<0.05). TICI 0-1 was associated with higher risk of HT (OR 2.80, 95% C.I. 1.21–6.48; p=0.015). Patients without HT had statistically more often mRS score ≤2 upon discharge.
Conclusion: Increased NIHSS, IV tPA, higher BG and TICI score 0-1 were associated with higher risk of HT and worse clinical outcomes.
Disclosure: Nothing to disclose.

EPO-272

Influence of antithrombotic pre-treatment and time window on hemorrhagic complications of ivt in ischemic stroke

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Background and aims: The risk of haemorrhagic complications of iv-thrombolysis in acute ischemic stroke may depend on the type and intensity of antithrombotic pre-treatment at the time of stroke onset. This study aimed to investigate the bleeding risk in a multicentre, longitudinal real-world-clinical cohort of patients with ischemic stroke.

Methods: This study bases on the Stroke Research Consortium in Northern Bavaria (STAMINA). Patients treated with iv-thrombolysis were categorized according to their antithrombotic pre-treatment: No pre-treatment, mono antiplatelet therapy, dual antiplatelet therapy, or oral anticoagulation. We investigated the incidence of asymptomatic and symptomatic haemorrhagic complications according to the patient category and time from symptom onset.

Results: 528 ischemic stroke patients with iv-thrombolysis were included. 272 (51.5%) had no antithrombotic pre-treatment, 216 (40.9%) were on mono antiplatelet therapy, 10 (1.9%) on dual antiplatelet therapy and 30 (5.7%) on oral anticoagulation. The incidence of asymptomatic intracranial haemorrhage differed between categories and was elevated among patients with mono antiplatelet therapy (5 (1.9%) vs. 14 (6.5%) vs. 0 (0.0%) vs. 2 (6.7%); p=0.036). The risk of symptomatic intracranial haemorrhage according to ECASS III criteria was similar (2 (0.7%) vs. 7 (3.3%) vs. 0 (0.0%) vs. 0 (0.0%); p=0.233). This result was consistent in the subgroup of patients treated in the unknown or extended time window beyond 4.5 hours from onset (n=97).

Conclusion: Pre-treatment with antiplatelet therapy was associated with asymptomatic haemorrhagic complications. The risk of symptomatic intracranial haemorrhagic was low and irrespective of antithrombotic pre-treatment in the early and extended time window of rt-PA application.

Disclosure: Nothing to disclose.

EPO-273

Serum Ferritin and D-Dimer as Possible Risk Factors in Ischaemic Stroke in Cancer Patients

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Background and aims: Ischemic stroke is frequently encountered in patients with malignant disease. The pathophysiology of stroke in such cases differs from other subjects with no malignant disease. This study was conducted to compare serum levels of ferritin and d-dimer in cases with ischemic stroke in cancer versus non-cancer patients.

Methods: The data of consecutive 264 patients presented with ischemic stroke, confirmed by clinical examination and radiological investigations, were retrospectively reviewed. The included cases were divided into two groups: Group A (non-cancer with stroke, 210 cases) and Group B (cancer with stroke, 54 cases). The collected data included patient demographics, systemic comorbidities, disease and tumor characteristics, in addition to platelet count, serum ferritin and d-dimer.

Results: Age, gender, and systemic comorbidities were statistically comparable between the two groups. Additionally, the etiology of stroke and its disability were not statistically different between the two groups. However, the incidence of mortality significantly increased in Group B (25.93% vs. 7.14% of Group A, p=0.005). Both serum ferritin and d-dimer showed a significant increase in association with cancer (Group B). The former had mean values of 294.54 and 867.87 ng/ml, while the latter had mean values of 463.83 and 888.13 ng/ml in the same two groups, respectively

Conclusion: Serum ferritin and d-dimer showed a significant rise in cancer-associated ischemic stroke. This confirms the role of the hypercoagulable state, associated with malignancy in the development of this morbidity.

Disclosure: The authors declare no conflicts of interest.

EPO-274

Consistency of poststroke disability assessment between stroke unit and rehabilitation ward physicians using MRS

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Background and aims: Modified Rankin Scale (mRS) is the most commonly used tool to quantify poststroke disability in everyday practice and by certified raters in clinical trials. However, interobserver variability may affect reliability of retrospective observational studies, including clinical registries. Our aim was to assess real life consistency between neurologists and rehabilitation physicians using mRS to rate poststroke disability in patients transferred directly from stroke unit to rehabilitation ward.

Methods: This is a retrospective analysis of 132 consecutive acute stroke patients transferred from single tertiary stroke unit to rehabilitation ward located in the same hospital in Warsaw, Poland. Patients were assessed by one rater from each department at the day of transfer. We distinguished between physicians previously certified in using mRS for clinical trials and never-certified physicians using mRS only for clinical purposes.

Results: mRS at discharge from stroke unit and on admission to rehabilitation ward was recorded for 105 of 132 patients. The overall agreement was 70.5% (Cohen's kappa 0.55). Similar agreement was observed in the subset of 30 patients rated by certified physicians in both departments (70.0%, kappa 0.57) and in the subset of 61 patients rated by a pair of certified neurologist and never-certified rehabilitation physician (73.8%, kappa 0.58).

Conclusion: According to our findings, everyday consistency between raters from stroke unit and rehabilitation ward using mRS is modest, irrespectively of prior certification. It emphasizes the need for regularly repeated and easily accessible training in conduction conventional mRS interviews or implementation of specialized tools with predefined questions.

Disclosure: Nothing to disclose.

EPO-275

Endovascular management of carotid artery stenosis with one and double-mesh stents – single-center results.

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Background and aims: The advantage of double-mesh stents over the one-mesh is uncertain. The aim of this study was therefore to compare clinical and MRI data in patients with one-mesh and double-mesh stenting.

Methods: The study included 112 patients with hemodynamically significant stenoses of the ICA: 53 without type 2 diabetes mellitus (DM2) (mean age in the group 64.9 ± 6.2 years) and 59 with DM2 (mean age in the group 65.8 ± 7.4 years). According to the indications, patients underwent transluminal balloon angioplasty with ICA stenting, and Acculink single-mesh stents (SMS) (n=66) and Casper double-mesh stents (DMS) (n=46) were placed.

Results: The patients were divided into 2 groups. Group I included 66 patients (37 men, 28 women) with ICA stenosis, who were placed with single-mesh stents (SMS). Group II included 46 patients (26 men, 20 women) with ICA stenosis, who were placed with double-mesh stents (DMS). Single ischemic foci larger than 5 mm after the intervention were observed more often in the group of patients without DM2 operated on using SMS (6%). In the group of patients without DM2 operated on using DSS, the total number of silent ischemic post-procedural lesions (SIPL) was found in the smallest number of patients (19%).
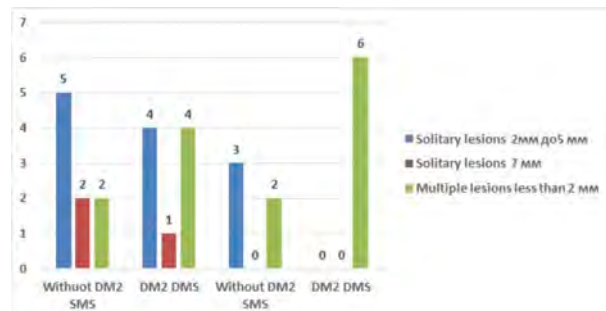
Distribution of silent ischemic leasions by groups

Conclusion: Differentiation of the nature of SIPLwas revealed, depending both on the type of stents used and on the presence of DM2. The use of DMS both in patients with DM2 and without it showed significantly better results (p<0.05), including those determined by the state of the brain substance.

Disclosure: Nothing for disclosure.

EPO-276

Biofeedback Gait Training in Cerebral Stroke Patients in the Early Recovery Phase with Stance Phase as Target Parameter

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Background and aims: Biofeedback technology (BFB) is currently considered effective and promising for training walking function. The aim of our study was to investigate the feasibility of using BFB training targeting one of the basic parameters of gait symmetry stance phase duration in cerebral stroke (CS) patients.

Methods: The study included 20 hemiparetic patients in the early recovery period after the first hemispheric ischemic CS. The control group included 20 healthy subjects. The BFB training and biomechanical analysis of walking (before and after all BFB sessions) were done using an inertial system. The mean number of BFB sessions was nine (from 8 to 11) during the three weeks in clinic.

Training process. The patient is on a treadmill. Inertial sensors are installed on his shins to register gait parameters. Before him is a screen with a virtual task.

Results: The spatiotemporal parameters of walking showed the whole syndrome complex of slow walking and typical asymmetry of temporal walking parameters, and did not change significantly as a result of the study therapy. The changes were more significant for the kinematics of hip and knee joints. The contralateral hip amplitude returned to the normal range. For the knee joint, the amplitude of the first flexion increased and the value of the amplitude of hyperextension decreased in the middle of the stance phase. Muscle function, the observed significant decrease in the function of m. Gastrocnemius and the hamstring on the paretic side remained without change at the end of the treatment course.

Conclusion: We obtained positive dynamics of the biomechanical parameters of walking in patients after the BFB training course. The feasibility and efficacy of their use for targeted correction need further research.

Disclosure: The authors declare no financial or other interest. The study was carried out under the state order Reg. no. AAAA-A19-119042590030-2.

EPO-277

DOES THE DYNAMIC OF RELEASING OF ST2 PREDICT ISCHEMIC STROKE OUTCOME?

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Background and aims: The aim was to investigate prognostic accuracy of the protein Suppression of Tumorigenicity 2 (ST2) serum dynamic in ischemic stroke (IS) outcome.

Methods: We prospectively enrolled acute IS patients who presented to our hospital 24 h within an onset between September and December 2019. Patients with score using the NIH Stroke Scale ≥8 were included. Sampling was performed in 7-time points, after admission (T1) and further in 24 hours-interval (T1-T6). Additional aliquots of serum were stored at -20°C for subsequent analysis of the concentration of ST2. The primary outcome was functional outcome according to the modified Ranking scale at 90 days; 0-1 good and 2-6 poor outcome. The secondary outcome was mortality caused by all causes after 90 days.

Results: We studied 20 patients; baseline characteristics are shown in Table 1. All patients had a poor outcome, and 8 died. Friedman ANOVA test has shown statistically significant differences between concentrations in various time points (P=0.013) (Figure 1). Mann-Whitney test showed a statistically significant difference in ST2 concentrations between good and poor outcomes in T0 (P=0.044), T1 (P=0.044) and T2 (P=0.044). The difference in ST2 concentrations was also found for the T1 (P=0.014) and T2 (P=0.009) between survivors and deceased. Prognostic accuracy was the highest in T2 for cut-off >10.3 µg/L (sensitivity 99.4% and specificity 100%) (Table 2).

Female sex, n (‰)	13 (0.65)
Age, years— median (IQR)	84 (46-94)
Body mass index, kg/m2 – median (IQR)	24.5 (23.7–29.3)
Smoking, n (‰)	5 (0.25)
Alcohol, n (‰)	4 (0.2)
Drugs, n (‰)	0
Arterial hypertension, n (‰)	18 (0.9)
Atrial fibrillation, n (‰)	9 (0.45)
Presence of a heart valve, n (‰)	1 (0.05)
Dyslipidaemia, n (‰)	9 (0.45)
Diabetes mellitus, n (‰)	3 (0.15)
Coronary heart disease, n (‰)	1 (0.05)
Peripheral arterial disease, n (‰)	1 (0.05)
Prior stroke/TIA, n (‰)	4 (0.2)
Average time from onset to sampling, hours— median (IQR)	14 (6–16)
NIHSS at admission— median (IQR)	13 (8–17)
Infarct volume, cm2 - median (IQR)	12.6 (1.6–105.7)
Stroke etiology, TOAST subtype	
Large-artery atherosclerosis, n (‰)	4 (0.2)
Small-vessel occlusion (lacune), n (‰)	9 (0.45)
Cardioembolism, n (‰)	7 (0.35)
Stroke syndrome, OCSP classification	
TACS, n (‰)	1 (0.05)
PACS, n (‰)	13 (0.65)
LACS, n (‰)	4 (0.2)
POCS, n (‰)	2 (0.1)

IQR – interquartile range. TIA – transient ischemic attack. TOAST – Trial of Org 10172 in Acute Stroke Treatment. OCSP – Oxfordshire Community Stroke Project. TACS – total anterior circulation syndrome. PACS – partial anterior circulation syndrome. LACS – lacunar syndrome. POCS – posterior circulation syndrome.

Table 1. Baseline characteristics of patients with ischemic stroke (n=20)
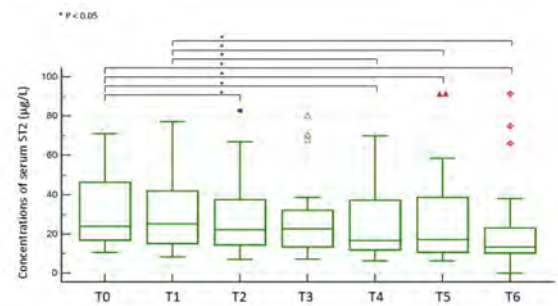
Figure 1. Statistically significant differences between concentrations of serum ST2 in various time points (T0-T6) according to Friedman ANOVA test.

Time point	Cut-off	Sensitivity (95%CI)	Specificity (95%CI)	PPV (95%CI)	NPV (95%CI)	LR+ (95%CI)	LR- (95%CI)	AUC
T0	> 13.8	88.89 (65.3-98.6)	100.0 (15.8–100.0)	100.0 (79.4–100.0)	50.0 (6.8–93.2)	/	0.11 (0.03–0.4)	0.944
T1	> 10.8	94.44 (72.7–99.9)	100.0 (15.8–100.0)	100.0 (80.5–100.0)	66.7 (9.4–99.2)	/	0.06 (0.008–0.4)	0.944
T2	> 10.3	99.4 (72.7–99.9)	100.0 (15.8–100.0)	100.0 (80.5–100.0)	66.7 (9.4–99.2)	/	0.06 (0.008–0.4)	0.944
T3	> 9.0	94.1 (71.3–99.9)	100.0 (15.8–100.0)	100.0 (79.4–100.0)	66.7 (9.4–99.2)	/	0.06 (0.009–0.4)	0.941
T4	> 11.3	88.2 (63.6–98.5)	100.0 (15.8–100.0)	100.0 (8.2–100.0)	50.0 (6.8–93.2)	/	0.12 (0.03–0.4)	0.912
T5	> 9.7	88.2 (63.6–98.5)	100.0 (15.8–100.0)	100.0 (78.2–100.0)	50.0 (6.8–93.2)	/	0.12 (0.03–0.4)	0.912
T6	> 10.6	75.0 (47.6–92.7)	100.0 (15.8–100.0)	100.0 (73.5–100.0)	33.3 (4.3–77.7)	/	0.25 (0.1–0.6)	0.813

ST2 – Suppression of Tumorigenicity 2. CI – confidence interval. PPV – positive predictive value. NPV – negative predictive value. LR+ – positive likelihood ratio. LR- – negative likelihood ratio. AUC – area under the curve.

Table 2. Prognostic accuracy of ST2 concentrations in time points (T0-T6)

Conclusion: Our findings show high prognostic accuracy of serum ST2 dynamic in IS outcome, which could be helpful for clinicians in early predicting of unfavourable outcomes and making a clinical decision.

Disclosure: Nothing to disclose.

EPO-278

THE SIGNIFICANCE OF HELIOS MARKER EXPRESSION IN T REGULATORY CELLS RESPONSE TO STROKE

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Background and aims: Adaptive immunity participates in the body's stroke response by inducing activation of T regulatory (Treg) cells. The role of Treg's in ischemic stroke is not fully understood, with conflicting findings across various studies. Treg cells express transcription factor Helios, which may fluctuate to either a more proinflammatory (Treg Helios-) or suppressive (Treg Helios+) state. Analyzing Treg subpopulation behavior during the development of inflammation and stroke associated infection (SAI) may be insightful in better understanding the pathophysiology of ischemic stroke.

Methods: 52 patients and 32 controls with risk factors of cardiovascular diseases were recruited. Blood samples in 1 (W1), 3 (W3), 10 (W10) and 90 (W90) days after stroke onset were obtained to measure inflammatory indicators and to detect Treg cells levels with flow cytometry analysis.

Results: Treg Helios- cell levels increased (p<0,0001), and Treg Helios+ levels decreased in stroke patients (p<0,0001), particularly in women (p=0,037). SAI+ patients presented a higher percentage of Treg Helios+ in the acute phase (p=0,03). Increased levels of Helios+ 3 days post-stroke correlated with increased neurological deficits after 90 days (p<0,01, rS=0,62).
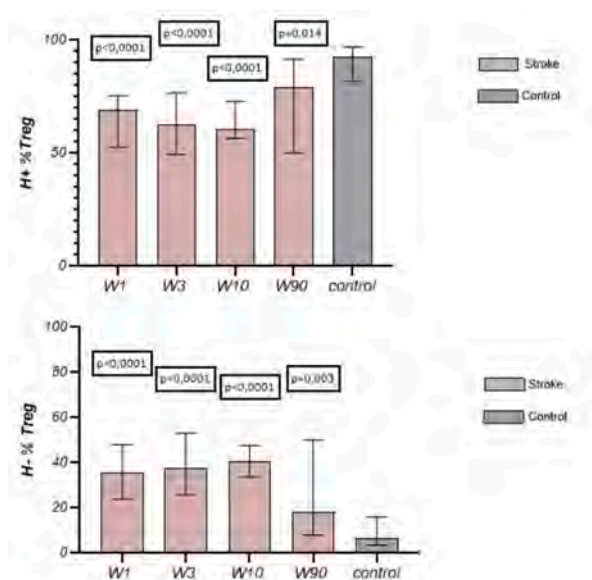
Comparison of Helios+ and Helios- percentage of Treg cells in stroke patients (in day 1, 3, 10 and 90) and controls (median, IQR)
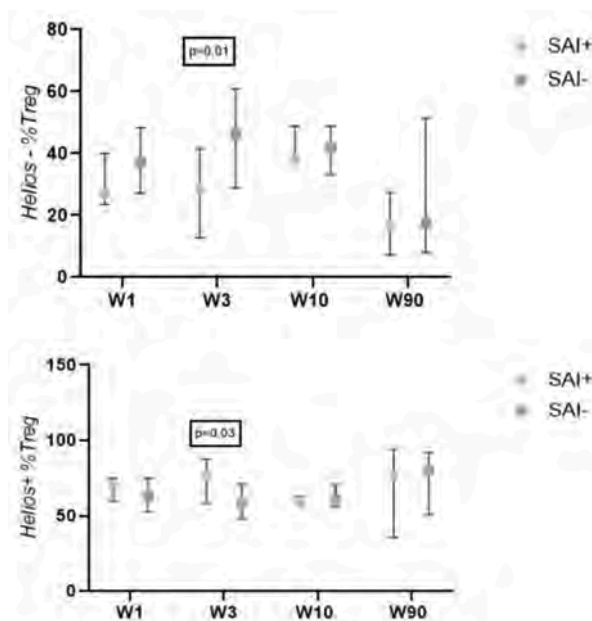
Comparison of Helios+ and Helios- percentage of Treg cells in patients SAI+/SAI- (median, IQR)
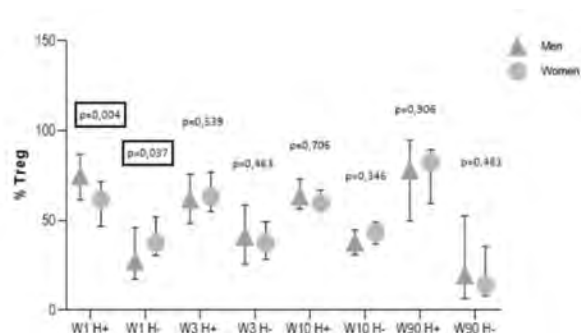
Comparison of Helios+ and Helios- percentage of Treg cells in male/female (median, IQR)

Conclusion: 1. Treg response to ischemic stroke is associated with altered Helios marker intracellular expression. It is gender-dependent, and its deleterious effects are due to transition to the proinflammatory Helios-type, particularly in women. 2. Time-shifted suppressive Treg function (increased Helios+ percentage) and delayed proinflammatory activity (decreased Helios- percentage) may lead to SAI development.

Disclosure: The research was financed from the funds for the activity of the Neurology Department of the Poznan University of Medical Sciences and a grant from the National Science Center in Poland (2014/15/B/NZ4/00736)

EPO-279

Short-term outcomes after carotid stenting in patients with metabolic syndrome

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Background and aims: Metabolic syndrome (MetS) is a cluster of several risk factors for cardiovascular and cerebrovascular disease. MetS has been linked with increased severity and prevalence of carotid artery disease. Aim of the study was to evaluate the short-term outcomes after carotid artery stenting in patients with metabolic syndrome.

Methods: 108 patients with carotid artery disease who underwent carotid artery stenting were enrolled in the study (aged 43–78 years, mean age 57.12 ± 14.0 years, male=53%). Patients were divided into two groups by 54 weather diagnosed concomitant MetS or not. MetS was defined international diabetes federations criteria. Mean follow-up consisted of 2.8 ± 1.0 years. All anthropometry, laboratory and instrumental data were obtained at baseline and during the follow up period. All statistical analysis were performed by STATA software.

Results: During the follow up period MACE including post-operative stroke and restenosis of carotid artery were significantly higher in patients with MetS than those without it (12.9 % vs. 7.4%, $p<0.05$). Among MetS components high blood sugar (1.6, CI 95% 1.2–2.3, $p<0.05$), dyslipidemia (1.4, CI 95% 1.15–2.1, $p<0.05$) and higher abdominal obesity (1.2, CI 95% 1.05–1.7, $p<0.05$) were positively associated with elevated risk of MACE. There were not significant changes between male and female.

Conclusion: MetS is associated with increased number of MACE in short-term period in patients with carotid artery disease. Among MetS components high blood sugar, dyslipidemia and abdominal obesity were strong predictor for the MACE. Further studies are required with large amount of participants.

Disclosure: Nothing to disclose.

EPO-280

Central Nervous System Vasculitis in Primary Immune Deficiency

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Background and aims: To illustrate the wide etiologic profile and interdisciplinary approach in childhood arterial ischemic stroke (AIS) in a tertiary center.

Methods: We present two cases with immunodeficiency and central nervous system (CNS) vasculitis with AIS.

Results: Case 1, 13-year-old girl with common variable immunodeficiency, autoimmune adrenal insufficiency developed sleepiness and right hemiplegia after gastroenteritis. Magnetic resonance imaging (MRI) revealed acute ischemia, diffuse saccular and fusiform aneurysms in the left anterior and middle cerebral arteries (MCA) and branches, and a chronic right caudate infarct. Irregularities and stenosis of major and perforating cerebral arteries suggested vasculitis. The chronic infarct, calcifications on ICAs on cranial CT, sulcal and basal ganglia collaterals on MR angiography suggested an acute exacerbation of a slowly progressive, probably non-infectious, vasculitis. Steroid, immunoglobulin and cyclophosphamide were given. Subsequently, mycophenolate mofetil was started. However, she was readmitted 3 weeks later for right hemispheric AIS with hemorrhage. Case 2, a three-year-old boy diagnosed with immunodeficiency when 6 months old, underwent corneal transplantation for CMV retinitis and keratitis at 1 year but received no antivirals. He was admitted 2 years later with left hemiplegia and left central facial paralysis. MRI showed acute infarction in both MCA territories and bilateral diffuse vascular stenosis at the circle of Willis. Treatment included steroid, unfractionated heparin, and valganciclovir added for high serum CMV load. Hemiparesis improved within 2 months.

Case 1: At admission Flair, DWI, ADC
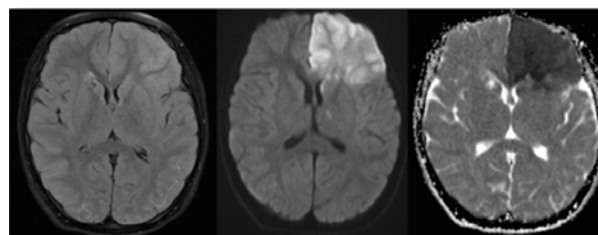
Case 1: Second attack Flair, DWI, ADC
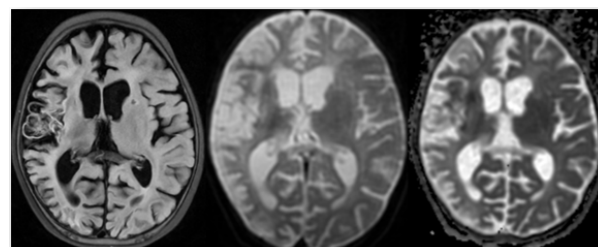
Case 2: At admission Flair, DWI, ADC

Conclusion: The first patient had vasculitis of autoimmune and the second, viral etiology. A complex course with recurrent AIS, bleeding and infection is conceivable in immunodeficiency/dysregulation.

Disclosure: Nothing to disclose.
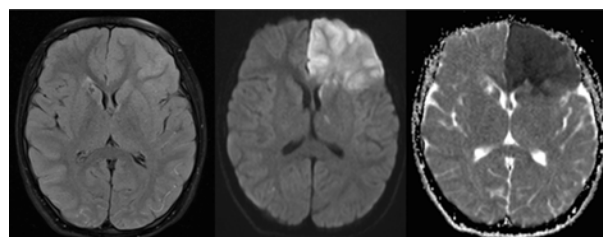
Clinical neurophysiology

EPO-281

Neurophysiological reappraisal of light-evoked blink reflex in migraine: preliminary data

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Background and aims: Light-evoked blink reflex (L-BR), is a brainstem reflex induced by light stimuli. Afferent visual pathway carries the impulses to lateral geniculate body and pretectum; the efferent muscular pathway originates from the facial nuclei in the pons. It consists of two distinct EMG bursts, referred to as R50 and R80 based on their typical onset latencies. Aim of this study was to evaluate the feasibility and reliability of L-BR in healthy subjects (HS) and patients with migraine without aura (MO).

Methods: 14 patients with MO were compared to 14 HS matched for age and sex. Surface EMG electrodes (Ag–AgCl) were placed over the right orbicularis oculi muscle. Signal was amplified and band-pass filtered (1–1,000 Hz). After dark adaptation, 80 white flashes were delivered by a xenon lamp. EMG responses were rectified and averaged to measure the onset latency and area under the curve (AUC) of R50/R80 components.

Results: The R50 was reliably recorded in 11/14 HS and 9/14 MO, whereas R80 in 10/14 HS and 13/14 MO. Mean R50 onset latency was 50.3 ± 2.5ms in HS and 49.2 ± 3.6ms in MO ($p>0.05$); mean R80 latency was 82.1 ± 7.4ms in HS and 85 ± 7.7ms in MO ($p>0.05$). As to the area, no significant differences between groups ($p>0.05$) were shown.

Conclusion: L-BR proved to be a simple and reliable tool to study brainstem circuitry. Two components can be easily measured in the majority of HS and MO patients, with similar latencies and areas, suggesting a normal eyeblink reflex in migraine.

Disclosure: Nothing to disclose.

EPO-282

Subcortical Neurophysiological Recordings Derived form Fully Implantable DBS Systems in Movement Disorders

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Background and aims: Although deep brain stimulation (DBS) has an established role in the treatment of refractory movement disorders, outcome is still heterogeneous and side-effects often occur. With the recent availability of implantable DBS devices that are able to sense local neurophysiological activity (i.e. Local Field Potentials; LFP's), the optimal amount of stimulation can be titrated based on LFP activity. However, in order to apply this adaptive form of DBS (aDBS) in clinical practice, the signal-to-noise ratio, correlation with clinical symptoms and behaviour of LFP's under different conditions need to be established.

Methods: LFP's from chronically implanted DBS symptoms were recorded in 17 Parkinson's disease (PD), 3 Essental tremor (ET) and 2 dystonia patients shortly after DBS battery replacement. Conditions included rest, bradykinesia (PD) and tremor (PD and ET) assessment as well as speech, gait and cognitive tasks (all patients) and were performed with DBS switched OFF and ON.

Results: Key findings were 1) the marked presence of ECG artefacts that can be removed off-line by applying template subtraction filters 2) the presence of a peak in the low beta (13-20) range in PD that was more outspoken in de most affected hemisphere and decreased during the DBS ON condition and 3) oscillatory activity in the tremor frequency range (4Hz) contralateral to the tremor (ET).

Conclusion: LFP data of sensing enabled DBS systems is, after considerable artefact suppression, comparable with data derived from externally recorded signals. This holds great promise for chronic recordings and the automated optimisation of DBS systems.

Disclosure: Nothing to disclose.

EPO-283

Pupil size: a new biomarker for transcutaneous vagal nerve stimulation?

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Background and aims: Mechanisms of action and optimal stimulation parameters of transcutaneous auricular vagus nerve stimulation (taVNS) are currently unknown. Pupil size has gained attention as a promising biomarker of vagal activation in different studies on animal models. The aim of this study is to investigate the effects of taVNS on pupil diameter in healthy subjects.

Methods: All subjects received taVNS at the left external acoustic meatus and control stimulation at the left earlobe during the same experimental session. Different intensities (0.5 mA; 1.0 mA; 2.0 mA; 3.0 mA) for both conditions were tested. Tonic pupil size was recorded in both eyes at baseline and during each stimulation using an infrared-automated pupillometer in three different illuminance conditions (scotopic, mesopic, photopic).

Pupil size in different illuminance conditions.

Results: In scotopic illuminance condition, a significant interaction between intensity and condition (real vs control) was found for the left eye. Post-Hoc analysis showed that during real taVNS at 2 mA, pupil size was significantly larger in comparison to baseline and 2 mA control stimulation.

Effects of stimulation intensity and condition on pupil size under different light levels.

Conclusion: Our study demonstrates that taVNS induces pupil dilation under specific illuminance conditions and at specific stimulation intensity.

Disclosure: The authors have no disclosures related to this abstract.

EPO-284

Fluency Type Index: a neuropsychological marker to predict amnestic Mild Cognitive Impairment progression to AD

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Background and aims: Category fluency (CF), mainly dependent on linguistic functions, reveals a temporal disfunction, while letter fluency (LF), mainly dependent on attentive-executive functions, reveals a prefrontal dysfunction. Fluency Type Index (FTI = adjustedCF − adjustedLF / adjustedCF + adjustedLF) quantifies relative proficiency of each subject on CF and LF. A positive value (FTI+) suggests an attentive-executive deficit and a negative value (FTI-) a semantic deficit, that has been shown to characterize Alzheimer's Disease (AD). The study aims to investigate FTI's ability to predict amnestic Mild Cognitive Impairment (aMCI) evolution in AD and his correlation with a CSF parameter (Tau/ABeta) in aMCI patients.

$$FTI = \frac{aCF - aLF}{aCF + aLF} \qquad \begin{array}{l} aCF = \text{adjusted CF} \\ aLF = \text{adjusted LF} \end{array}$$

FTI formula

Methods: A total of 165 aMCI patients have been divided considering evolution (aMCI-E, n=41) or non-evolution (aMCI-NE, n=124) to AD within 1 year. FTI values, the prevalence of FTI- and FTI+ in each group have been compared. Pearson correlation coefficient between FTI and Tau/ABeta has been calculated and frequency of pathological (<-0.22 and >0.5) and normal FTI in patients with pathological (>0.52) and non-pathological Tau/ABeta has been compared with X^2 test.

Results: FTI values are significantly different in the 2 groups (t=2.28, p<0.01). In aMCI-E group prevalence of FTI- is higher that FTI+, while no difference emerges in aMCI-NE (X^2=5.36, df=1, p<0.05). FTI and Tau/ABeta result negative correlated (r=-0.18, p=0.05). Frequency of pathological/non-pathological FTI and pathological/non-pathological CSF result correlated (X^2=3.45, df=1, p<0.05).

Conclusion: FTI is a neuropsychological marker that, similarly to T/ABeta, predicts aMCI evolution to AD.

Disclosure: No conflict of interest to disclose for this abstract.

EPO-285

Neurophysiological and behavioural correlates of Ocrelizumab therapy on manual dexterity in patients with PPMS

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Background and aims: Hand dexterity impairment is common in pwPPMS. Ocrelizumab, the only therapy approved for PPMS reduce the risk of upper limb disability progression. Neural mechanisms underlying hand impairment in pwPPMS and the brain networks behind the effect of ocrelizumab on manual dexterity are not fully understood. Aims of our study were: to investigate neurophysiological and behavioural correlates of hand function in subjects with PPMS; to use neurophysiologic and behavioural measures to track the effects of ocrelizumab therapy on manual dexterity.

Methods: Neurophysiological protocols assessing the integrity of cortico-spinal and somatosensory pathways and advanced TMS protocols assessing intracortical excitability were applied in 17 PPMS patients. All subjects underwent behavioural analysis of hand dexterity by means of nine-hole peg test, finger movement analysis, hand strength with handgrip and three-point pinch test. Neurophysiological and clinical assessment of hand functionality were also performed after about one year of ocrelizumab therapy.
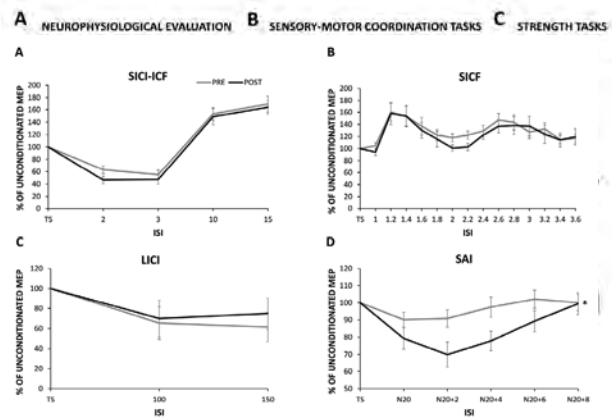
Figure 3

Results: At baseline PPMS patients displayed a significant impairment of hand dexterity and strength (all p<0.03). Neurophysiological study disclosed prolonged latencies of standard somatosensory and motor evoked potentials (all p<0.025), an overall reduction of intracortical excitability at TMS protocols, involving excitatory and inhibitory circuits. Hand dexterity impairment, indexed by delayed 9HPT was strictly associated to TMS protocols investigating cortical sensory-motor integration SAI), p=0.009. 9HPT (p=0.01) and SAI (p=0.01), displayed a significant improvement after one year of therapy with ocrelizumab.
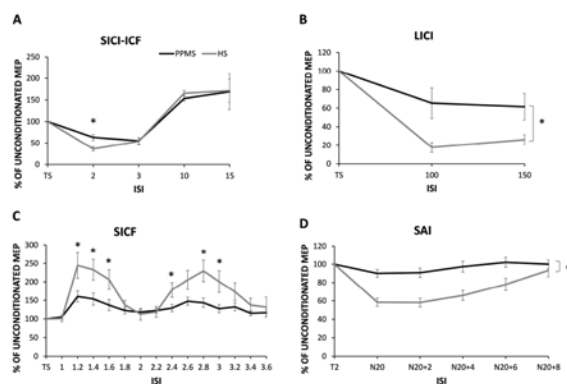
Figure 2

Conclusion: Ocrelizumab therapy displays a beneficial effect on hand dexterity impairment trough intracortical networks implicated in fast sensory-motor integration.
Disclosure: Nothing to disclose.

EPO-286

Characterising recovery from acute brachial neuritis using high-density surface EMG

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Background and aims: High-density surface EMG is a non-invasive technology capable of recording from greater muscle volumes and for longer durations than traditional needle EMG. We sought to track the axonal recovery of a patient with acute brachial neuritis using HDSEMG, anticipating this reverse model may paradoxically elucidate the profile of axonal degeneration in ALS.

Methods: We performed measurements of the affected right triceps and asymptomatic left triceps using HDSEMG at 7, 11, 15, 20 and 34 weeks after symptom onset. For each assessment, we recorded up to 90s of muscle contraction at 25%, 50%, 75% and 100% of the maximum voluntary contraction (MVC).

Results: At 25% MVC, we observed a near-normal distribution of the motor unit potential amplitudes in the unaffected left triceps, whereas the affected right triceps produced multiple amplitude peaks early on covering a large range of amplitudes. By week 20, the distribution of motor unit potential amplitudes in the right triceps normalised with improvement of the patient's strength and restoration of the corresponding reflex. The amplitude profiles detected at 75–100% MVC were stable at all timepoints.

Conclusion: The early amplitude pattern from the affected triceps was reminiscent of the fasciculation potential amplitude profiles previously reported in ALS and its recovery pattern is consistent with early axonal loss and compensatory reinnervation followed by axonal regrowth and recovery of motor unit number. HDSEMG showed a promising ability to track the axonal recovery in ABN. This also raises the question whether this non-invasive technique could help to monitor the complex neurodegenerative nature of ALS.

EPO-287

Efficiency of neurophysiological methods for monitoring of the brain in temporal pharmacoresistant epilepsy

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Background and aims: The basis of pre-surgical neurophysiological examinations of patients with pharmaco-resistant structural epilepsy is the method of monitoring bioelectrical activity of the brain, video-electroencephalographic monitoring and, if indicated, long-term invasive monitoring. The goal of the study is to estimate the diagnostic efficacy of the monitoring's methods on the basis of long-term results of patients with temporal structural pharmaco-resistant epilepsy surgical treatment.

Methods: 61 patients with temporal lobe pharmaco-resistant epilepsy were divided into two groups: performance of video-EEG monitoring only (33 patients) and the additional use of invasive monitoring for the localization of the epileptogenic zone (28 patients). Each group was divided into subgroups depending on the outcome : patients with ceased seizures (Engel 1) and patients with seizures persisted to some degree (Engel 2–3–4). The reference method to calculate diagnostic efficacy was invasive monitoring with ictal event recording.

Results: Invasive monitoring as a part of the pre-surgical evaluation of patients with temporal lobe pharmaco-resistant epilepsy has a higher sensitivity (72.7%) and accuracy (82.4%) than video-EEG monitoring (sensitivity 50%, accuracy 45.9%).

Conclusion: The diagnostic efficiency of video-EEG monitoring doesn' t allow an invariant description of the structural and functional organization of complex epileptic systems. Invasive monitoring of the brain, performed as part of a pre-surgical examination of patients with pharmacoresistant temporal lobe epilepsy, has a high sensitivity (72.7%) and accuracy (78.6%). The phenomenon of convergence of neurophysiological phenotypes leads to a decrease in the diagnostic efficiency of non-invasive and invasive monitoring of the bioelectric activity of the brain in temporal lobe pharmacoresistant epilepsy.

Disclosure: Nothing to disclose.

EPO-288

Clinical and electrophysiological changes after platinum- and taxane-based chemotherapy

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[2] *University Clinical Centre of Kosova, Clinic of Oncology, Kosovo*

Background and aims: Patients undergoing chemotherapy for cancer were examined to determine the neuropathological effects of different chemotherapy agents, and to determine the distribution of peripheral nerve involvement.

Methods: 120 patients were examined clinically and by ENG prior to chemotherapy, and again 4 to 6 cycles after the chemotherapy treatment. All patients underwent standardized neurological examination, and studies of sensory and motor nerves. Peripheral nerve involvement was evaluated through a reduced version of the total neuropathy score (TNSr).

Results: Almost 90% of patients reported neuropathic symptoms, especially affecting tactile sensation. The mean TNSr was 11.2, with higher values in patients treated with platinum-based compounds only or in combination with taxanes. Voltage amplitudes in all sensory and motor nerves were low. Conduction velocities for all motor nerves and of the sensory median nerve were slowed. Patients treated with platinum-based compounds had significantly lower compound motor action potentials in the motor ulnar and tibial nerves.

Conclusion: Polyneuropathy is very frequent finding of patients treated with chemotherapy. Clinical examination finds pronounced sensory symptoms, and electrophysiological examination shows that motor findings are also severe. Certain drugs can have greater effects on certain nerves, and further imaging methods can shed light on patterns of involvement.

Disclosure: Nothing to disclose.

EPO-289

Cathodal transcranial direct current stimulation: impact of the ring radius of a 4x1-ring electrode configuration

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Background and aims: Transcranial direct current stimulation (tDCS) is a non-invasive brain stimulation technique capable of modifying cortical excitability. To increase its spatial specificity, a 4x1-ring electrode configuration has been developed. The ring radius significantly influences intracranial electrical field characteristics and therefore may modify its therapeutic effects, especially for cathodal tDCS (c-tDCS) given its non-linear effects. Reliable sham conditioning is a challenge in tDCS trials. We investigated 1. whether motor evoked potential (MEP) modulation by 4x1-ring c-tDCS is ring radius-dependent, and 2. differences in reported sensations between sham and true c-tDCS and the efficacy of a de facto blinding procedure.

Methods: 15 healthy adults underwent three 4x1-ring c-tDCS sessions: sham tDCS (ramp-up/ramp-down only), true 3.5cm and true 7cm radius 4x1-ring c-tDCS (10min,2mA). Participants were told that stimulation parameters differed between study visits without further details (de facto blinding). MEP amplitude was measured before and after tDCS (Figure1). tDCS-induced sensations and blinding efficacy were evaluated by questionnaires.
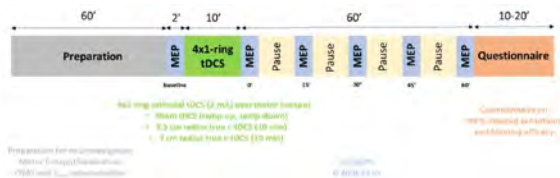
Figure 1: Study protocol

Results: Compared to sham, both 3.5cm and 7cm radius true 4x1-ring c-tDCS significantly reduced the MEP amplitude (p=0.004) (Figure2); no significant differences between both true conditions were found. True c-tDCS was associated with higher local sensation scores than sham c-tDCS (Figure3), in particular for sensation durations. Blinding efficacy was largely unaffected: 42/45 sessions were believed to be active c-tDCS and only one subject correctly identified sham stimulation.
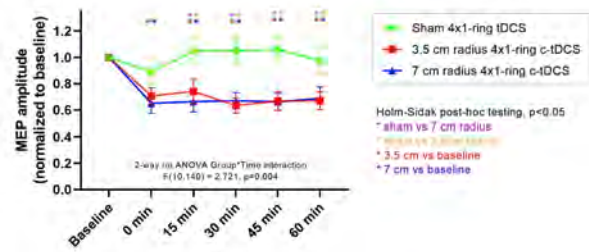
Figure 2: MEP amplitude modulation by sham, 3.5 cm radius and 7 cm radius 4x1-ring cathodal tDCS
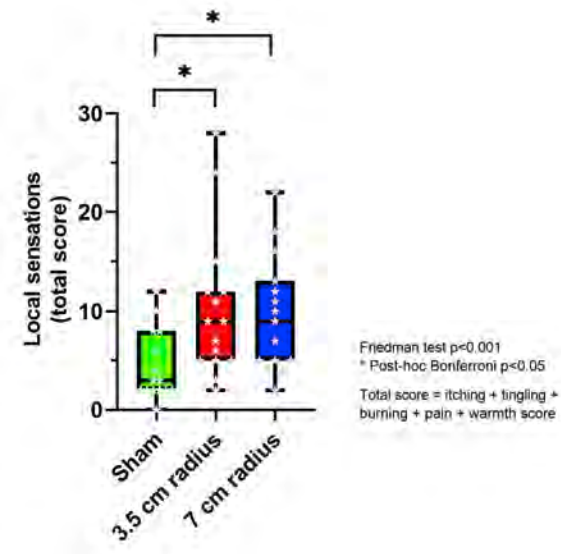
Figure 3: Local sensations induced by 4x1-ring cathodal tDCS

Conclusion: Both 3.5cm and 7cm radius 4x1-ring c-tDCS significantly reduced MEP amplitude in healthy volunteers. Despite more local sensations with active c-tDCS, participants were successfully blinded using a de facto blinding procedure.

Disclosure: The study is part of the PerStim project funded by a PPP allowance grant from Health Holland TKI-LSH. Non-disposable hardware was temporarily provided by Vandelanotte Consulting, disposables were purchased from the same provider.

EPO-290

Supraspinal modulation of the cutaneous silent period in healthy subjects

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Background and aims: Cutaneous silent period (CSP) is defined as a temporary reduction or cessation of voluntary muscle activity following a noxious stimulus. Here, we aimed to examine the modulation of the cutaneous silent period (CSP) by maneuvers, such as teeth clenching and contralateral tonic and phasic voluntary limb movements, that have various effects on other reflexes.

Methods: We included 18 healthy subjects aged between 20 and 31 years. Recording electrodes were placed on the abductor pollicis brevis (APB) muscle of the dominant hand. We performed the recordings at baseline, during maximum teeth clenching (TC), contralateral tonic dorsiflexion (TD) of the foot, and at the beginning (RT1), in the middle (RT2), and at the last part (RT3) of the phasic wrist extension of the contralateral non-dominant upper limb. The suppression indices of the I1, I2, and long loop reflex (LLR) were calculated.

Results: The onset latency of the CSP was earlier in RT1 condition than that at baseline. Duration of I1 in RT1 and RT3 were longer compared to the duration of I1 at baseline. Duration of I2 in RT2 and RT3 were longer compared to the duration of I2 at baseline. The suppression index of I2 during RT1, RT2, RT3 and TC were significantly higher than that at baseline. The suppression index of I1 was reduced in TD.

	Baseline	TC	TD	RT1	RT2	RT3
CSP onset (ms)	38.6±3.9	37.9±3.9	37.6±7.1	33.3±11.8*	34.7±10.4	35.1±6.2
I1 end (ms)	51.2±6.2	50±5	47.3±10.9	52.2±9.7	50.1±12.7	51.7±7.9
LLR end (ms)	75.5±8	74.2±7.5	73.4±10.2	74.2±10.8	73±13.6	73.4±12.2
CSP end (ms)	120.2±9.4	118.6±9.3	119.1±7.4	123.7±12.1	125.9±19.6	123.6±9.6
I1 duration (ms)	12.6±4.5	12.1±5.1	12.1±3.6	18.9±7.7*	15.5±8.7	16.6±6.0*
LLR duration (ms)	24.3±8.9	24.2±7.7	22.5±8.2	21.9±6.4	21.1±8.2	21.9±10.4
I2 duration (ms)	44.7±7.9	44.4±8.4	45.7±8.8	49.6±15	52.9±19.4*	50.3±11.5*

Mean ± standard deviation, MC: Maximal teeth clenching, TD: contralateral tonic dorsiflexion of the foot, RT1: Onset of the reaction time, RT2: Middle of the reaction time, RT3: End of the reaction time, *p<0.05 (Wilcoxon test)

Latencies and durations

	Baseline	TC	TD	RT1	RT2	RT3
I1 (%)	68.7±52.2	49.4±20.5	41.4±26.6*	50.5±25.8	64.1±29.9	94.8±88.2
LLR (%)	136.7±95.1	95.3±38.6	152.1±127.8	114.5±77.7*	159.1±101.3	130.7±74.1
I2 (%)	34.2±23.6	48.1±19.3*	51.5±34.6	75.7±60*	85±73.8*	95.8±78.4*
E3 (%)	162.6±89.1	180.2±30.2	146.3±66.2	169.7±107.5	163.5±116.4	159.6±87.1

Mean ± standard deviation, MC: Maximal teeth clenching, TD: contralateral tonic dorsiflexion of the foot, RT1: Onset of the reaction time, RT2: Middle of the reaction time, RT3: End of the reaction time, *p<0.05 (Wilcoxon test)

Suppression indices

Conclusion: Phasic hand movements occupying both cortical and spinal motor networks have an inhibitory effect on the inhibition potential of CSP. It seems that CSP is under the influence of these networks.

Disclosure: Authors have nothing to disclose.

EPO-291

Assessing the effect of taVNS at 25Hz and 100Hz on the activity of the cerebello-thalamo-cortical pathway: a TMS study

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Background and aims: Transcutaneous auricular vagal nerve stimulation (taVNS) is a noninvasive electrostimulation method with a propensity to modulate upstream vagal afferents. However, there is limited evidence of its neurophysiological effects. Modulation of cerebellar function with taVNS could be potentially useful in treatment of tremor disorders or movement disorders with decreased cerebello-cortical inhibition (CBI), such as dystonia and Parkinson's disease. We used CBI, a transcranial magnetic stimulation (TMS) paradigm, to compare the effect of a single session of taVNS at 100Hz (taVNS100), 25Hz (taVNS25), and sham (xVNS) on the activity of the cerebello-thalamo-cortical pathway.

Methods: 32 healthy adult participants were included in a randomized, within-subject, double-blind, sham-controlled study. CBI was assessed at baseline, and during 3 types of stimulation: taVNS100, taVNS25, and xVNS (Figure 1). TaVNS was applied at the left cymba conchae with the following parameters: square-shaped pseudobiphasic pulse, interpulse duration 80μs, pulse width 300μs, pulse intensity 0,1mA above the perceptual threshold. During xVNS no electrical current was applied. CBI was performed as described by Chen et al. (2001), with an interstimulus interval of 5ms. CBI during all conditions was compared with a Friedman test, followed by Wilcoxon signed-rank tests.
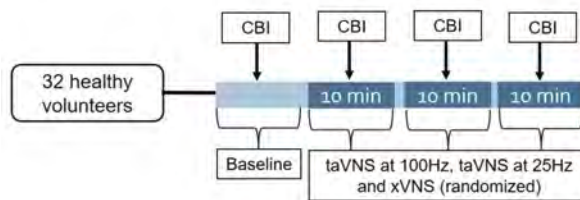
Figure 1. Study design. CBI – cerebello-cortical inhibition; taVNS – transcutaneous auricular vagal nerve stimulation; xVNS – sham stimulation.

Results: There was a significant difference in CBI between different stimulation conditions (p=0.005). Follow-up pairwise comparisons revealed that this difference was due to CBI being significantly increased during taVNS100 compared to baseline (p=0.012) (Figure 2).
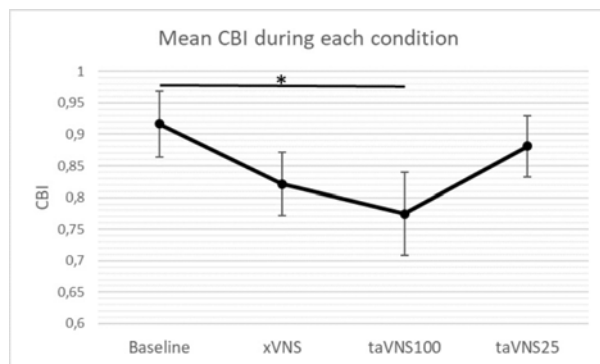
Figure 2. Mean CBI during each condition. CBI - cerebello-cortical inhibition; xVNS – sham stimulation; taVNS100 - transcutaneous auricular vagal nerve stimulation (taVNS) at 100Hz; taVNS25 - taVNS at 25Hz.

Conclusion: CBI was increased during taVNS100, but not during xVNS or taVNS25, suggesting that taVNS has a frequency-dependent potential to modulate the activity of the cerebello-thalamo-cortical pathway.
Disclosure: Nothing to disclose.

EPO-292

The clinical value of generalized irregular theta activities in EEG

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Background and aims: The electroencephalographic irregular waves in theta and delta frequency bands are often associated with an underlying pathological process. In our study, we aimed to investigate the clinical significance of generalized irregular theta activities (GITA) that appear during the waking state.
Methods: The EEG recordings of 2,156 patients who were referred to our EEG laboratory were reviewed retrospectively: 50 patients who had GITA without another identified electroencephalographic abnormality and 303 patients with normal EEG recordings were included. The term GİTA was used to identify a burst of bilateral synchronous irregular waves of at least one-second duration at a dominant theta frequency with maximum amplitude over the frontocentral regions. The relationship between the presence of GITA and demographic characteristics, previous history of metabolic or central nervous system or psychiatric disorders, antiepileptic use, and the nature and localization of cranial lesion was assessed.

EEG showing a burst of generalized irregular theta activity in a patient with normal EEG recording.

Results: The frequency of GITA was statistically significantly higher in females (n=39, 78%) than in males (n=165, 54.5%) (p=0.002). Besides, the median age of the patients with GITA was 28 years (18–74 years) and 40 years (18-82 years) for the patients with normal EEG recording, and this difference statistical significance (p=0.002). However, no significant difference was found in the terms of the presence of other variables (p>0.05).
Conclusion: Our results imply that GITA occurring as a single finding on electroencephalography should not be interpreted as a specific abnormality. GITA may be related to a normal physiological process of the brain.
Disclosure: Nothing to disclose.

Epilepsy 2

EPO-293

The standardized EEG array recommended by the IFCN versus 10-20 system in detecting abnormalities

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Background and aims: The International Federation of Clinical Neurophysiology (IFCN) recommends the use of the 10–20 EEG array with six electrodes in the inferior temporal chains (F9/F10, T9/T10, P9/P10) in order to sample the inferior-basal and anterior part of the temporal lobe. We pretended to investigate the supplementary capability of this extended array compared to the classic 19-channel EEG in detecting interictal epileptiform discharges (IED) and slow activity (SA).
Methods: Cross-sectional study enrolling consecutive adult patients who underwent routine and sleep deprived EEGs between August 2019 and March 2020. The EEG recordings were anonymized, randomized and blindly reviewed by the same expert, using both systems, aiming the index of abnormalities regarding its category (IED or SA) and topography.
Results: 258 patients were included, with a median age of 59 years and were mainly female (55.4%). Although a strong agreement was observed for abnormality detection using both methods (k=0.881), 11.5% of patients with abnormalities in the IFCN array had normal results in the 10–20 system. There was a strong agreement of both methods in detecting focal abnormalities in temporal regions (kappa>0.6). Despite this fact, the 10–20 system did not detect IED in 36.4% in right temporal region and 42.1% in left temporal region, as well as SA in 23.1% in right temporal region and 20.0% in left temporal region.
Conclusion: Using additional EEG electrodes in the inferior temporal chains, according to the IFCN recommendations, substantially improves the detection rate of EEG abnormalities, particularly in the temporal regions.
Disclosure: Conflicts of interests: none declared.

EPO-294

Epilepsy in tubulinopathies: a case with a new de novo mutation in TUBB2A

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Background and aims: Tubulinopathies are autosomal dominant disorders caused by mutations in seven known genes, encoding different tubulin isoforms. We describe the drug-resistant epilepsy in a patient with a new de novo mutation in TUBB2A.
Methods: Data on seizures, EEGs, brain MRIs were collected in our epilepsy centre. Genetic analysis was performed using exome sequencing(ES).
Results: In addition to profound intellectual and motor disability, he presented post-natal microcephaly and mild facial dysmorphisms. Brain MRI showed enlarged lateral ventricles, corpus callosum and brainstem hypoplasia. Epilepsy onset was at 1 year old with myoclonic seizures, followed by generalized tonic-clonic seizures(GTCSs). Thus, valproate was started and levetiracetam was added-on. From the age of 7 years he has been presenting monthly GTCSs upon awakening and multiple per day focal tonic seizures, both in wakefulness and during sleep. Thus, he added-on felbamate. When he was 12 years old multiple per day atonic and myoclonic-atonic seizures with drop appeared. Since the age of 7 years, the EEGs showed spike-wave discharges over the left frontal-temporal areas with bilateral diffusion, strongly exacerbated by sleep. The sleep figures were absent, configuring a pattern of Electrical Status Epilepticus in Sleep(ESES). ES performed at the age of 11 years revealed a de novo heterozygous mutation c.1172G>A(p.Arg391His) in TUBB2A.
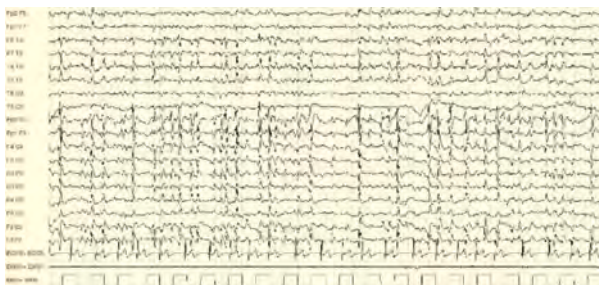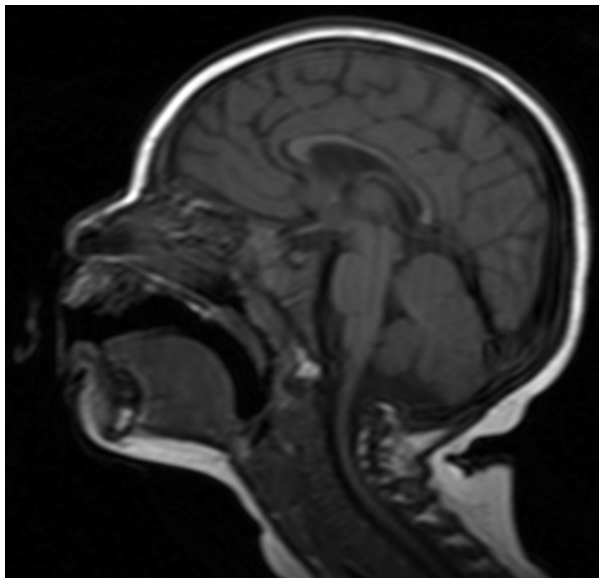
Conclusion: Despite the incidence of epilepsy seems higher in patients with TUBB2A compared with other tubulinopathies, to date a detailed description is not available. The description of the epilepsy features in other TUBB2A cases might help clarify whether a Developmental and Epileptic Encephalopathy is a consistent phenotype.

Disclosure: The authors have nothing to disclose.

EPO-295

Social and psychiatric background of patients with psychogenic non-epileptic seizures

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Background and aims: Psychogenic non-epileptic seizures (PNES) are functional neurological disorders that can be highly disabling. Adverse life events, psychological and social factors are associated with these conditions. We aimed to describe the social and psychiatric background of a PNES cohort.

Methods: Retrospective descriptive analysis of all patients with PNES admitted to a Portuguese epilepsy monitoring unit (EMU) between 2011–2020.

Results: From 456 non-invasive VEEG monitoring from the EMU, we included 28 patients with PNES. 86 percent were female, with mean age of 41 years (SD 14.3), mean age of PNES onset of 32 years (6–60 yrs) and mean time to diagnosis of 12 years (sd 10.3). 12 (43%) of patients suffered from weekly episodes. Six (23%) of patients identified anxiety as a trigger. Only 5 (18%) patients had higher education, and 12 (43%) had previously failed a course. Regarding social background, most patients (53.6%) were married, and one-third were unemployed. Almost one-third (29%) of patients had a dysfunctional family, and psychological abuse was present in 18%. A psychiatric disorder was present in 64% of patients: 14 (50%) had depressive disorder, 7 (25%) suffered from anxiety and 2 (5%) had a conversive disorder. Most patients (79%) were under psychoactive drugs: 64% were on anti-depressants, 25% on anxiolytics, and 25% on neuroleptic drugs. After discharge of the EMU, fifty-four percent of patients had a follow-up in the outpatient psychiatric clinic.

Conclusion: Adverse life conditions may be frequently found in PNES patients, as well as psychiatric comorbidities which require appropriate management.

Disclosure: The authors have no disclosures.

EPO-296

The European Reference Network for Rare and Complex Epilepsies EpiCARE: a european collaboration improving care pathways

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Background and aims: Share with the members of the European Academy of Neurology our experience in constructing a cross-border network for rare and complex epilepsies at the service of care and research, funded by the European Commission.

Methods: We will present the structure and missions of one of the 24 European Reference Networks launched by the European Commission in 2017 and discuss the achievements and future plans of the ERN for rare and complex epilepsies, EpiCARE (https://epi-care.eu).

Results: Today, the ERN EpiCARE is composed of 52 full and affiliated HCP members (Fig.1) and several collaborating partners. We use a referral system for patients and share medical results in a secure platform developed by the EU, aiming to ensure the same level of access to healthcare across Europe: the patient does not need to travel, the information does. Experts in different fields of epileptology meet regularly online to discuss optimal diagnostics and treatment for non-surgical and surgical cases. EpiCARE members share, compile and assess best practices, disseminate them in the form of publications, clinical guidelines and protocols.

Fig.1 : Map of EpiCARE current members

Conclusion: After 5 years of experience in developing an EU based network of experts in epilepsy, the ERNs are one of the most original and innovative initiative taken in the field of health care. Sharing of competencies and knowledge generation are facilitated, always at the service of the patients. Collaboration between ERNs is another important achievement, supporting the construction of highly interactive networks, both at national and EU level.

Disclosure: Nothing to disclose.

EPO-297

The development of cognitive functions and speech in children with idiopathic generalized epilepsy treated with AEDs

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Background and aims: The side effects of antiepileptic drugs (AEDs) on cognitive functions and speech are assessed in idiopathic generalized epilepsy (IGE) as this form influences cognitive status minimally.

Methods: The authors developed and validated a toolkit for rapid assessment of neuropsychological and speech status to track changes in children and adolescents (C&A) with IGE from 4 to 18 years old treated with AEDs. Control group (CG) included 30 neurologically healthy C&A, study group (SG) – 30 C&A with IGE receiving AEDs. C&A from SG were tested by the neuropsychological battery: a) before treatment; b) after 3, 6, 9, 12, 18, 24, 30 months. C&A from CG were tested at the same time intervals. Video-EEG monitoring with sleep deprivation was carried out in SG.

Results: There was revealed statistically significant decrease in SG: 1) in the productivity of verbal thinking (understanding of figurative meaning, generalization) which manifests after 18 months; 2) in the volume of auditory-verbal memory which manifests after 18 months; 3) the presence of dysgraphia signs in writing samples after 12 months with further decrease after 18 months; 4) in the functions of the energetic block of the brain after 9 months; 5) in the functions of the serial organization of movements after 18 months with worsening after 30 months.

Conclusion: Neuropsychological assessment should be recommended in treating epilepsy after 12 months from the start of therapy, further at least once a year.

EPO-298

How do astrocytes affect epileptogenesis? A brain slice study.

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Background and aims: Studies indicate that release of glutamate from astrocytes mediated by intracellular calcium signals via the inositol-1,2,5-trifosfat (IP 3) receptor 2 may trigger epileptiform activity. We have found an increase in mortality and epileptic activity in IP 3 receptor 2 knockout mice. Here we investigate the role of astrocytic glutamate handling and IP 3 receptor mediated calcium signalling in epileptogenesis.

Methods: IP 3 R2 knockout mice and wild-type mice were injected in the right hippocampus with calcium indicator GFAP-gCaMP6f or glutamate indicator syn-iGluSnfr. Status epilepticus was triggered 3 weeks later by deep cortical injection of kainate above the right hippocampus in an epileptogenesis and mesial temporal lobe epilepsy model. Day one or 10 post injection mice were terminated and fresh 400 μm hippocampal slices prepared. Two photon microscope recordings of astrocytic calcium signals and extracellular glutamate concentrations and electrophysiological recordings were made.

Results: Preliminary results indicate that electrophysiological stimulation induces substantially stronger calcium signalling in astrocytes of wild-types compared to knockouts. Stimulation elicits robust glutamate responses in both genotypes. We are currently mapping potential differences in glutamate responses and calcium signalling from day one to 10 and between genotypes. Analyses are done in Clampex (Molecular Devices) and the software Begonia. Results will be presented at the EAN 2022 Congress.

Conclusion: We have shown that mice with reduced calcium signalling display increased epileptic activity and mortality in a mouse model for mesial temporal lobe epilepsy. By mapping the mechanisms at play we hope to identify possible future pharmacological targets for curbing epileptogenesis.

Disclosure: Nothing to disclose.

EPO-299

Abstract withdrawn.

EPO-300

Overall and cause-specific mortality in epilepsy patients: A retrospective cohort study

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Background and aims: We analyzed the overall and cause-specific mortality in a large hospital-based epilepsy population.

Methods: Retrospective analysis of adult epilepsy patients at the Department of Neurology, Medical University of Vienna who died between January 1993 and December 2020. Patients with brain tumors or nonepileptic seizures were excluded. Database was linked to national death registry of Statistics Austria. Causes of death assessed by demographic, clinical information, death certificates and postmortem examination reports and were classified as 1) epilepsy related, 2) unrelated to epilepsy and 3) unknown. Study was approved by local Ethics Committee.

Results: 339 patients, 135 female (40%), 19–95y (median 57y±18.3y) with 22y median duration of disease (0.5–80y) were included: 247 patients (73%) with focal (temporal lobe epilepsy 85/25%, extratemporal lobe epilepsy 20/6%, and focal epilepsy not otherwise specified 142/42%), 48 patients (14%) with generalized, 44 patients (13%) with unclassified epilepsy. 30 patients (8%) had additional nonepileptic seizures. Diagnosis was verified in 50% of cases with video-EEG-monitoring. At last follow-up 68 patients (20%) were seizure-free, 105 patients (31%) had low seizure frequency (1/month) and seizure frequency was unknown in 46 patients (14%). 5.7% of patients were off-medication, 43.6% had monotherapy and 50.7% of patients had more than one antiseizure medication. There was an epilepsy-related cause of death in 66 patients (19.4%), no relation in 249 patients (73.5%) and unknown in 24 patients (7.1%).

Conclusion: Epilepsy-related mortality still remains underappreciated and underestimated by death certificates and forensic autopsy reports.

Disclosure: The authors declare no conflicts of interest.

EPO-301

Study of the cognitive neuropsychological functioning in epilepsy

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Background and aims: Chronic neurological diseases are the main cause of disability. Epilepsy is among the neurological diseases that cause disability. This disability is partly due to cognitive dysfunction. The aim of this prospective-retrospective observational study is to analyze the existence of cognitive neuropsychological dysfunction in patients with different epilepsies.

Methods: We used standard neuropsychological tools to evaluate the neuropsychological functioning in 91 adult patients with different types of epilepsy, separated into four groups: 20 patients with drug-resistant (DR) focal epilepsy, 27 with drug-responsive focal epilepsy, 21 with genetic generalized epilepsy (GGE), and 23 with developmental and epileptic encephalopathies (DEE).

Results: Disturbances in cognitive neuropsychological functioning were found in 48 of 91 patients with epilepsy (52.7%). Cognitive dysfunction was found in 16 of 20 patients in the DRE group, in 9 of 27 patients in the drug-responsive focal epilepsy group. Cognitive dysfunction was found in 2 of 21 patients in the GGE group and in 21 of 23 patients with DEE. There were significant differences, $p<0.05$ in the two groups of focal epilepsy, and in the two groups of generalized epilepsies, cognitive dysfunction was characterized for focal DRE and DEE.

Conclusion: Cognitive dysfunction in patients with different epilepsies was found in 52.7%. Cognitive dysfunction may be a single or additional disabling factor besides seizures and neurological deficits. Neuropsychological evaluation of cognitive functioning in patients with epilepsy serves for timely appropriate treatment aiming to decrease the burden of the disease for the patient, family, and society.

Disclosure: Nothing to disclose.

EPO-302

Transcranial Magnetic Stimulation in Drug Resistant Epilepsy and anti-GAD65 antibodies

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Background and aims: Epilepsy is a chronic neurological disease that manifests itself in the body's predisposition to sudden seizures. In some cases, drug treatment of this disease is ineffective, therefore, transcranial magnetic stimulation (TMA) remains the therapy of choice in the management of patients with epilepsy. The effectiveness of such treatment is difficult to assess in the initial stages.

Methods: Under our observation were 65 epilepsy patients, treated in clinic of Ogarev Mordovia State University, men and women from 46 to 73 years old. Control group comprise from 54 healthy doinors. We stimulated motor cortex, causing certain peripheral muscles to contract according to their topographic representation in the cortex. Motor responses evoked by TMS (Motor Evoked Potentials (MEP) were recorded using the electromyography method. GAD Ab were detected by using ELISA incubating patient sample in plates wells containing human recombinant GAD65.

Results: It was found that GAD65 AB levels were increased in 68% of epilepsy patients and 14% donors. After 2 months of TMA treatment convulsive paroxysms occurred much less frequently, GAD65 AB concentrations were increased only in 21 per cent of patients.
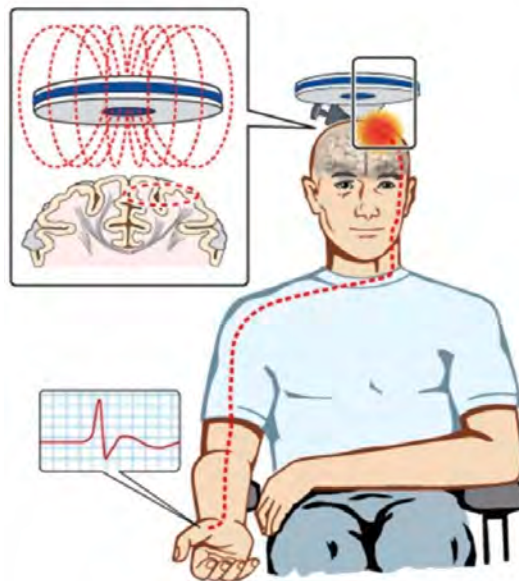
Transcranial Magnetic Stimulation

Conclusion: GAD65 AB play a significant role in epilepsy pathogenesis/ The use of anti-GAD65 antibodies as a marker of the degree of readiness for seizures seems to be a justified approach.
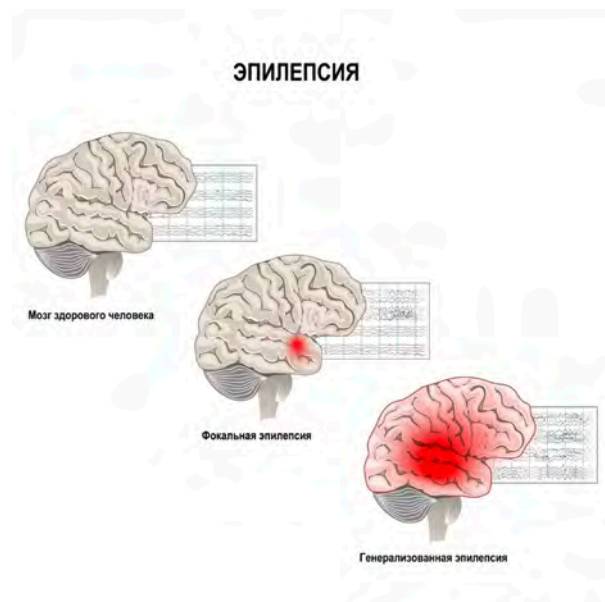
1. Healthy person; 2. Focal epilepsy; 3. Generalized Epilepsy

Disclosure: Nothing to disclose.

EPO-303

EEG findings in patients diagnosed with COVID-19

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Background and aims: Neurological complications have been reported in up to a third of patients with severe COVID-19 disease, including seizures. Some studies have noted a preponderance of frontal findings in the EEG of these patients. The aim of this work was to develop a clinical and electroencephalographic description of 80 patients diagnosed with COVID-19 who performed an electroencephalogram (EEG) at the Hospital Prof. Dr. Fernando Fonseca between March 2020 and September 2021.

Methods: Retrospective analysis of the electroencephalographic and clinical findings. Statistic analysis in SPSS software, with a significance level of $p<0.05$.

Results: There was a median of age of 75 years (IQR 22–94) and 48.8% of patients were female. The most frequent indication for ordering an EEG was depression of mental status (57.5%). The most common EEG finding was diffuse slowing (75.4%). There was a preferential location of the epileptiform discharges in the frontal lobe (48.7% of the first EEGs). Non-Convulsive Status Epilepticus (NCSE) was present in 9.7% of EEGs. No tendency of NCSE was found throughout the categories of the severity of COVID-19 disease nor any relation between the degree of encephalopathy and the severity of COVID-19 disease.

Conclusion: Similarly, to articles published on this matter, the most common electroencephalographic finding was diffuse slowing and the preferential location of the epileptiform discharges was the frontal lobe.

Disclosure: The authors deny having a conflict of interest.

EPO-304

How to find epileptogenic lesion in non-lesional focal epilepsies?

I. Rektor

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Background and aims: Surgical treatment of pharmaco-resistant MR-negative epilepsy is a major problem in neurology. The presentation will be focused on advanced diagnostic methods identifying the epileptogenic zone in MR-negative epilepsy.

Methods: 150 patients with MR negative epilepsy and 100 healthy controls were investigated. Thirty seven metabolic, imaging and EEG methods were tested. The results were checked and confirmed in 38 operated patients.

Results: For detection of epileptogenic zone in MR negative epilepsy combination of multimodal methods is optimal. The best results were obtained with: PET, SISCOM (ictal and interictal SPECT), EEG source imaging, in MRI GMV (Gray Matter Volume), ASL (arterial spine labelling), ReHo (regional homogeneity), DWI (diffusion tensor imaging), DKI (diffusion kurtosis imaging). Other methods may increase probability of epileptic zone detection. In 36 patients the location of epileptogenic lesion identified with multimodal methods was confirmed by resection surgery results; only in 2 patients the lesion was not found.

Conclusion: Optimal combination of techniques for visualization of seizure onset zone in MR negative epilepsies is presented. Patients with previously unremarkable MRI scans should be rescanned using novel advanced methods. Supported by grant AZV NU21-04-00254 Four studies were published in 2021 (Gajdoš et al.-ASL, Scientific Report; Kojan et al. – comparison of ASL and PET – Epilepsy and Behavior; Bartonová et al. DTI/DKI- Scientific Report; Marecek et al. Automatic fusion of data, Human Brain mapping; other papers are prepared).

Disclosure: Nothing to disclose.

EPO-305

Video-EEG documented bilateral Todd's palsy in a patient with left fronto-opercular epilepsy

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Background and aims: Todd's paralysis is a classic lateralizing postictal sign. It is usually a unilateral, transient weakness, lasting minutes to hours, after focal or focal to bilateral tonic-clonic seizures, contralateral to the epileptogenic zone. Bilateral postictal paresis is exceedingly rare and could be misinterpreted, namely as supporting a diagnosis of generalized epilepsy.

Methods: Clinical case report of postictal bilateral arm weakness in a case of focal epilepsy.

Results: We report the case of an 18-year-old right-handed patient with refractory focal epilepsy and seizure onset at age three. He had no relevant comorbidities and interictal neurological examination was normal. Seizures were predominantly nocturnal, consisting of a laryngeal somatosensory aura evolving to bilateral tonic or tonic-clonic seizures, with asymmetrical limb extension during the tonic phase (right arm extended). Postictally consciousness recovery was fast and at that stage we documented, on video-EEG, severe dysarthria and bilateral symmetrical arm paresis lasting several minutes. The ictal pattern was projected on the fronto-central midline and interictal epileptiform activity had the same topography. Brain MRI was highly suggestive of a bottom of the sulcus cortical dysplasia with underlying transmantle sign on the left premotor, fronto-opercular region. FDG-PET showed a concordant left fronto-operculo-insular hypometabolism.

Conclusion: Bilateral postictal paresis is extremely rare and we could only find two cases previously reported in the literature. We can speculate that, in our patient, a left fronto-opercular cortical dysplasia ictal onset with an early spread to both primary motor cortices and relative sparing of consciousness networks allowed the emergence of a clinically detectable postictal bilateral paresis.

Disclosure: Nothing to disclose.

EPO-306

Decrease in daily defined dose of antiseizure medications in phase 3 trial of adjunctive cenobamate for focal seizures

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Background and aims: An ongoing phase 3 safety study (C021), evaluated adjunctive cenobamate, an antiseizure medication (ASM) approved in Europe for adults with inadequately controlled focal seizures. This post-hoc analysis evaluated changes in concomitant ASM drug load and incidence of adverse events.

Methods: Patient ASM drug load was quantified using World Health Organization defined daily dose (DDD) at baseline and during post-baseline periods up to 30 months. Patients were grouped into 3 categories based on baseline DDD (0-<1, 1-<3, ≥3). Changes in DDD over time and incidence of treatment emergent adverse events (TEAEs) were reported for DDD categories.

Results: As of the June 2020 data cutoff (median treatment duration=33.4 months), 1340 patients were included in the post hoc analysis. Overall, the mean (SD) DDD at baseline was 2.86 (1.63) units, with 137 (10%) patients with DDD 0-<1, 607 (45%) with DDD 1-<3, and 596 (44%) with DDD ≥3. At month 30, the overall mean DDD reduction from baseline was 0.61 (1.01) units; in patients with baseline DDD ≥3, the mean DDD reduction was 1.14 (1.28) units. Patients with lower DDD at baseline and at year 1 had a lower incidence of TEAEs and serious TEAEs within 1 year and after 1 year of starting cenobamate, respectively (Table).

	DDD at Baseline			
	Overall (N=1340)	0 - <1 (N=137)	1 - <3 (N=607)	≥3 (N=596)
Subjects with TEAE that start before 1 year, n (%)	1147 (85.6)	99 (72.3)	506 (83.4)	542 (90.9)
Subjects with Serious TEAEs that start before 1 year, n (%)	127 (9.5)	3 (2.2)	49 (8.1)	75 (12.6)
	DDD at 1 Year			
	Overall (N=1054)	0 - <1 (N=158)	1 - <3 (N=582)	≥3 (N=314)
Subjects with TEAE that start after 1 year, n (%)	754 (71.5)	107 (67.7)	413 (71.0)	234 (74.5)
Subjects with Serious TEAEs that start after 1 year, n (%)	126 (12.0)	8 (5.1)	72 (12.4)	46 (14.6)

Table

Conclusion: A reduction in concomitant ASMs DDD in patients with focal epilepsy initiating adjunctive cenobamate was observed, with more than 1 unit reduction in patients with DDD ≥3 at baseline. Patients with adjunctive cenobamate treatment and lower DDD had fewer TEAEs and serious TEAEs.

Epilepsy 3

EPO-307

Psychogenic non-epileptic seizures in the emergency department: clinical characteristics, monitoring and evolution.

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Background and aims: Psychogenic non-epileptic seizures (PNES) are episodes of altered movement, sensation or experience resembling seizures, but not associated with epileptic activity. The aim of this study is to describe the PNES' care process in the emergency department (ED) and to analyze the factors which influence their subsequent demand for urgent care.

Methods: We performed a retrospective single-center study of patients attended due to PNES in the ED of our tertiary hospital. Clinical characteristics, type of long-term monitoring, complementary tests, final diagnosis and urgent care needed during one year of the follow-up period were analyzed.

Results: Between 2008 and 2018, 151 patients were fulfilled the inclusion criteria. Mean age was 43 years old, 72% were female and frequent comorbidities were anxious-depressive syndrome (66%) and epilepsy (18%). Patients were followed-up by Psychiatry (57%) and/or Neurology (47%) departments. In 32% of patients there was no follow-up. The final diagnosis was "documented PNES" in 15% and 6% of the patients had a final diagnosis of epilepsy. Hyperkinetic PNES (50%) were more followed-up by Neurology or Psychiatry and reached the "documented PNES" final diagnosis in a higher proportion. 37% of the patients required new urgent care due to PNES, which was associated with the presence of comorbid anxious-depressive syndrome and being followed-up by Neurology or Psychiatry.

Conclusion: Patients with PNES have an uneven care, with low follow-up and most do not reach a definitive diagnosis. The medical care provided by the Neurology department increases the likelihood of documented diagnosis, but does not decrease subsequent demand for urgent care.

Disclosure: The authors disclose no relationships/activities/interests related to our manuscript.

EPO-308

Are there differences in EEG between epileptic patients with vagal nerve stimulation (VNS) and healthy controls?

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Background and aims: The presented work is based on the results of our published work, in which we focused on the VNS efficacy prediction in patients with drug-resistant epilepsy. We found that there are differences in power spectra between VNS responders and non-responders. We asked two more questions. Are there differences between the epileptic patients with VNS and healthy controls? Do the EEG power spectra in healthy controls resemble more responders or non-responders to VNS therapy?

Methods: We identified retrospectively EEG recording in epileptic patients with VNS and in healthy controls. The epileptic patients were classified based on the VNS efficacy as responder and non-responders EEG was segmented into several time-intervals (resting-state, eyes-opening 1, resting state, photic stimulation, hyperventilation, eyes opening 2, resting state 3 and resting state) and frequency bands. Subsequently, we established relative EEG power spectra in pre-defined frequency bands and time-intervals.

Results: We identified EEG in 56 healthy controls and in 60 epileptic patients with VNS (35 responders, 25 non-responders). When compared healthy controls and epileptic patients, we identified EEG power spectra differences in theta (eyes-opening 1, 2), alpha (eyes-opening 1,2) and beta frequency range (eyes-opening 1). When compared responders to VNS therapy and healthy controls, we found more significant differences than in non-responders.

Comparison of healthy controls and VNS responders

Theta

Alfa

Beta

Gamma

Comparison of healthy controls and VNS non-responders

Theta

Alfa

Beta

Gamma
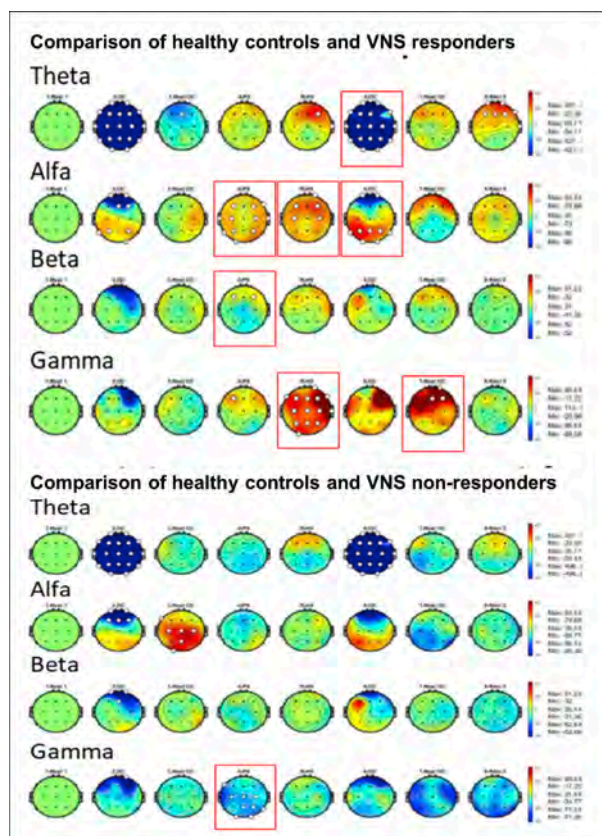
The differences between controls and VNS responders, non-responders

Conclusion: There are differences in EEG power spectra between epileptic patients treated with VNS and healthy controls. These differences are present in more frequency bands and time-intervals. However, non-responders resemble healthy population more than responders. The question is whether we can employ these results for pre-implantation VNS prediction.

EPO-309

Improved assessment of P-gp activity at the blood-brain barrier of epilepsy patients with [11C]metoclopramide PET

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Background and aims: [11C]Metoclopramide is a new positron emission tomography (PET) radiotracer for measuring the activity of the efflux transporter P-glycoprotein (P-gp) at the human blood-brain barrier (BBB). Using [11C]metoclopramide PET we have found +15% higher volume of distribution (VT) and a 14% decreased elimination rate from the brain (k2) in elderly subjects as compared to the young controls. This points to an age-related decrease of P-gp activity at the BBB. In contrast, higher P-gp activity is expected to occur in the focus area of patients with drug resistant temporal lobe epilepsy.

Methods: In our Franco-Austrian multicentre phase II study, 80 patients with drug-resistant and drug-sensitive focal epilepsy and 20 healthy volunteers will receive a single [11C]metoclopramide PET scan to investigate P-gp activity at the BBB.

Results: Five epilepsy patients (mean age: 44 ±17 years), four drug-resistant and one drug-sensitive, and 10 healthy volunteers (mean age: 26+/-5 years) were scanned so far. In comparison to the healthy volunteers, the epilepsy group shows lower [11C]metoclopramide VT (VT : 1.72+/-0.29 versus 1.85+/-0.28 respectively) and higher k2 (k2: 0.045+/-0.009 versus 0.039+/-0.005 respectively), pointing to increased P-gp activity. Co-medication of patients did not affect [11C]metoclopramide metabolism.

Conclusion: Our preliminary data indicate that patients with focal epilepsy may have increased P-gp activity at the BBB and that this could be measured with [11C] metoclopramide PET.

EPO-310

Headache and the quality of life of people living with epilepsy at the Douala general hospital

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Background and aims: Headache occurs frequently in people living with epilepsy (PWE) and it contributes greatly to an altered quality of life for these people. However, despite the frequent association between these two health conditions, there is limited data on this subject in Cameroon.

Methods: We conducted a 4-months cross-sectional study from February to May 2021 at the neurology unit of the DGH. We included PWE aged 18 years and above. A previously designed questionnaire was administered. Data on epilepsy and headache were collected. We classified headache according to International classification headache (ICH-3beta). Data on quality of life was assessed using quality of life in epilepsy-31 (QOLIE-31).

Results: 100 participants were included, 52.1% were males. The mean age was 38±16 years. A majority of our participants reported a history of generalized seizure with no significant difference between the two groups. 48 participants had headache. The most frequent headache was migraine (50%). Headache occurred mainly in the post ictal period (32%). Impaired emotional well-being (p=0.013), impaired social functioning (p=0.047) was significantly higher in those with headache. On multivariate analysis, having a family history of headache (OR 12.66, 95% CI 1.86–86.22) and lack of headache treatment (OR 16.28, 95% CI 2.31–114.41; p=0.005) were found to be independent predictors of poor quality of life.

Conclusion: About half of PWE had headache. Having a family history of epilepsy, not being on treatment for headache were independent predictors of poor quality of life in our participants.

Disclosure: Nothing to disclose.

EPO-311

Epilepsy and Episodic ataxia type 2 (EA2): report of clinical case

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Background and aims: Episodic ataxia type 2 (EA2) is a rare disorder characterized by self-limited episodes of ataxia due to mutations in the CACNA1A gene, which encodes the alpha-1A subunit of the voltage-dependent calcium channel, usually inherited, although de novo mutations have also been described.

Methods: We present a case of episodic ataxia type 2 and epilepsy.

Results: A 37-year-old male followed by the department of neurology for Juvenile myoclonic epilepsy consults for ataxia, nausea and vomiting episodes lasting hours. His family history includes a sister and a maternal first cousin diagnosed with EA2 with a mutation in the CACNA1A gene. Due to the compatible clinical manifestations and favourable family history, treatment was started with acetazolamide, and a genetic study was performed, with a heterozygous mutation in the CACNA1A gene, p. Gly297 Arg (C.889G>A). A positive genetic study was also performed on his mother and maternal uncle, and they were classified as asymptomatic carriers.

Conclusion: We describe a patient with EA2 and Juvenile myoclonic epilepsy caused by a mutation in the CACNA1A gene, which is associated with EA2 and epilepsy among others entities. It is suggested that the mutation lead to a reduction in the function of the voltage-dependent calcium channel, which sequentially causes an increase in thalamocortical excitation and predisposition to epileptic discharges. Generalized and focal epilepsy have been related to this mutation and same genetic mutation can lead to different clinical phenotypes. The correlation between epilepsy and AE2 is often underestimated. As the diagnosis often requires a high suspicion, family history is frequently decisive.

Disclosure: Nothing to disclose.

EPO-312

Seizure prediction after a first unprovoked epileptic seizure: Current status of the Swiss First Study

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Background and aims: If patients present with a first unprovoked epileptic seizure, uncertainty is a frequent companion for the patient and the caregiver. Diagnosing an epileptic seizure is challenging. Epileptiform discharges, the best objective biomarker are rarely detectable. Estimating seizure recurrence, and therefore diagnosing epilepsy, is even more sophisticated. The risk for seizure recurrence can be estimated, but not precisely calculated with the present diagnostics. Therefore, after a first seizure it often cannot be distinguished if anti-seizure medication is inevitable or not necessary.

Methods: In the ongoing Swiss First study, we prospectively analyze patients with a first unprovoked epileptic seizure, review their MRI and EEG, and observe them over a period of two years. We screen for potentially epileptogenic lesions within the MRIs. We additionally apply automatic brain morphometry and a novel MRI-sequence to detect high-frequency oscillations. EEGs are analyzed regarding functional connectivity and microstate-architecture. After the observational period, multimodal data from the work packages are employed to set up a deep-learning algorithm to predict the individual risk of seizure recurrence based on clinical and quantitative features.

Results: Currently, approx. 400 patients have been included in the Swiss First study, and the study is open until December 2022. Diagnosis posed at the emergency department was upheld in only 88%, showing us the large potential in diagnostics. Also, 49 patients had subsequent seizures, that could have potentially prevented by establishing antiseizure medication.

Neuronal current imaging of a 20 year old female with suspected seizure onset zone in the right temporal lobe
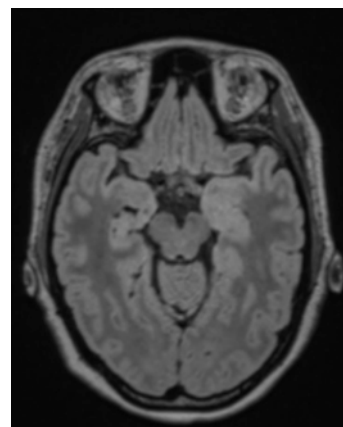
FLAIR image of a 36 year old female with swelling of the left amygdala. The entity of that lesion is unknown, and if that lesion is epileptogenic is still discussed.

Confusion chart of all patients with initial and present diagnosis. Remark: Observation period is still ongoing, follow-up information therefore frequently not available.

Conclusion: We will present the preliminary outcomes of these patients and show, in what setting our diagnostic tools can be applied in clinical environment.

Disclosure: Nothing to disclose.

EPO-313

Implications of anaesthetics' utilization in NCSE prognosis

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Background and aims: Status epilepticus (SE) derives from the failure of the terminating mechanisms in a seizure or the beginning of those who allow it to continue. Literature is not consensual regarding anaesthetics' utilization in non-convulsive status epilepticus (NCSE). This work aimed to analyze anaesthetics' use in NCSE.

Methods: Retrospective study including patients older than 18 years, with an electroencephalographic diagnosis of NCSE, from July 2020 to October 2021. Statistical analysis made with SPSS® and Microsoft Excel®.

Results: 85 patients [88.9% male, a median of 76 years old, 77.8% with a modified Ranking Scale (mRS) 0–1, 30.8% with a Status Epilepticus Severity Score (STESS) =6] were analysed. In 4 patients, anaesthetics were initiated for other reasons but kept posteriorly to the diagnosis; in two patients, they were initiated to terminate NCSE; in three, they were reinitiated after its diagnosis. In 6 cases, NCSE was resolved (83.3% used benzodiazepines, and 16.7% levetiracetam and lacosamide simultaneously as the last medication). Anaesthetics' utilization seemed to favour a fatal disclosure, although not statistically significative (p=0.084). A multinominal analysis suggested that complications inherent to intensive care unit stay (88.9% had a qSOFA ≥ 2) and a worse STESS contributed to a greater variation in mRS at discharge (p<0.05).

Conclusion: Anesthetics' utilization might be associated with worse outcomes, but a causal relationship is unclear. Larger prospective studies are needed to clarify which situations might benefit from a more aggressive strategy.

Disclosure: No conflict of interest is declared by the authors.

EPO-314

Benzodiazepines' utilization in non-convulsive status epilepticus

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Background and aims: Status epilepticus (SE) derives from the failure of the terminating mechanisms in a seizure or the beginning of those who allow it to continue. Recent studies show that benzodiazepines' underutilization, as well as their late positioning in non-convulsive status epilepticus (NCSE) treatment algorithms, might contribute to a worse prognosis. This work aimed to evaluate benzodiazepines' use in NCSE.

Methods: Retrospective study including patients older than 18 years, with an electroencephalographic diagnosis of NCSE, from July 2020 to October 2021. Statistical analysis made with SPSS® and Microsoft Excel®.

Results: Eighty per cent of 85 patients' NCSE [56.99% female, a median of 76, 43% with a modified Ranking Scale (mRS) 0–1] was ended after a medium of 5.47 days, utilizing a medium of 2.46 anticonvulsants. Benzodiazepines were used in 75.3%. The subgroup that used them as the first anticonvulsant (10.5%) had a lesser variation in mRS at discharge (52.6% vs. 88.9%, p=0.038). Although negatively influenced by higher scores of SE's severity (STESS) and medical complications (qSOFA), a multivariate analysis showed that benzodiazepines' precocious usage had a statistically significant value (p=0.012). In the subgroup where NCSE ended after benzodiazepines' introduction (43.8%), a greater mRS' variation was also verified (0.025); however, STESS and qSOFA's negative effects seem to overlap.

Conclusion: As suggested by some authors, benzodiazepines' underutilization, as well as their late positioning in treatment algorithms of NCSE, might associate with a worse prognosis; however, clinical variability (eg, qSOFA and STESS) has a negative effect on these results.

Disclosure: No conflict of interest is declared by the authors.

EPO-315

Consideration of surgical treatment in pharmacoresistant epileptic patients in Czechia – reality and a recommendation

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Background and aims: The aim of the study was to determine changes in the duration of pharmacoresistant epilepsy in individual patients who are referred by outpatient neurologists to the Brno Epilepsy Center to be assessed for surgical treatment of epilepsy.

Methods: A total of 605 patients with pharmacoresistant epilepsy were enrolled in the study. The patients were referred to the Brno Epilepsy Center between 1995 and 2020 to be assessed for their suitability for surgical treatment of epilepsy. Another condition for inclusion in the study was performed epilepsy surgery, either an intracranial procedure or a VNS implantation. Three periods were compared statistically 1995–2000, 2001–2010, and 2011–2020). We studied the duration of intractable epilepsy before referral to the centre, and the duration of the diagnostic process.

Results: The mean age of the patients was 30.7 years; SD=12.91. In terms of surgical intervention, 384 patients underwent intracranial surgery and 221 patients had implanted VNS. In the three analysed time periods, the duration of epilepsy before referral to the centre has not decreased (17, 18.2 and 18.1 years for 1995–2000, 2001–2010 and 2011–2020 respectively, p=0.72). The average time of the diagnostic process in the centre was significantly reduced from 2.6 years to 1.4 year, p<0.001.

Conclusion: The results are similar to those previously published. Since 1995, the duration of epilepsy before a surgical solution has not been significantly shortened within the epilepsy surgery program. There is however a clear increase in the speed of the diagnostic evaluation prior to surgery.

Disclosure: Authors declare no competing interests and have nothing to disclose.

EPO-316

Non-convulsive status epilepticus due to benzodiazepine deprivation. An entity not suspected until the EEG is performed

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Background and aims: Benzodiazepines (BZD) are a common treatment whose abrupt withdrawal can cause generalized non-convulsive status epilepticus (NCSE) due to GABAergic disinhibition and hyperexcitability. We present a case series of 13 patients.

Methods: Unicentric observational study of NCSE due to BZD deprivation (2009–2021) of 13 patients (7 women, median age of 71 years [range 51–87], only 1 with known epilepsy).

Results: All patients presented with an acute altered mental status with confusion (n=9) and/or episodes of disconnection from the environment (n=8); six had generalized tonic-clonic seizures. Ten were brought to the emergency department from home, while three presented during hospitalization (ICU n=2; conventional ward n=1). In all cases there was an abrupt discontinuation or reduction of chronic benzodiazepine treatment, 1–5 days before the episode (Figure 1), either by patient choice (n=8) or by medical indication (n=5). In none of them this etiology was suspected (Figure 2) until an EEG recorded continuous or recurrent seizures with generalized 2–3Hz polyspike-wave activity (Figure 3). Treatment with antiepileptic drugs was not effective. Only reintroduction of BZD achieved complete remission in all cases.
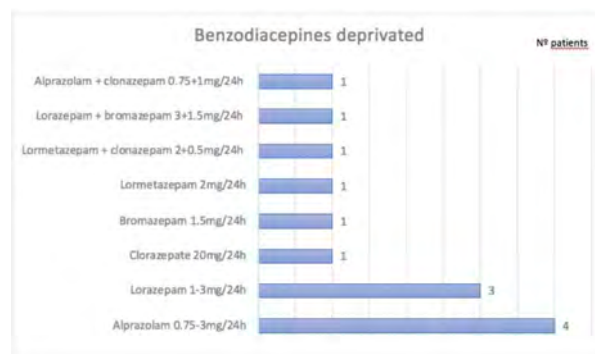
Figure 1: Benzodiazepines used, with more than 1 year duration of treatment in all patients.
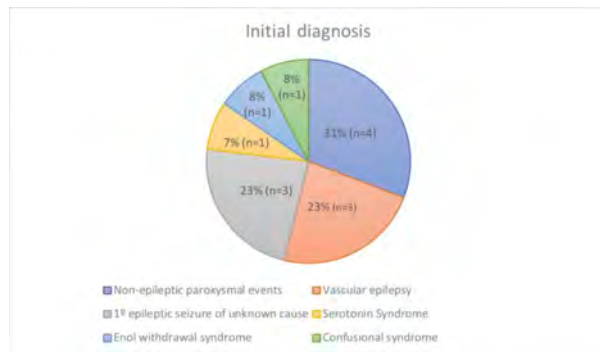
Figure 2: Initial diagnosis. An epileptic etiology was only suspected when patients presented with motor symptoms (46%).
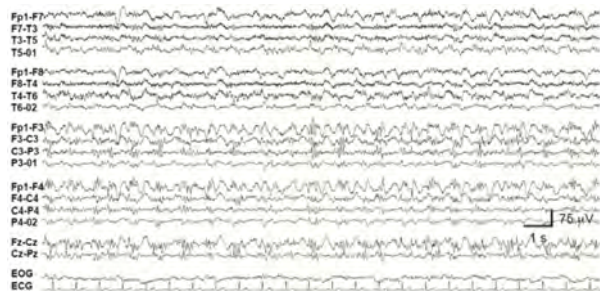
Figure 3: Electroencephalogram (EEG). Longitudinal bipolar montage showing polyspike - wave at 2–3Hz generalized with anterior and central predominance.

Conclusion: NCSE due to recent BZD withdrawal may present as an acute or intermittent confusional syndrome in the emergency department or in critically ill patients without epilepsy history. In the absence of a known etiology, it is important to rule out BZD withdrawal and perform an EEG to diagnosis this unsuspected complication. Treatment with antiepileptic drugs is ineffective and reintroduction of BZD is necessary.

Disclosure: The authors have no financial disclosures or conflicts of interest.

EPO-317

Dramatic response to carbamazepine in a patient with epileptic encephalopathy related to a de novo CACNA1A mutation

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Background and aims: Epilepsy has been recognized as part of the CACNA1A mutations related phenotype, including a severe developmental epileptic encephalopathy minimally responsive to antiepileptic treatment.

Methods: Case report of a girl with epileptic encephalopathy, apparently pharmacoresistant, ataxia, cognitive impairment and significant social behavioral abnormalities, due to a de novo pathogenic CACNA1A gene mutation, who became seizure-free with carbamazepine (CBZ).

Results: After failing valproic acid (500 mg twice daily) and levetiracetam (1,250 mg twice daily), at the age of 23 years, she was admitted because of uncontrolled seizures and occasional nonconvulsive status epilepticus. The girl had a dramatic response to CBZ, up to 400 mg twice daily, with a complete control of any types of seizures. This improvement has persisted over two years. Clinical exome sequencing revealed the presence in heterozygosis of c.4186G>A (p.V1396M) mutation of CACNA1A gene.

Conclusion: The CACNA1A mutation V1396M has recently been studied in HEK293 cells using transient expression of mutant cDNA. It resulted in a gain-of-function of CaV2.1 channels with facilitated current activation. In addition to the classic action on sodium channels, CBZ has also antagonistic effects on calcium channels, as documented in several experimental models in vitro. We observed a complete seizure freedom with CBZ in our patient, for over two years, suggesting that the calcium antagonistic property of CBZ could reduce the gain-of-function related to mutated calcium channels. A similar effect has been reported with lamotrigine, likely due to calcium antagonistic properties. These findings suggest that calcium channel blocking drugs may be useful in CACNA1A-mutations associated epilepsy.

Disclosure: Nothing to disclose.

EPO-318

Frequency and risk factors for acute post-stroke seizures

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Background and aims: Stroke is one of the leading causes of death and disability worldwide. Acute post-stroke seizures (early seizures, occurring within the first week of stroke onset, ASS) increase the risk of mortality and poor stroke outcome. The reported incidence of ASS varies significantly from 1 to 18%. We aimed to identify all ASS in a cohort of post-stroke patients and to reveal the risk factors of ASS.

Methods: 424 patients with acute stroke were enrolled. Patients themselves, relatives and ambulance teams were interviewed at the emergency room to reveal ASS occurred before the admission. The presence of ASS observed during the hospital stay was confirmed by a neurologist with expertise in epileptology and specially trained hospital staff. A qualified epileptologist was available at all hours to verify a seizure in cases of uncertainty.

Results: ASS occurred in 97 (23%) of all post-stroke patients. Over 60% of people with ASS experienced only focal aware seizures. The first ASS occurred within 24 hours after the stroke onset in 85% of all cases. Multivariate logistic regression revealed the initial stroke severity measured in NIHSS (OR=1.1, p<0.001), hemorrhagic stroke type (OR=2.1, p=0.01) and atrial fibrillation (OR=1.9, p=0.01) to be independent risk factors for ASS. ASS was an independent predictor for in-hospital mortality; 47 (48%) patients with ASS died during the in-hospital stay.

Conclusion: The frequency of ASS, especially ASS without tonic-clonic features may have been underestimated in previous studies. ASS are associated with a significantly increased risk of in hospital death.

Disclosure: Nothing to disclose.

EPO-319

Efficacy of Perampanel in refractory myoclonic epileptic syndromes of different etiology: A series of four patients

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Background and aims: Perampanel is an antiepileptic drug (AED) acting as a selective, non-competitive alpha-amino-3hydroxy-5-methyl-4-isoxazolepropionic acid (AMPA) receptor antagonist.

Methods: We present four patients with refractory epileptic syndromes of different etiology [Progressive Myoclonic Epilepsy (PME), refractory myoclonic epilepsy of degenerative etiology, Opercular Myoclonic-Anarthric Status Epilepticus (OMASE), Epilepsia Partialis Continua (EPC)], to assess the efficacy of Perampanel as add-on therapy.

Results: Patient 1: A 23-year-old male with PME experienced GTCS, multiple daily myoclonias and absences with frequent recurrent myoclonic seizures under four-fold antiepileptic treatment with valproate, levetiracetam, zonisamide and clonazepam. Perampanel was added to eliminate GTCS and reduce myoclonus and absences. Patient 2: A 43-year-old male with rapidly progressive dementia of degenerative etiology gradually established severe cognitive decline and myoclonic epilepsy with limb and trunk myoclonus and frequent episodes of myoclonic status. Perampanel was added to levetiracetam and clonazepam as 3rd AED resulting in complete suppression of myoclonus. Patient 3: A 74-year-old female was admitted with new onset refractory status epilepticus (NORSE) presented as OMASE of possible autoimmune origin. She was treated with methylprednisolone, levetiracetam, phenytoin, diazepam without response. Eventually Perampanel was added to achieve seizure control. Patient 4: A 47-year-old female with multiple sclerosis developed progressive multifocal leukoencephalopathy (PML) while on treatment with fingolimod and was admitted with EPC. The patient was treated with brivaracetam, lacosamide, diazepam with poor response. Perampanel was lastly added leading to seizure control.

Conclusion: The heterogeneity of our sample in terms of etiology, course and clinical symptomatology of drug-resistant epileptic syndromes, emphasizes the broad spectrum of effectiveness of Perampanel.

Disclosure: Nothing to disclose.

EPO-320

Connectome Analysis in an Individual with SETD1B-Related Neurodevelopmental Disorder and Epilepsy

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Background and aims: Causative variants in SETD1B, encoding a lysine-specific methyltransferase, have recently been associated with a neurodevelopmental phenotype encompassing intellectual disability, autistic features, pronounced language delay and epilepsy. It has been noted that long-term and deep phenotype data are needed to further delineate this rare condition.

Methods: Here, we provide an in-depth clinical characterization with long-term follow-up and trio exome sequencing findings to describe one additional individual affected by SETD1B-related disorder. The diagnostic work-up was complemented by a functional magnetic resonance imaging study.

Results: We report a 24-year-old male individual with an early-onset neurodevelopmental disorder with epilepsy due to the de novo missense variant c.5,699A>G, p. (Tyr1900Cys) in SETD1B (NM_015048.1). He exhibited delayed speech development, autism spectrum disorder and early-onset epilepsy with absence and generalized tonic-clonic seizures. In spite of profoundly impaired communication skills, ongoing improvements regarding language production have been noted in adulthood. Functional magnetic resonance imaging findings demonstrate abnormal language activation and resting-state connectivity structure.

	Previously published patients	Patient reported in this study
Gender (male)	25/39	Yes
Global DD/ID	37/39	Yes
Language impairment	37/39	Yes
Autistic features	25/39	Yes
Epilepsy	30/38	Yes
Generalized seizures at onset	24/29	Yes
ASM response (yes or partly)	18/26	Partly

ASM = antiseizure medication, DD = developmental delay, ID = intellectual disability.

As some phenotype characteristics were not available for all reported individuals, the frequencies of previously published patients in Table 1 differ between the clinical features.

Brief comparative phenotype analysis of previously published patients with (likely) pathogenic sequence variants in SETD1B (as reviewed in Weerts et al., 2021)9 and our reported index patient.
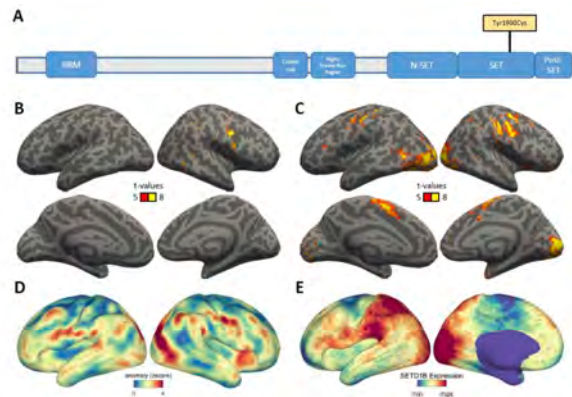
Genetic and connectome analysis in SETD1B-related neurodevelopmental disorder.

Conclusion: Our report expands the previously delineated phenotype of SETD1B-related disorder and provides novel insights into underlying disease mechanisms.

Disclosure: Nothing to disclose.

Headache 3

EPO-321

Long-Term Prophylactic Transcranial Direct Current Stimulation Improves Clinical Outcomes in Migraineurs with Allodynia

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Background and aims: Migraine is a common and substantially debilitating disorder that may associate with allodynia, a marker of central sensitization in the pain circuits and which is an indicator of drug resistance and chronicity. Several unmet needs like limited adherence to drugs due to adverse events and cost-effectivity still occur in the prophylactic treatment of migraine. Transcranial direct current stimulation (tDCS) has recently been indicated to be beneficial in migraineurs. There are no studies, however, evaluating the efficacy of 6-month tDCS in migraine so far.

Methods: In this randomized double-blind sham-controlled study, three consecutive sessions of 2 mA 20-minute tDCS over the left primary motor cortex every month for 6 months were applied to a total of 23 migraineurs with allodynia. Migraine features, allodynia, depression, anxiety, and disability due to migraine were assessed.

Results: Improvements in allodynia levels (p = 0.007), attack frequency (p = 0.034), number of rescue medications (p = 0.003), attack duration (p = 0.001) were higher, and mostly gradual during the trial, in the active group. And also higher responder rates of attack frequency (56.8% vs 25%; p = 0.012), the number of headache days (56% vs 16.7%; p = 0.012) and attack duration (90.9% vs 8.3%; p = 0.01) were observed. MIDAS grades were also lower in the active group (p = 0.005), whereas no between-group differences were found in depression and anxiety scores.

Conclusion: Long-term tDCS comes forward as a safe, efficacious and plausible modality for the prophylactic treatment in migraineurs with allodynia.

Disclosure: Nothing to disclose.

EPO-322

New daily persistent headache as the main neurological headache symptom in long-covid patients: an observational study

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Background and aims: New daily persistent headache (NDPH) is a primary headache characterized by persistent and daily painful symptoms, with pain becoming continuous and non-remitting within 24 h, and lasting more than 3 months. Aim of our study is to establish the impact of NDPH in our COVID-19 population.

Methods: 390 patients with COVID-19 have been hospitalized in San Martino Hospital, Genova, from march 2020 to march 2021. Among the surviving subjects we enrolled in the study 109 patients followed for neurologic post covid symptoms in our Neurologic Clinic outpatients. We analyzed which was the major neurologic longcovid-19 related symptom, and which was the percentage of NDPH (in accord to the International Classification of Headache Disorders ICHD-3) and its features.

Results: The characteristics of the patients and the course of their COVID-19-related illness are schematized in the figure n.1. 42 (45%) patients reported having acute headache among the symptoms of the acute phase of covid-19, while 17 of our patients (15%) experienced headache as the main neurological symptom related to post COVID-19 condition. 3 patients had headache like secondary neurologic symptom. Oh those, 7 patients (41%) meet the criteria for NDPH. 5 are migraine like (pulsating headache with photophobia and phonophobia or with nausea and vomiting,) and 5 improved without specific therapy after 12 months.

Sex (male:female)	1:1		
Age: mean (range)	57.17 years (18-80)		
Smoking habit			
non-smoker	55%		
smoker	10%		
ex-smoker	35%	**Oxygen therapy**	
BMI		no oxygen therapy	31.2%
underweight	3%	nasal cannula/mask	20.2%
healthy weight	51%	NIV	18.3%
overweight	46%	intubation/tracheostomy	30.3%
Manifestation of acute COVID		**Prone ventilation**	0,23
pneumonia	81%	**Days of admission stay**	
upper respiratory tract symptoms	16%	no admission	18.3%
gastrointestinal symptoms	1%	< 30 days	36.7%
Number of symptoms of acute infection		> 30 days	45%
		Severity of acute phase	
no symptoms	2.8%	low	50.5%
1 symptom	5.5%	moderate	18.9%
2 symptoms	36.7%	severe	30.6%
3 symptoms	27.5%		
4 symptoms	14.7%		
5 symptoms	9.1%		
6 symptoms	2.7%		
7 symptoms	1%		

Figure 1

Conclusion: In conclusion, NDPH is one of the most common headache related to COVID-19, with a prevalent migraine features and spontaneously improving course. Further data are still ongoing.

Disclosure: I declare that there is no conflict of interest

EPO-323

Use of CGRP monoclonal antibodies and patient-reported improvement: Results from the OVERCOME (EU) study

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Background and aims: Real-world data are limited for people who use a calcitonin gene-related peptide (CGRP) monoclonal antibody (mAb) for preventive treatment of migraine. We assessed respondent characteristics and patient-reported improvement among current CGRP mAb users in the OVERCOME (EU) study.

Methods: Data were obtained from a cross-sectional web-based survey (2020–2021). Adult respondents fulfilled International Classification of Headache Disorders (ICHD-3) criteria for migraine or had a self-reported physician diagnosis. This analysis assessed clinical and demographic characteristics in those who had ever used erenumab, fremanezumab or galcanezumab. Moreover, current users of a single mAb completed the Patient Global Impression of Improvement (PGI-I) to assess improvement in current migraine condition. Analyses were descriptive.

Results: Of 20,756 respondents, 2,167 (10.4%) reported ever using a CGRP mAb. Among these, the mean (standard deviation [SD]) age was 32.9 (10.4) years, 38.8% were female, and the mean (SD) headache days/month (HD/m) was 3.4 (4.4). More than 1/3 of respondents (34.1%) had severe migraine-related disability (MIDAS score ≥21), 30.8% moderate (11–20), 21.8% mild (6–10), and 13.3% little to none (≤5). The vast majority had used at least 1 additional traditional preventive medication (Figure 1). A total of 940 respondents (43.4%) had used a single CGRP mAb within the past 3 months. Among them, most respondents (77.3%) reported their migraine condition as "better" based on the PGI-I since starting the CGRP mAb. This was consistent across HD/m categories (Figure 2).

Figure 1. Proportion of patients using additional preventive medication.

Figure 2. PGI-I response in those currently using a single mAb.

Conclusion: Most respondents taking a CGRP mAb for the preventive treatment of migraine reported their migraine as better since starting the medication.

Disclosure: JP: advisory boards for Allergan-Abbvie, Amgen-Novartis, Eli Lilly, and Teva. SE: consultation/speaker for Allergan-Abbvie, Eli Lilly, Lundbeck, Novartis, Perfood and Teva. TP, GDA and DN: full-time employees and stock-holders of Eli Lilly.

EPO-324

Facial neuropathy secondary to cocaine use: an infrequent and refractory entity

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Background and aims: The trigeminal terminal branch neuropathy is a rare trigger of drug-resistant facial neuralgia in which non-traumatic causes are difficult to suspect. We present a case of infraorbital and external nasal dysautonomic neuropathy of otorhinolaryngologic aetiology, with excellent response to anaesthetic infiltration.

Methods: A 28-year-old man, regular consumer of cocaine, initiated a paroxystic intense burning pain on the nasal wing radiated to infraorbital and cygomatic alternating bilateral regions and dysautonomia (local edema and erythema, eye redness and bilateral tearing). This clinical presentation was associated to millimetric ulcers in both nostrils with posterior nasal septum perforation and formation of a bacterial abscess. Blood tests including herpes virus serology and autoimmunity tests delivered normal results. No pulmonary infiltrates and pleural effusion were observed on the chest x-ray. Vascular damage was not found on the cerebral magnetic resonance imaging with angiography. The facial/sinus computerized tomography only showed a deviation of the nasal septum.
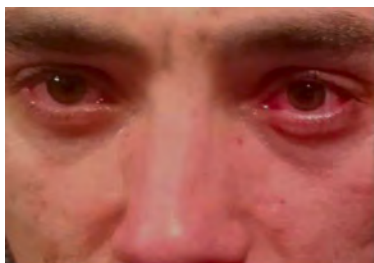
Dysautonomia in infraorbital and external nasal nerve territories

Results: The patient started treatment with gabapentin, amitriptyline, eslicarbazepine acetate and intranasal lidocaine, with no favourable results. Afterwards he initiated local infiltrations with 1 cm^3 of 2%-lidocaine in each infraorbital and external nasal nerves with complete resolution of pain and remaining asymptomatic for two months.

Conclusion: We want to highlight with this clinical case the importance of an adequate otorhinolaryngologic examination when searching for non-traumatic causes of trigeminal terminal branch neuropathy, given its anatomic location and bilateral crossed innervation (nasal septum anomalies, rhinosinusitis or granulomatosis with polyangiitis) as well as its frequent refractoriness to treatment, with an optimum medium-term response to anaesthetic infiltration.

Disclosure: Nothing to disclose.

EPO-325

Real-world study of migraine patients treated with galcanezumab or topiramate in the German NeuroTransData network

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[2] PricewaterhouseCoopers AG, Zurich, Switzerland, [3] Eli
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Background and aims: Recent approvals of calcitonin-gene-related-peptide (CGRP) monoclonal antibodies (mAbs) for the prophylactic treatment of migraine provide new therapeutic opportunities. We report baseline results from an ongoing real-world study aimed to improve our understanding of prescribing patterns of galcanezumab, a novel CGRP mAb launched in Germany in 2019, and topiramate, a conventional prophylactic treatment.

Methods: We collected retrospective data from a nation-wide registry in Germany (NeuroTransData) including patients treated with galcanezumab or topiramate for a descriptive assessment of socio-demographic factors, clinical characteristics, patient-reported outcomes (PROs), and treatment sequences. The study included adult patients with ≥4 monthly migraine days (MMDs), required in the European galcanezumab label indication (study interval May-1-2018 to Nov-16-2021; see Figure 1 for study design/methodology details).
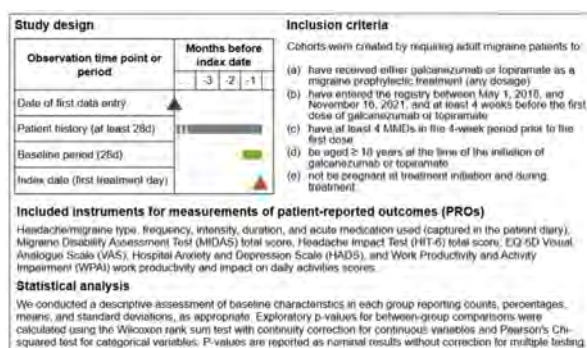
Figure 1: Study design, inclusion criteria, PRO instruments used, and statistical methodology of the retrospective cohort study

Results: We identified 65 patients treated with galcanezumab and 111 with topiramate. Core socio-demographic data showed that the age at diagnosis was similar in the two groups while employment status differed (Table 1). Exploratory comparisons of clinical characteristics revealed that galcanezumab-treated patients had more baseline monthly migraine days (MMDs) and monthly headache days (MHD) and were more likely to suffer from chronic migraine (CM) (Table 2). Pre-treatment assessments of PROs showed similar values between groups, but interpretation is limited due to incomplete responses. Galcanezumab was mostly used as the first (n=30) or second (n=26) CGRP mAb.

Variable	Statistic	Galcanezumab	Topiramate
Sample size	N	65	111
Age at migraine diagnosis	mean	27.0	27.9
	standard deviation	11.8	12.5
	missing	1	2
	P-value*	0.66	
Employment status n (percent)	education	1 (1.6)	3 (3.6)
	employed (full time)	23 (37.1)	50 (59.5)
	employed (part time)	18 (29.0)	17 (20.2)
	retired	14 (22.6)	2 (2.4)
	homemaker	2 (3.2)	7 (8.3)
	unemployed	4 (6.5)	5 (6.0)
	missing	3 (4.6)	27 (24.3)
	P-value**	< 0.001	

n: number of observations for this outcome
* P-values based on Wilcoxon rank sum test with continuity correction
** P-values based on Pearson's Chi-squared test

Table 1: Core baseline sociodemographic data

Variable	Statistic	Galcanezumab	Topiramate
Sample size	N	65	111
Monthly migraine days (MMDs)	mean	13.2	9.7
	standard deviation (sd)	6.5	4.8
	missing	0	0
	P-value*	< 0.001	
Monthly headache days (MHDs)	mean	14.4	11.1
	sd	7.4	5.5
	missing	0	0
	P-value*	< 0.01	
Type of migraine (based on MMDs|MHDs) n (percent)	CM	25 (38.5)	21 (18.9)
	HFEM	26 (40.0)	48 (43.2)
	IFEM	14 (21.5)	42 (37.8)
	P-value**	< 0.01	

* P-values based on Wilcoxon rank sum test with continuity correction
** P-values based on Pearson's Chi-squared test
n: number of observations for this outcome; sd: standard deviation
IFEM (Intermediate-frequency episodic migraine) 4-7 MMDs
HFEM (High-frequency episodic migraine): 8-14 MMDs and < 15 MHD
CM (chronic migraine): 8-14 MMDs and at least 15 MHDs or at least 15 MMDs

Table 2: Core baseline clinical characteristics

Conclusion: This real-world study revealed similarities and differences between patient groups receiving galcanezumab and the conventional prophylactic treatment topiramate when including patients with ≥4 MMDs. Future studies on comparative real-world effectiveness will need to take these characteristics into account.

Disclosure: M. K. has received consulting fees from advisory board/speaker/other activities for Janssen-Cilag and Novartis. H. I.-W. has received consulting fees from advisory board/speaker/other activities from Novartis, TEVA, Allergan/Abbvie, and Eli Lilly and Company. F. R. is an employee of NeuroTransData GmbH, V. T. and S. P. are employees of PricewaterhouseCoopers AG, and J. K., I. S., and N. L. are employees of Eli Lilly and Company. M. K., V. T., H. I.-W., S. P., and F. R. performed the work under contract with Eli Lilly and Company, who provided funding for the study.

EPO-326

A more than unusal wearing-off effect in antiCGRP monoclonal antibody: A multicenter prospective study with Fremanezumab

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Background and aims: The presence of a wearing-off effect is a determining factor in the efficacy of antiCGRP monoclonal antibodies. Post-hoc analyses of pilot studies suggest a low rate of wearing-off with galcanezumab and fremanezumab compared to erenumab. Our objective is to analyze the presence of fremanezumab-related wearing-off in a real-life scenario.

Methods: This was a multicenter, prospective, open label study in a cohort of patients receiving fremanezumab monthly for high-frequency episodic migraine (HFEM) or chronic migraine (CM). Baseline clinical and demographic characteristics were collected. Migraine diaries were analyzed throughout a 3-month period. Wearing-off was defined as the occurrence of at least 50% of the total migraine days in the last week of the month, as compared to the first three weeks.

Results: 142 patients were recruited from 4 different centers. A total of 42 patients (32.39%) showed a wearing-off effect. Mean age was 47.5 (SD 12.01). 122 were women (85.92%). 26 (18.3%) reported aura. 109 (76.76%) were CM whereas 33 (23.2) were HEFM. Mean previous preventive oral treatments was 6.62 (SD 2.56). 100% of patients had been on onabotulinumtoxinA. History of migraine lasted 26.14 (SD 13.55) years with high-frequency (>8) phase of 7.65 (SD 7.56) years. 26 (18.3%) patients had migraine with aura. 58 (40.84%) were predominantly unilateral migraine.

Conclusion: According to the data, 1 out of 3 patients exhibited a wearing-off effect. Since this is a short study, long studies are required to propose a change in posology to every three weeks.

Disclosure: Honoraria for participation in oral presentations from Abbvie, Lilly, and Teva.

EPO-327

The economic and personal burden of cluster headache. A controlled cross-sectional study.

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Background and aims: Cluster headache is a less-prevalent primary headache but is overrepresented with regards to use of healthcare and social services. Insight into the socioeconomic impact is required.

Methods: We investigated both the personal and societal burden and cost in 400 patients with well-classified cluster headache (ICHD-criteria) and 200 sex- and age matched controls. All participants completed a cross-sectional questionnaire and semi-structured interview.
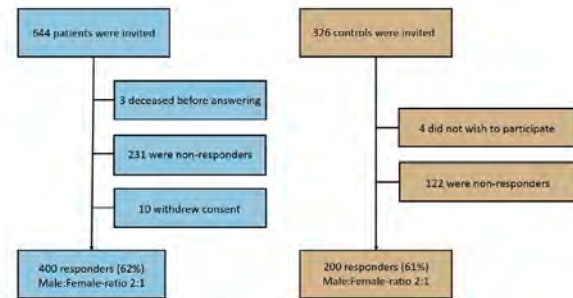
Flowchart of inclusion.

Results: Patients with chronic cluster headache constituted 146 out of 400 (37%). Overall, restriction in personal and/or professional life was reported by 94% of patients during attack periods. In remission, nine times as many episodic patients rated their health as poor compared to controls (9% vs 1%, p=0.002). For chronic patients, the odds of rating health as good were ten times lower compared to controls (OR:10.10, 95% CI: 5.29–18.79. p<0.001) and three times lower compared to episodic patients in remission (OR:3.22, 95% CI: 1.90–5.47, p<0.001). The mean direct annual costs amounted to 9,158 € and 2,763 € for chronic and episodic patients, respectively (p<0.001). We identified a substantial absence from work resulting in an indirect cost of 11,809 €/year/chronic patient and 3,558 €/year/episodic patient.
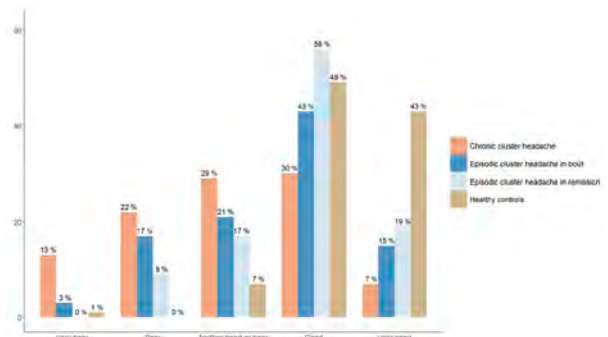
Self-rated health among patients with cluster headache and controls
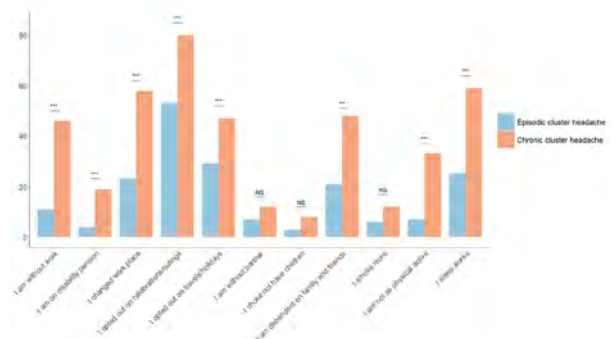
Negative impact of cluster headache on professional, social and family life.

Conclusion: Cluster headache has a negative impact on personal-life, self-perceived health, and societal cost. Patients with the chronic variant are vastly more burdened. Patients with the episodic form were still markedly affected during the remission period. This study highlights the need for more effective therapy to lighten the burden on patients and society.

Disclosure: Dr. Petersen: Current sub-investigator in trial for Lundbeck. Previous sub-investigator in trials for Eli-Lilly, and CCH pharmaceuticals. Dr. Lund reports no disclosures. Dr. Snoer: Current sub-investigator in trial for Lundbeck. Previous sub-investigator in trial for Eli-Lilly. Dr. Jensen: Lectures for Pfizer, Eli-Lilly, Merck, TEVA, Novartis, Lundbeck and Allergan. Investigator in clinical trials with Eli-Lilly, Novartis and Lundbeck. Dr. Barloese reports no disclosures.

EPO-328

Acute treatment for trigeminal neuralgia severe exacerbation – an unmet need in the emergency department

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Background and aims: Trigeminal neuralgia (TN) is characterized by recurrent and intense pain episodes in the trigeminal distribution, usually too brief to allow acute abortive treatment. Nevertheless, some patients experience severe exacerbation in pain frequency and/or intensity requiring acute treatment in the emergency department (ED).

Methods: Retrospective review of clinical records of adult TN patients admitted to the ED of a university hospital during a period of twelve years.

Results: 139 episodes of TN exacerbation treated in the ED were included. Opioids were the most prescribed drugs (78% of episodes), followed by nonsteroidal anti-inflammatory drugs (42%), corticosteroids (21%), phenytoin infusion (18%) and lidocaine infusion (6%). Of the 108 cases treated with opioids, 78 (72%) required additional drugs for pain management. When discharged from the ED, pain relief status was reported in 99 patients: complete in 73%, partial in 22% and absent in 5% (all referred to a pain specialist). 63 of those patients needed more than one drug to achieve at least partial pain control.

Conclusion: In our sample, opioids were the preferred treatment option for TN severe exacerbation, despite not being recommended in this setting and requiring additional drugs to control the pain. Lidocaine and phenytoin infusions, both described as highly effective in other studies, were infrequently used. Management by non-specialized teams without expertise in TN could explain these results.

Disclosure: The authors report no conflict of interest.

EPO-329

Long-term grey matter structural changes in the transition from chronic migraine to episodic migraine

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Background and aims: The objective was to assess grey matter longitudinal changes in patients with chronic migraine (CM) who reverse to episodic migraine (EM) compared to those who do not reverse.

Methods: High-resolution 3D brain T1-weighted Magnetic Resonance Imaging data were obtained twice from migraine patients. The first acquisition was performed immediately after the first visit to the Headache Unit, before taking preventive treatments. The second timepoint was at least three years after the first acquisition. From the longitudinal pipeline of FreeSurfer (v6.0), the mean values of cortical thickness, surface area and grey matter volume of 68 cortical, 14 subcortical regions and the cerebellum were extracted. Longitudinal changes between patients with CM and those who reversed to EM were assessed with linear mixed-effects models, setting $p < 0.05$ (false discovery rate corrected) as threshold for statistical significance.

Results: 22 patients were included, and 10 of them (45.5%) reversed to EM. No statistically significant differences of age (42.0±9.0 years) and sex (21 women, 95.5%) were found between patient groups. Higher statistically significant values of the three parameters in patients who reversed to EM were found in the pericalcarine, parietal, orbitofrontal cortex, and amygdala (Table 1, Figure 1). In contrast, lower values were detected in the cingulum, caudal middle frontal cortex, cerebellum, caudate nucleus and pallidum (Figure 2). In the insula, higher thickness but lower area was appreciated in patients who reversed.

Region	Thickness		Surface Area		Grey matter volume	
	Left	Right	Left	Right	Left	Right
Caudal middle frontal			↓			
Lateral orbitofrontal			↑	↑		
Medial orbitofrontal				↑		
Superior parietal	↑					
Pericalcarine		↑				
Paracentral				↓		
Isthmus cingulate		↓				
Posterior cingulate			↓		↓	↓
Rostral anterior cingulate					↓	
Insula		↓	↑			
Cerebellum	NA	NA	NA	NA		↓
Caudate	NA	NA	NA	NA		↓
Pallidum	NA	NA	NA	NA		↓
Amygdala	NA	NA	NA	NA		↑

NA = not applicable. ↓ = lower values in patients who reversed to episodic migraine. ↑ = higher values in patients who reversed to episodic migraine

Table 1: Grey matter regions with longitudinal changes in patients with chronic migraine who reversed to episodic migraine compared to patients with persistent chronic migraine.
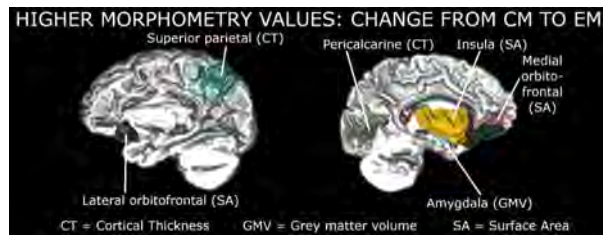
Figure : Grey matter regions with statistically significant higher values of cortical thickness, surface area or grey matter volume in patients with chronic migraine (CM) who reversed to episodic migraine (EM) compared to patients with CM.

Figure 2: Grey matter regions with statistically significant lower values of cortical thickness, surface area and/or grey matter volume in patients with chronic migraine (CM) who reversed to episodic migraine (EM) compared to patients with CM.

Conclusion: Patients with CM who reverse to EM present distinct patterns of increased and decreased morphometric parameters propagated in the orbital frontal cortex and the cingulum, respectively.

Disclosure: Nothing to disclose.

EPO-330

Descriptive analysis of response to Galcanezumab in 7 patients with refractory cluster headache

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Background and aims: Cluster headache is the most frequent trigeminal autonomic headache. It is characterized by facial unilateral painful attacks associated to autonomic features and important restlessness and psychomotor agitation. Duration of episodes is among 15 and 180 minutes and they occur grouped in daily or weekly periods, usually with a nocturn predominance. It is more frequent among men and it has an important impact on the quality of life of patients. It is known that in the pathophysiology of pain, levels of calcitonine-gene related peptide (CGRP) are high in serum and CSF. Among anti-CGRP monoclonal antibodies, Galcanezumabas been included in guidelines of clinical practice as a possible third line therapy according to two published clinical trials.

Methods: Descriptive prospective study about clinical response to Galcanezumab by compassionate use in 7 patients with refractory cluster headache.

Results: Five patients (7.4%) had a diagnosis of chronic cluster headache and two of episodic cluster headache (28.6%). Average of previous treatments was 5.58 ($\pm$1.9). Mean number of headache attacks before treatment with Galcanezumab was 3.6 per day ($\pm$1.57). After treatment with Galcanezumab, patients presented an average of 1.51 headache attacks per day ($\pm$2.03).

Conclusion: The analysis of response to Galcanezumab in patients diagnosed with cluster headache shows favorable results due to reduction of at least 50% of headache attacks in 85% of the patients.

Disclosure: Nothing to disclose.

EPO-331

Anti-CGRP treatment in difficult-to-treat chronic migraine patients

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Background and aims: Calcitonin gene-related peptide (CGRP) antagonists have proven efficacy in the prevention of Episodic (EM) and Chronic Migraine (CM). Real life evidence in resistant and refractory migraine is still poor.

Methods: The present study was conducted at the Headache Centre of Spedali Civili of Brescia. Patients were treated with Erenumab 140 mg every 4 weeks. Inclusion criteria were: history of migraine for at least 12 months, ≥8 mean migraine days per month (MMD) for at least 3 months, ≥8 previous prophylactic failures. Data about outcome, analgesics consumption and disability (Migraine Disability Assessment Score Questionnaire – MIDAS; Headache Impact Test – HIT-6) were collected.

Results: 76 patients with CM and medication overuse (MO) were enrolled. Baseline clinical and demographic characteristics are presented in Table 1. A significant reduction from baseline to week 4, 12, 24 and 48 in MMD, analgesics consumption, pain intensity and MIDAS score per month was found (Table 2). The percentage of non-responders (<30% MMD reduction), partial-responders (<50%) and responders (>50%) at week 4, 12, 24 and 48 is shown in Figure 1. When comparing our cohort to patients who had previously failed 3 to 5 previous prophylaxis no significant differences in the percentage of responders were found.

	SUBJECTS (n=76)
AGE, years (mean, SD)	48.2 (9.1)
FEMALE, number (%)	62 (81.6%)
DISEASE DURATION, years (mean, SD)	28.5 (10.1)
PREVIOUS PROPHYLAXIS, number (mean, SD)	8.6 (1.8)
TRIPTAN RESPONSE, number (%)	59 (77.6%)
MEDICATION OVERUSE, number (%)	76 (100%)

Table 1: subjects baseline demographic and clinical features.

	BASELINE	WEEK 4	WEEK 12	WEEK 24	WEEK 48	p
MMD Mean (SE)	20.5 (1.2)	10.2 (1.5)	8.7 (1.1)	9.4 (1.1)	7.6 (0.9)	<0.0001
SEVERE MMD Mean (SE)	12.9 (1.1)	5.5 (0.9)	3.5 (0.6)	4.6 (0.7)	3.2 (0.7)	<0.0001
TOTAL ANALGESICS/MONTH Mean (SE)	20.9 (1.6)	11.3 (2.2)	9.1 (1.4)	10.3 (1.5)	7.2 (0.9)	<0.001
NSAIDs/MONTH Mean (SE)	6.9 (1.8)	3.9 (1.4)	3.3 (0.7)	4.3 (1.3)	2.8 (0.6)	NS
TRIPTANS/MONTH Mean (SE)	13.1 (1.6)	6.6 (1.9)	5.2 (1.4)	5.5 (1.1)	4.1 (0.6)	<0.001
PAIN INTENSITY – NRS Mean (SE)	7.5 (0.1)	6.0 (0.3)	5.7 (0.4)	6.2 (0.3)	5.5 (0.3)	<0.001
MIDAS Mean (SE)	104.1 (17.9)	N/A	25.2 (4.7)	31.2 (7.9)	17.2 (5.6)	=0.004
HIT-6 Mean (SE)	66.6 (2.8)	N/A	58.2 (1.8)	57.7 (2.7)	55.7 (2.4)	=0.05

Table 2: between-subjects ANOVA results documenting a statistically significant reduction in MMD, analgesics consumption, pain intensity and disability.
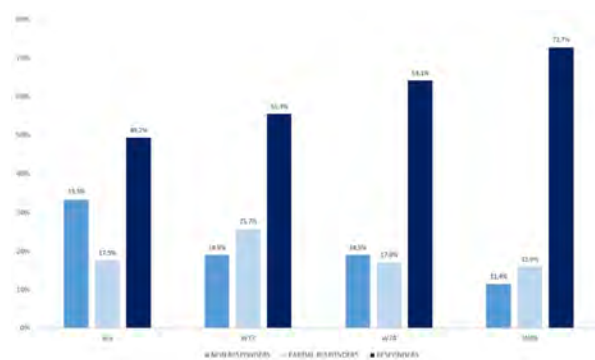
Figure 1: responders rates at week 4, 12, 24 and 48 of treatment

Conclusion: The data confirm Erenumab efficacy in difficult-to-treat patients, with a long-standing history of treatment failure. Nearly 50% of patients documented a significant improvement from the first cycle. Moreover, Erenumab was as effective in difficult-to-treat patients as in those who only failed up to 5 prophylactic treatments.

Disclosure: Nothing to disclose.

EPO-332

Fremanezumab in the cluster headache treatment.

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Background and aims: Cluster headache (CH) is a disorder that is difficult to treat. A monoclonal antibody against calcitonin gene-related peptide (CGRP), galcanezumab, is currently used as a pathogenetic therapy for episodic cluster headache. It has not yet been registered in Russia, but the monoclonal antibody fremanezumab, which mechanism of action is similar to galcanezumab, is available for purchase by prescription. Thus, it may potentially be effective for cluster headache treatment.

Methods: Ten patients with episodic and chronic cluster headaches were referred to a tertiary headache center. They did not have a positive effect after verapamil treatment and had contraindications or poor tolerance to alternative prophylactic therapy for cluster headache. Therefore, the patients were offered treatment with fremanezumab. The medication was administered to patients on day 1 or 2 of the beginning of their cluster period (in patients with episodic CH) at a dose of 225 mg subcutaneously.

Results: Seven of ten patients (all of them had episodic cluster headache) responded to fremanezumab therapy: the cluster period ended an average of 5.2±2.8 days after injection instead of 44.8±26.6 days (a reduction of 87.1%). The 3 patients who did not respond to therapy had chronic cluster headache.

Conclusion: In our study, we cannot exclude the placebo effect. However, the non-effectiveness of anti-CGRP therapy in patients with chronic cluster headache compared to episodic cluster headache may be due to the fact that the CGRP levels in chronic cluster headache patients are usually lower.

Disclosure: Nothing to disclose.

EPO-333

Cluster headache patients' phenotypes according to their verapamil response

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Background and aims: Cluster headache is one of the primary headaches characterized by high intensity, presence of associated autonomic symptoms and/or agitation. Currently, there are several options for cluster headache prophylactic therapy, with verapamil as the golden standard.

Methods: A retrospective and prospective analysis of 23 patients referred to a tertiary headache center was carried out. A structured interview focused on headache intensity, frequency, cluster period duration in weeks, response to verapamil treatment was perfomed.

Results: We found that verapamil responders' average age was 33.2±6.4 years old compared to non-responders, whose average age was 42.7±9.8 (p=0.04). Verapamil responders had shorter attack duration (108±51.3 minutes vs. 121±92.0 minutes (p=0.8)), less intense pain on the Numerical Pain Rating Scale (9.3±0.8 vs. 9.9±0.4 (p=0.1)), more attacks per day (3.0±2.1 vs. 1.7±1.5 (p=0.2)), agitation (67% vs. 17% (p=0.04)). Migrainous signs were more prominent in non-responders to verapamil: photophobia in 100% (non-responders) vs. 33% (p=0.006)) and phonophobia 71.4% vs. 33% (p=0.1). Also, patients who did not respond to therapy had higher frequencies of ptosis 71% and 16% (p=0.04), redness of the eye (86% vs. 50% (p=0.1)), lacrimation (100% and 50% (p=0.04)), rhinorrhea (100% and 50% (p=0.04))

Conclusion: Our study is the first phenotypic description of patients with cluster headache who responded or did not to verapamil treatment. The differences between attack duration, intense pain on the Numerical Pain Rating Scale, number of attacks per day, presence of phonophobia, and eye redness were statistically insignificant. More patients need to be investigated for a more detailed description and accurate data.

Disclosure: Nothing to disclose.

Miscellaneous 1

EPO-334

Training Of The Emergency Medical Center Doctors And Paramedics in Kyrgyzstan

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Background and aims: In the framework of the Roadmap for Stroke implementation in Kyrgyzstan the educational resource should include personnel's training on the prehospital level. We aimed to train the EMS specialists in FAST algorithm and NIHSS use for the improvement of the accurate stroke diagnostics.

Methods: In the 6-month period three vascular neurologists conducted 30 on-site and online trainings on FAST and NIHSS for EMS specialists and led 12 video seminars on recognition of stroke, neurovisualization and prehospital stroke management in Bishkek, Kyrgyzstan. After the 2-month period there were follow-up training sessions to assess the doctors' and paramedics' accuracy in NIHSS filling out.

Results: 91 doctors and 68 paramedics participated in stroke recognition trainings. 535 medical records of stroke patients were analyzed by stroke experts. We found out that stroke patients in prehospital settings are mostly examined by medical doctors (95,7%) and the most – by a neurological crew (78,5%), less by reanimation (11,2%), cardiological and paramedic crews. In 73,3% of stroke cases EMS specialists correctly evaluated a patient's neurological deficit using the NIHSS scale. Among the mistakes in filling the NIHSS scale were incorrect evaluations of patients with impaired consciousness, wrong assessment of cerebellar lesions, and incorrect calculation of total NIHSS scores.
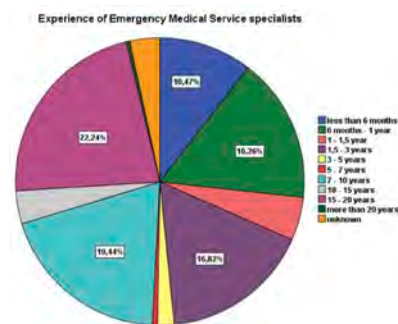
Experience of Emergency Medical Center specialists

Conclusion: We succeeded in implementing NIHSS evaluation of each stroke patient by an internal order of the EMS after an effective set of trainings. NIHSS use on the prehospital level will shorten the "onset-to-door" time in stroke patients and their selection for the future thrombolytic therapy.

Disclosure: Nothing to disclose.

EPO-335

Impact of Atrial Fibrillation on Outcomes in Acute Stroke Patients receiving Endovascular Treatment: A Meta-Analysis

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Background and aims: Atrial fibrillation (AF) is a significant risk factor for ischemic stroke and is linked to an increased risk of poor outcomes following an acute ischemic stroke (AIS). The meta-analysis sought to investigate the impact of AF status on clinical and safety outcomes in AIS patients receiving endovascular thrombectomy (EVT).

Methods: Studies with AIS patients treated with EVT and data stratified according to AF status (AF vs no-AF) were included. Relevant data on clinical outcomes, such as functional outcome at 90 days, mortality at 90 days, angiographic reperfusion, symptomatic intracerebral hemorrhage (sICH), hemorrhagic transformation (HT), and onset to reperfusion therapy time (OTRT), were collated and analyzed. Random-effects meta-analysis was performed to test the association of AF with clinical outcomes.

Results: Overall, 11,285 AIS patients from 11 studies were included. AF was significantly associated with worse 90-day functional outcome (OR 0.71, 95% CI 0.56–0.91; p=0.007) and worse angiographic reperfusion (OR 5.11, 95% CI 1.04–25.22; p=0.045), increased mortality (OR 1.63, 95% CI 1.44–1.84; p<0.0001), increased rates of sICH (OR 1.24, 95% CI 1.03–1.50; p≤0.024) and ICH of any cause (OR 1.69, 95% CI 1.34–2.13; p<0.0001). No significant difference in OTRT was observed between AF vs non-AF cohorts.

Conclusion: AF is significantly associated with worse clinical and safety profiles in AIS patients undergoing EVT, however, the difference in demographic factors between cohorts with and without AF may play a factor. These significantly worse outcomes suggest the need for targeted stroke pathways for patients with AF and the need for AF (pre-and/or in-) hospital screening.

Disclosure: Nothing to disclose.

EPO-336

Neurological manifestations associated with SARS-CoV-2 infection in children

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Background and aims: Neurological manifestations are found in more than 1/3 of cases of SARS-Cov-2 infection. Actually acute epileptic seizures and Epileptic Status (SE) in children currently demonstrate a high mortality rate (between 5% and 39%) in combination and post-infection with SARS-CoV-2.

Methods: To estimate the prevalence of the association of neurological manifestations, including acute seizures and status epilepticus (SE) after infection with Covid-19 in children.

Results: Within this group of children neurological recurrences during and post-SARS-CoV-2 was as follows: 30 (63.8%) represented in-hospital onset, whereas 12 (25.5%) had outpatient onset, and 5 (10.6%) presented with unclear onset. Neurological symptoms consistent with SE was diagnosed in (31.2%), whereas other frequently reported symptoms were hypo/anosmia (11.7%), encephalopathies (9.3%), stroke (5.6%), hyperkinesia (5.6%), irritability (27.8%), cognitive impairment (22.2%), and asthenia (18.7%). EEG findings and imaging data correlated with cerebral distress (r=0.62), (r=0.78), respectively. No significant difference was noticed between the recurrence of in-hospital (p>0.01) and out-of-hospital SE (p>0.02).

Conclusion: Although a possible association between SE and Covid-19 has been reported, the neuroinvasive and neurotropic properties of SARS-CoV-2 are insufficiently elucidated. The cytokine storm and hyperactivation of immune cells lead to secondary dysfunction in CNS with subsequent occurrence of neurological sequelae.

Disclosure: Nothing to disclose.

EPO-337

Acute Motor Axonal Neuropathy presenting as Person-in-a-Barrel syndrome

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Background and aims: Person-in-a-barrel syndrome (PIBS) is clinically characterized by brachial diparesis, with preserved cranial and crural muscle strength. It is a rare neurological syndrome most commonly caused by bilateral and symmetric injury of the motor neurons that control the upper limb movements, including bilateral injury to the brain hemispheres, brainstem, cervical spinal cord, brachial plexus, or peripheral nerves.

Methods: N/A

Results: A 70-year-old male patient with a history of hypertension, dyslipidaemia and hyperuricemia was admitted with an acute and rapidly progressive (10 days of evolution) bilateral upper limb weakness. The patient denied respiratory or gastrointestinal symptoms, fever or recent cervical trauma/pain. Two weeks earlier he was given the first dose of the Pfizer-BioNTech™ vaccine for COVID-19. The neurological examination revealed severe brachial diparesis and generalized hyporeflexia. Ancillary testing revealed positive serum anti-GM1 and GD1b antibodies. The PCR for SARS-CoV-2 was negative (with positive serum T-Spike antibodies). CSF analysis and Brain/Spinal MRI were normal. The electromyography and nerve conduction studies disclosed diffuse motor conduction blocks in the upper extremities, ultimately fulfilling criteria for Acute Motor Axonal Neuropathy (AMAN) with reversible conduction failure. Intravenous human immunoglobulin (0.4g/kg/day, 5 days) and rehabilitation were started, with subsequent motor improvement.

Conclusion: To our knowledge this is the first case of AMAN presenting as PIBS. We intend to highlight that AMAN should be added to the list of causes of this syndrome. The role of the COVID-19 vaccine in this case remains uncertain, and it is not possible, at this moment, to infer causality.

Disclosure: I have nothing to disclose.

EPO-338

Predicting the Quality of Clinical Performance in Neurology Residents

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Background and aims: It is very difficult to predict how well a medical student, still in university, will develop as a competent or even superior clinical neurologist during Neurology residency.

Methods: We collected data available at the time of application for Neurology residency positions and sought factors that could correlate with clinical excellence during residency, including: age, US Medical Licensing Examination ("step") scores; performance evaluations in university Internal Medicine, Neurology, and overall rotations; perceived reputation of the student's university; research experience, publications, and other factors.

Results: Data were collected covering 211 Neurology residents who began residency from 2008 until 2019 and completed residency training by June 2021 in two Neurology residencies affiliated with the same university. For this study, being chosen as chief resident in the final year of residency was the 'favorable' outcome. It was correlated with (in order) superior performance on the university Neurology rotation, on clinical rotations overall, and on Internal Medicine; university reputation; and least among these, examination scores. Few correlations were particularly strong.

Conclusion: Several factors correlate with clinical excellence in Neurology residency, but few have very strong correlations. Prediction of resident performance remains complicated and challenging. Terminology and discussion will be adapted for suitability to European and other medical education systems.

Disclosure: Drs Drislane and Milligan have no disclosures related to this abstract.

EPO-339

ALAMEDA – a new dawn in predicting brain disease aggravation

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Background and aims: The care of patients with brain disorders is complex and manifestations can seriously impair the quality of life of patients and their caregivers. ALAMEDA is a research project, involving 15 international partners, encompassing three pilot studies in 3 sites, one for each disease (Greece for Parkinson, Italy for Multiple Sclerosis, Romania for Stroke). The objective of ALAMEDA is to develop innovative methods and technologies for patient monitoring, in the case of neurological diseases which require a constant evaluation of the evolution due to variability of symptoms and high possibility of worsening or relapsing.

Methods: Using a multi-structured approach by engaging the patients, the caregivers and the medical practitioners in the research mission, we created Local Community Groups (8 members from Greece, 12 members from Italy, 12 members from Romania) and applied the Shared Decision-Making model by organizing round-table interviews and circulating questionnaires.

Results: The main subjects of discussion were regarding: – patient reported outcomes submission options – primary use of the Chatbot – methods to view data – device type preferences – localization monitoring Considering all of the above, we designed a model that can help predict the aggravation of neurological disease using smart devices (Smart watch, Smart bracelet, Shoe pressure sensors, Belt sensors, Sleep Monitoring Mattress, Smartphone/Tablet Camera).

Conclusion: We decided to present this project in order to highlight the importance of a personalized rehabilitation treatment and of an improved management of a clinical status likely to aggravate in patients with Parkinson's disease, Multiple Sclerosis and Stroke.

Disclosure: Nothing to disclose.

EPO-340

Small fiber neuropathy following SARS-COV-19 vaccination. A case series

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Background and aims: Small fiber neuropathy (SFN) is a polymorphous disease affecting thin nervous fibers conducting temperature and pain sensations and involved in autonomic transmission. Etiology is diverse and remains elusive in 70% of cases.

Methods: We describe a case series of 6 patients who developed symptoms of SFN following SARS-COV-19 vaccination. Neurologic examination was normal whilst paraclinical results were consistent with SFN. Confirmation by skin biopsy was obtained in 4 cases.

Results: Six patients, 5 female and 1 male, ages 31, 34, 39, 42, 44 and 62 years, consulted our department with intense pain and numbness involving the arms and legs 2 to 15 days following SARS-COV-19 vaccination. Neurologic examination was normal. A preliminary diagnostic protocol comprising autoimmune, metabolic, infectious and inflammatory panel, cerebral and spinal cord magnetic resonance imaging and electromyography was normal. Functional neurophysiologic testing showed reduced activation of fibers involved in sweat gland control indicating SFN. Skin biopsy of distal calf and thigh in 4 patients, three female and one male, showed rarefaction of thin intraepidermal nerve fibers in a non length dependent manner, allowing for a diagnosis of SFN.

Conclusion: Whereas autoimmune, infectious, metabolic, toxic and genetic causes are well described in SFN, evidence of possible association with vaccination is confounding. Given their small caliber and richness of surface antigens, small nervous fibers are vulnerable to a wide spectrum of disease. Immunologic factors intervening on a predisposing substrate could be a hypothesis for the mechanism involved in development of SFN following SARS-COV-19 and possibly other vaccination.

Disclosure: Nothing to disclose.

EPO-341

Burst suppression and intravenous anesthetic antiseizure drugs in patients with refractory status epilepticus

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Background and aims: The International League Against Epilepsy (ILAE) recommends to treat refractory status epilepticus (rSE) with intravenous anesthetic antiseizure drugs (IVAAD) to achieve a burst attenuation/suppression (BS) EEG pattern. This study investigates duration of BS and IVAAD in patients with rSE.

Methods: Retrospective analysis between 1 January 2011 and 31 December 2019 of adult patients with rSE receiving IVAAD in a Swiss academic tertiary medical care center. The first two minutes of each one-hour-epoch EEG were analyzed for BS. Continuous EEG (cEEG) was defined as recordings longer than one hour. BS was defined according to the American Clinical Neurophysiology Society's (ACNS) Standardized Critical Care EEG Terminology 2021.

Results: A total of 171 patients (74 female, median 64 years) were included with 130 (76%) receiving midazolam (MDZ), 85 (50%) propofol (PRO), 6 (4%) thiopental (TP) and 1 (0.6%) pentobarbital (PB) as IVAAD. All patients treated with TP or PB received MDZ or PRO beforehand. The median IVAAD duration was 71.5h for MDZ, 21.1h for PRO, 88.2h for TP and 442.5h for PB. In 144 (84%) patients EEG was performed, thereof 115 (67%) with cEEG with a median recording duration of 17.2h. While EEG suppression pattern during IVAAD not meeting the ACNS BS criteria was recorded in 25 patients (15%), BS was documented in 33 (19%) for a median 30% of EEG recordings.

Conclusion: Our results underscore the challenges of achieving BS patterns during IVAAD treatment. Further analysis of clinical outcome in relation to IVAAD and BS are undergoing and will be presented at the meeting.

Disclosure: Nothing to disclose.

EPO-342

Obstructive sleep apnoea in patients with Guillain-Barré syndrome

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Background and aims: Sleep apnoea (SA) has been proved a risk factor of cardiovascular and metabolic diseases. The relation of SA and neuromuscular disorders has not been investigated enough. We have focused on monitoring of possible sleep disorders in a patient with Guillain-Barré syndrome (GBS) with the aim to determine the type and severity of SA in and to assess motor disability in the acute state and 3 months after disease beginning.

Methods: A prospective monocentric study of patients GBS patients was performed. All subjects have been examined with the polysomnography in the first 3 day after admission (V1) and 3 months later (V2). Movement deficit was assessed using the GBS disability scale and muscle weakness scale (MRC) at V1 and V2. Subjective increased daytime sleepiness was assessed with the Epworth Sleepiness Scale.

Results: Twelve patients have been enrolled from January to December 2020 (9 men, mean age 51±17.9 years) and underwent polysomnography on V1. Out of those obstructive SA has been found in 11 subjects (91.7%). The study has been completed with V2 measurements in 8 patients with persistent SA. Although there was a significant improvement in the GBS disability (p=0.016) and the MRC scale (p=0.008), the severity of SA correlated to MRC showed significant progression (p=0.027) at V2.

Conclusion: Obstructive SA is present in up to 90% of patients with GBS in the acute period. The high incidence of sleep apnoea in GBS suggests the inclusion of polysomnography in the diagnostic protocol.

Disclosure: Nothing to disclose.

EPO-343

Coasting in Taxane-induced Peripheral Neuropathy in Patients with Breast Cancer: A Systematic Review.

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Background and aims: Taxane-induced peripheral neuropathy (TIPN) is a common dose limiting adverse effect, that may be transient or become permanent after ended treatment. The taxane paclitaxel induces TIPN in 57–83% of patients treated. Case reports suggest, that the neuropathy may debut or progress after ended treatment, known as coasting, but little is known about the incidence. The aim of the review is to assess the incidence and severity of coasting in TIPN.

Methods: MEDLINE, Embase, clinicaltrials.gov and medrivx.org were searched using terms related to taxanes, adverse effects and breast cancer. Studies had to have a follow up of at least 3 months after end of treatment (EOT) and patients had to receive taxane in monotherapy. Additionally, studies had to be longitudinal and describe the neuropathy assessment method and timing.

Results: 16 studies met the eligibility criteria, with 4245 participants summarized. Of these, one study reported a coasting event in 14.3% (n=4) of patients. 8 studies reported no coasting events and 7 were unclear.

Conclusion: Few studies reported on coasting in TIPN. There may be several reasons for this. Among these are confounding factors, the choice of assessment methods and timing. More information is needed about coasting in TIPN to better characterize the neuropathies and aid in the development of interventions toward TIPN.

Disclosure: The work was conducted with a grant from The Lundbeck Foundation and during work on The CryoPac Project.

EPO-344

Vegetative nervous system reaction in the early period of stroke

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Background and aims: Disorder of autonomic regulation is one of the mechanisms for the implementation of cerebral damage, which leads to an increase in mortality in the acute period of stroke, the ANS plays a special role in the adaptive and trophic process. Assessment of the vegetative status of patient in the acute period of stroke is important to determine the beginning of rehabilitation of patients.

Methods: We examined 61 patients, who were in the intensive neurology departments of the TMA with diagnosis - stroke. All patients have been hospitalized in period of 11.2021–12.2021. We studied the hemodynamic parameters at rest and when changing position.

Results: The obtained results were systematized into 2 groups: 1: the results of patients without diabetes, 2: patients with diabetes. Based on the measurements of blood pressure, heart rate, respiratory rate, oxygenation at rest, the Kerdo index was calculated. In group 1: 52% –sympathicotonia prevailed, 38% – vagotonia, 10% – amphotonia. In group 2: 62.5% – sympathicotonia prevailed, 25% – vagotonia, 12.5% – amphotonia. After changing the position of the body, in group 1: 57% – sympathicotonia prevailed, 43% – vagotonia. Group 2: 50% – sympathicotonia, 50% – vagotonia.

Conclusion: High activity of the sympathetic nervous system was revealed in ischemic strokes, both with concomitant diabetes mellitus and without it. Cardiac arrhythmias are most common in right hemispheric brain lesions. With right hemispheric injuries, vagotonia is observed, and with left hemispheric injuries, which indicates the need to start early rehabilitation of patients with strokes.

Disclosure: Nothing to disclose.

EPO-345

Serial bedside Transcranial Doppler ultrasound in Comatose Patients after Out-of-Hospital Cardiac Arrest

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Background and aims: Early prediction of outcome in comatose patients after out-of-hospital cardiac arrest (OHCA) is challenging. Prognostication tools include clinical examination, biomarkers, neuroradiological and neurophysiological tests. We studied the association between transcranial doppler (TCD), biomarkers and outcome.

Methods: This was a sub-study of the prospective observational Norwegian Cardiorespiratory Arrest Study. Patients underwent standardized post resuscitation care, including target temperature management (TTM) to 33°C for 24 hours. TCD was performed at day 1, 3 and 5-7. Biomarkers NSE and S100B were measured at day 1, 3 and 7. Primary endpoint was cerebral performance category (CPC) at six months, dichotomized into good (CPC 1-2) and poor (CPC 3-5) outcome. We used linear mixed modelling time-series analysis.

Results: Of 139 TCD-examined patients, 81 (58%) had good outcome. Peak systolic velocity (PSV) in the middle cerebral artery was low during TTM, elevated after rewarming, continued to rise in patients with poor, but normalized in patients with good, outcome. This pattern differed between the outcome groups (p<0.001). At day 5–7, PSV was 1.0 m/sec (95% CI 0.9; 1.0) in patients with good outcome versus 1.3 m/sec (95% CI 1.1; 1.4) in patients with poor outcome. NSE-values at day 3 were associated with PSV, as were S100B values at day 1.
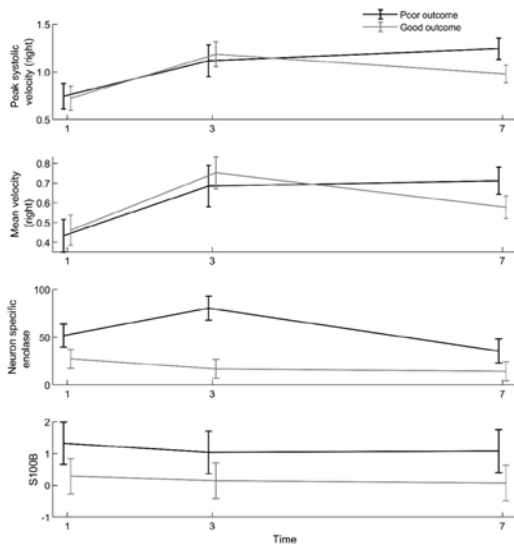
Time trend in PSV, MV, NSE and S100B; results of unadjusted linear mixed model
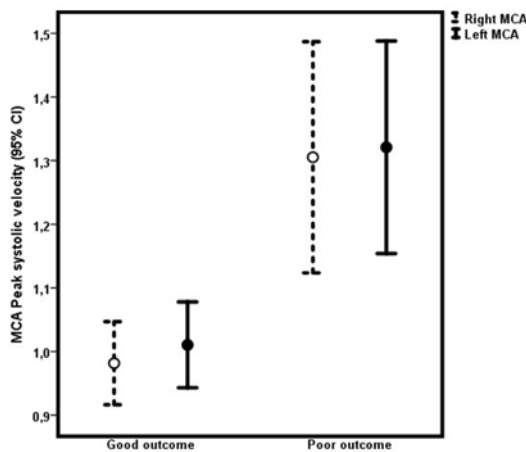
Relationship between day 7 peak systolic velocity and clinical outcome

Conclusion: Although TCD within the first 72 hours was not associated with outcome, the time course of PSV over the first week as well as elevated PSV at day 5-7 indicated poor outcome and may be interpreted as an indirect sign of serious brain injury.

Disclosure: The authors report no conflicts of interest related to the present study. The study had no additional outside funding beyond the ordinary employment of the authors and staff as noted under affiliations.

EPO-346

Multimodal Education in Advanced Parkinson's Disease Significantly Improves Identification and Treatment Decisions

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Background and aims: For patients with advanced Parkinson's disease (APD), device-aided therapies (DATs) have shown to decrease OFF time and improve quality of life. However, the advanced stage of PD is not uniformly defined and its identification can be challenging, leading frequently to late use of DATs when patients' quality of life has already deteriorated.

Methods: A series of 2 educational activities (a 30-min video panel discussion1 and interactive case-based activity2) were designed to address these gaps in APD care. The effects of education on knowledge and competence were assessed using a 3-question, repeated pairs, pre-assessment/post-assessment study design. One question for each activity assessed confidence. Differences from pre- to post-assessment were evaluated as described in the figures. The activities launched in March 2021 and, and data were collected through July 2021.

Results: Overall significant improvements were seen for both activities (Figure 1). Specifically, significant improvements were observed with regards to recognizing features of APD and selecting the most appropriate DAT for these patients (Figure 2). Regarding the latter, case-based education as compared with a panel discussion format was more effective. After participating, neurologists and primary care physicians had measurable improved confidence in identifying patients who have progressed to APD (31% and 49% respectively) and in choosing an appropriate DAT for APD (61% and 51% respectively).

Figure 1

CHANGES IN KNOWLEDGE & COMPETENCE AFTER PARTICIPATING IN EDUCATION ABOUT APD
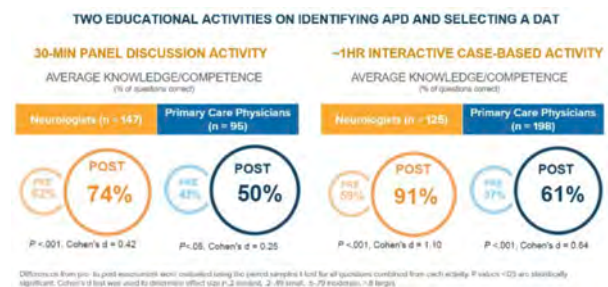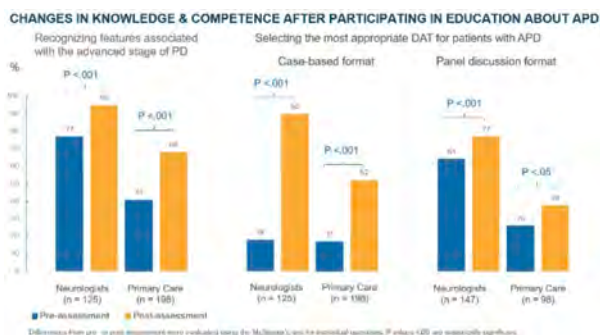
Figure 2

Conclusion: This study demonstrates the success of multi-format education in identifying and managing APD, especially using case-based clinical scenarios. Earlier and more effective intervention is likely to improve outcomes for patients.

Disclosure: SCRM, LF, and MV: None. AA: Advisor or consultant for: AbbVie; Bial; Kyowa Kirin; Neuroderm; Roche; UCB; Zambon. Speaker or a member of speakers bureau for: AbbVie; Bial; Boehringer Ingelheim; Zambon. Grant funding: Chiesi; Lundbeck; Roche.

EPO-347
Abstract withdrawn.

EPO-348
Acute corticosterone, delayed hippocampal damage and mortality after traumatic brain injury in rats: survivorship bias?

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Background and aims: Corticosterone (CS) is suggested to mediate both early excitotoxic hippocampal damage after traumatic brain injury (TBI) and further secondary neurodegeneration, putative morphological substrate for late TBI sequalae. Earlier we have demonstrated acute bilateral neuronal cell loss and microgliosis in the hippocampus and suggested an association of CS with this damage. In this study we aimed to assess delayed possibly CS-dependent hippocampal damage.

Methods: The study was performed on 51 male Sprague-Dawley rats, allocated to TBI, sham and control groups. TBI was modeled using lateral fluid percussion. CS blood levels were assessed by ELISA on day 7 before craniotomy and days 3, 7, and 3 months after TBI along with Nissl, Iba1 and GFAP staining on the last point.

Results: CS increased on day 3 after TBI, blood CS >860 nmol/L significantly raising risk of death. Morphological findings 3 months after TBI included thinning of cell layers in the dentate gyrus (DG) and CA3 area bilaterally ($p<0.02$), and in CA1 contralaterally ($p<0.016$), as well as neuronal cell loss in polymorph layer of the ipsilateral hippocampal DG ($p<0.04$) compared to sham and control groups. Unexpectedly, no associations of delayed hippocampal damage and acute CS elevation could be revealed.
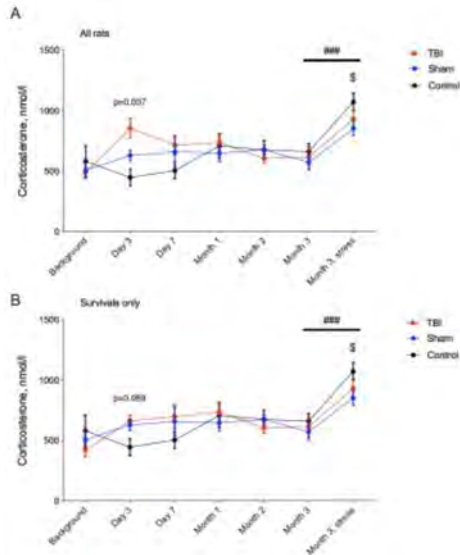
Figure 1: Corticosterone dynamic during 3 months after TBI in all rats (A) and in survived rats only (B). $ - p=0.090 (Kruskall-Wallis test), Sham vs. Control, p=0.098 ### - p<0.001, before and after forced swimming test, Wilcoxon test
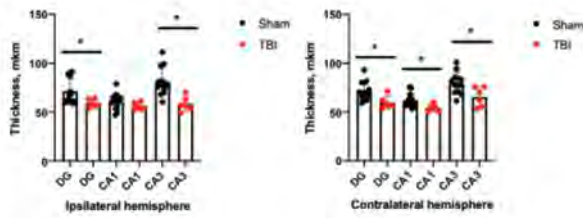
Figure 2: Thinning of cell layers in hippocampus 3 months after TBI. * - p
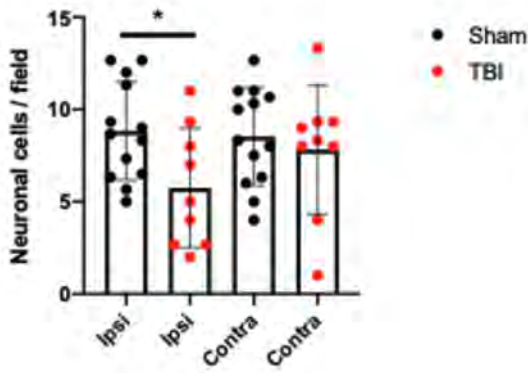
Figure 3: Ipsilateral neuronal cell loss in DG, polymorph layer, 3 months after TBI. * - p<0.05, Mann-Whitney test

Conclusion: Late TBI-induced hippocampal damage was not associated with acute CS elevation. However, early CS increase, a risk factor for high mortality, may cause preferential death in rats with severe hippocampal damage, thus masking putative associations of CS with alterations in the hippocampus since only survivors were counted.

Disclosure: Supported by RSF, grant № 22-25-00713.

Motor neurone diseases

EPO-349

Assessment of split-hand phenomenon in ALS with motor unit number index (MUNIX)

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Background and aims: Split-hand phenomenon in amyotrophic lateral sclerosis (ALS) is characterized by predominant wasting of abductor pollicis brevis (APB) and first dorsal interosseus (FDI) over the abductor digiti minimi (ADM) muscle. Its evaluation is generally based on the compound muscle action potential (CMAP) ratio recorded from these muscles. Our aim was to measure the split-hand phenomenon in ALS using motor unit number index (MUNIX).

Methods: 74 patients diagnosed with definite ALS (El Escorial criteria, 2,000) and normal findings on nerve conduction studies of the upper extremities were enrolled in the study: 31 patients (41.9%) had bulbar-onset ALS, while 43 patients (59.1%) presented with spinal-onset ALS. For the ALS group, disease duration, disease stage (King's College staging system), and ALSFRS-R score were measured. A subgroup of patients with ≤ 12 months since symptom onset was identified. The control group consisted of 36 healthy subjects with no neurological complaints. Both CMAP and MUNIX ratios ([APB+FDI]/ADM) were calculated for the ALS and the control groups.

Results: Both CMAP and MUNIX ratios were lower in ALS than in healthy controls ($p<0.05$). For the subgroup of patients with ≤ 12 months since symptom onset, CMAP and MUNIX ratios were lower than in the control group, yet this only reached statistical significance for the MUNIX ratio. The lowest MUNIX ratio was observed in patients with cervical-onset ALS. No correlations were found between electrophysiological data and clinical measures.

Conclusion: Our findings confirm that MUNIX can be a promising tool for evaluation of the split-hand phenomenon, serving as a potential electrophysiological biomarker of ALS.

Disclosure: The authors declare that there is no conflict of interest.

EPO-350

Multi-omics profiling of CSF from SMA type 3 patients after nusinersen: a multicenter retrospective study.

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Background and aims: Spinal muscular atrophy (SMA) is a neuromuscular disease caused by mutations in the SMN1 gene. Nusinersen is an antisense oligonucleotide that binds to the SMN2 gene resulting in the translation of a functional SMN protein. Intrathecal administration in SMA type 1 patients resulted in dramatic clinical improvement, while recent studies on SMA type 3 provided less striking, albeit encouraging, results. Here, we used high resolution mass spectrometry to assess proteome and metabolome in cerebrospinal fluid (CSF) from SMA type 3 patients treated with nusinersen, with the aim of identifying novel readouts of pharmacodynamics/response to treatment.

Methods: We included patients with a genetic and clinical diagnosis of SMA type 3. Nusinersen was intrathecally administered and CSF analyzed pre-treatment (T0) and after 2 years of follow-up (T1). CSF proteome and metabolome was measured using high resolution mass spectrometry analysis (nLC-HRMS) at UNITECH OMICs.

Results: A total of 27 proteins was found to be dysregulated between T0 and T1. Among them, Apoliprotein D was upregulated after treatment, and it is required for the maintenance of peripheral nerve function. Members of the semaphorin family, involved in axon guidance and dendritic growth, were also increased. Finally, the metabolome profiling revealed different expression of a spectrum of metabolites after treatment.

Conclusion: Together, these data confirm the utility of CSF multiomic profiling as pharmacodynamics biomarker for SMA type 3, while novel studies will be necessary to extend sample size and assess the pathogenetic role of identified molecules.

Disclosure: Nothing to disclose.

EPO-351

Search for potential surrogate biomarkers of upper limb function improvement in SMA adults treated with nusinersen

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Background and aims: SMA leads to progressive muscle weakness and atrophy. There is need for biomarkers of SMA severity/treatment response. Upper limb function is crucial for non-walkers. Aim: To evaluate biomarkers of treatment response in adult SMA patients.

Methods: 24 patients aged 20–66 years (4 SMA2, 20 SMA3, 50% women, 12 walkers), followed-up for 14 months (M14) of nusinersen treatment. Tests included abductor digiti minimi (ADM) CMAP amplitude and motor unit number estimate (MUNE), HFMSE, RULM, and serum creatinine. RULM was the endpoint to evaluate treatment effect.

Results: Baseline median values (range) were: for CMAP 4.5 mV(0.1–10.0), MUNE 61(22.2–144), HFMSE 33(0–64), RULM 34(2–37), creatinine 0.3 mg/dl (0.12–0.69). The patients with baseline HFMSE<35 points (13) had lower: serum creatinine 0.17 mg/dl (0.12–0.5), vs 0.445 (0.34–0.69), p 0.0008, CMAP 2.5 mV (0.1–8.4) vs 7.2 (4.6–10.4), p 0.0005, MUNE number 45.3 (5.06–80.4) vs 88.9 (27.7–144.45), p 0.01, as compared with patients with baseline HFMSE>35. Those who improved in RULM?1 point at M14 (50%), had lower baseline: HFMSE 5.5 vs 54 , p 0.0006, RULM 14.5 vs 37 , p 0.0003, serum creatinine 0.17 mg/dl vs. 0.44 ,p 0.01, CMAP 1.35 mV vs. 7.2 mV , p 0.001, MUNE 34.42 vs 88.78 , p 0.008. Walkers remained stable in RULM at M14 (p 0.04). CMAP, MUNE, creatinine, SMN2 copy number significantly correlated with baseline HFMSE, RULM.

Conclusion: ADM CMAP, MUNE, serum creatinine can serve as biomarkers of SMA severity. Severe non-ambulatory nusinersen-treated SMA adult patients demonstrate RULM improvement.

Disclosure: Anna Kostera-Pruszczyk Honoraria for advisory boards and speaking at educational events for Biogen, Novartis/AveXis, PTC and Roche, Principal Investigator for SUNFISH and JEWELFISH studies , Institutional grant support to Medical University of Warsaw from Biogen, POL-SMG-17-11166 (5BIOGEN01) 2. Anna Łusakowska Honoraria for speaking at educational events for Biogen and Roche, subinvestigator for SUNFISH, JEWELFISHand Ataluren(DMD) studies, Institutional grant support to Medical University of Warsaw from Biogen, POL-SMG-17-11166 (5BIOGEN01) 3. Anna Frączek Subinvestigator for SUNFISH 4. Katarzyna Pruszczyk none 5. Małgorzata Burlewicz Physiotherapist in SUNFISH 6. Zuzanna Gierlak-Wójcicka Physiotherapist in SUNFISH

EPO-352

Epidemiological study of amyotrophic lateral sclerosis in the province of Ourense (Galicia, Spain): period 2017-2021.

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Background and aims: Amyotrophic lateral sclerosis (ALS) is a fatal neurodegenerative disease of the motor neurons. ALS is characterized by clinical heterogeneity. About 5% of ALS is familial, with a Mendelian pattern of inheritance. Survival in ALS is dependent on phenotype, early respiratory failure, and nutritional status of patients. The objective of the present study was to know the survival of patients with ALS in our healthcare area.

Methods: Patients with ALS diagnosed between 01-Jan-2017 and 31-Dec-2021 were studied. The variables analyzed were: age, sex, clinical presentation, and time until the need for non-invasive mechanical ventilation, gastrostomy and wheelchair. The prevalence date was 31-Dec-2021. A Kaplan-Meier survival analysis was performed using the SPSS statistical program.

Results: Sixty-eight cases were registered (live patients were 29 (42.6%)). The population of the province of Ourense was 306,650 inhabitants (Jan 1, 2021). The mean incidence was 4.39 cases x100,000 inhabitants-year and the prevalence of 9.46 cases x100,000 inhabitants. The ratio (M / F) was 1.52. The median age was 73 years (38-91). Clinical presentation was: spinal (58.8%), bulbar (35.3%) and others (5.9%). Median survival was 16 months (CI95%= 10.9-21.1) and was significantly lower in patients older than 73 years [32 (CI95%= 9.9-52.1) vs 12 (CI95%= 10.2-13.8) months, p=0.013] (see figure). No significant differences were found for the other variables. In three cases a genetic mutation was identified (4.4%).

Kaplan-Meier survival analysis
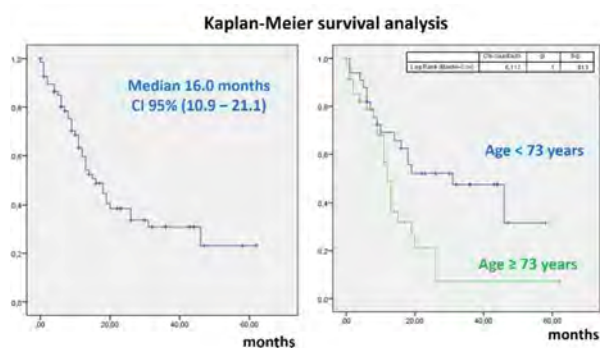
Conclusion: Our real-life study in ALS showed a male predominance, the incidence rate and prevalence were high, and that age at diagnosis was the main determinant of survival.

Disclosure: The authors declare that they have no conflict of interest in relation to this abstract.

EPO-353

Assessing the Value of Specialist Centres for the Diagnosis and Management of the Ataxias in Europe.

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[2] *University of Cambridge, United Kingdom,* [3] *ERN-RND,*
[4] *Takeda,* [5] *European Brain Council, Brussels, Belgium*

Background and aims: The Value of Treatment on rare neurological diseases research project (2019-2021) was coordinated by the the European Brain Council. The study is looking at the value of early diagnosis and intervention, aiming to assess the benefits of coordinated care and multidisciplinary care patterns on patient outcomes and costs. We present here the ataxia case study.

Methods: This project explores the patient pathways of individuals with progressive ataxias and compares their experiences attending specialist ataxia centres compared with care in non–specialist settings in terms of quality of care and health economic factors. We collected data in the UK, Germany and Italy using a patient survey, to gather information about the diagnosis and the management of the ataxias in specialist and non-specialist settings.

Results: Analysis of the patient care pathways identified several steps within the pathway to be improved. These included a reduction in the time to see a neurologist and the time to reach a specific diagnosis, and an increase in the access to specialist ataxia centres. The health economics evaluation of the specialist centres has revealed a higher cost due to higher resource use and cost of transport to centres. Overall, the symptoms management and care delivered to people living with ataxia in a specialist centre was better than in a non-specialist setting.

Conclusion: This study provides insight into the value of the specialist centres in terms of diagnosis, management of patients with rare neurological conditions, including cost implications.

Disclosure: The study received financial support from Reata and Takeda.

EPO-354

Ultrasound (US) examination of respiratory muscles (RMs) in motor neuron disease (MND)

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Background and aims: Respiratory failure is one of the main causes of death in MND patients. Early detection and monitoring of patients with respiratory failure is an important stage in the medical care provision.

Methods: US was performed on 20 MND patients: 11 (55%) men, 9 (45%) women; the age Me 64[57;67] years. The control group consisted of 18 patients without signs of neuromuscular pathology and respiratory problems: 6(33%) men, 12(67%) women, the age Me 57 [55; 64] years. MND patients: 15(75%) amyotrophic lateral sclerosis (ALS), 3(15%) progressive bulbar palsy, 2(10%) primary lateral sclerosis. Research was carried on HD11XE(Philips) device using sensors of linear and convexy formats, frequency 5–12 and 2-5 MHz along the midclavicular line symmetrically from 2 sides in the patient's supine position(Fig.1).

Parameters	MND (n=19) Me[LQ;UQ]	Control (n=18) Me[LQ;UQ]	U, p
ThD on the exhale Right, cm	0.18[0.16;0.20]	0.20[0.17;0.23]	0.06
ThD on the exhale Left, cm	0.18[0.16;0.20]	0.20[0.19;0.22]	0.01*
ThD at the end of quiet breath Right, cm	0.21[0.18;0.25]	0.24[0.21;0.32]	0.03*
ThD at the end of quiet breath Left, cm	0.21[0.18;0.23]	0.24[0.23;0.31]	0.0005*
ThD at the end of deep breath Right, cm	0.27[0.22;0.31]	0.32[0.29;0.37]	0.002*
ThD at the end of deep breath Left, cm	0.28[0.24;0.32]	0.36[0.32;0.45]	0.0003*
ADM while quiet breathing Right, cm	1.07[0.60;1.74]	1.53[1.17;1.84]	0.04*
ADM while quiet breathing Left, cm	0.97[0.7;1.33]	1.32[1.22;1.80]	0.008*
ADM while deep breathing Right, cm	4.3[1.71;5.38]	5.65[4.11;6.37]	0.02*
ADM while deep breathing Left, cm	3.06[1.85;4.31]	4.79[4.17;5.81]	0.004*
IcS on the exhale Right, cm	1.90[1.78;2.13]	2.09[2.05;2.21]	0.02*
IcS on the exhale Left, cm	1.90[1.81;2.08]	2.13[2.06;2.19]	0.02*
IcS at the end of quiet breath Right, cm	1.96[1.82;2.20]	2.19[2.16;2.36]	0.02*
IcS at the end of quiet breath Left, cm	2.04[1.85;2.19]	2.26[2.19;2.38]	0.006*
IcS at the end of deep breath Right, cm	2.08[1.96;2.38]	2.43[2.37;2.54]	0.003*
IcS at the end of deep breath Left, cm	2.23[2.04;2.46]	2.47[2.42;2.59]	0.002*
RMK while quiet breathing Right, cm	1.15[0.70;1.41]	1.51[1.32;1.83]	0.004*
RMK while quiet breathing Left, cm	0.94[0.86;1.11]	1.38[1.31;1.55]	0.0003*
RMK while deep breathing Right, cm	2.71[2.54;4.50]	4.53[3.69;5.35]	0.03*
RMK while deep breathing Left, cm	3.40[1.92;4.40]	4.22[3.57;4.69]	0.02*
ThRD Right	1.10[1.08;1.20]	1.13[1.10;1.33]	0.11
ThRD Left	1.13[1.06;1.16]	1.23[1.16;1.33]	0.002*

Table 1 – Results of the study of the structure and function of the main RMs (* - significant differences at $p<0.05$ according to the Mann-Whitney test)

Conclusion: US examination revealed parameters allowing to assess the motor capabilities of the RMs: significant decrease in the ThD and ADM, decrease of the IcS, deterioration of the RMK, reducing of the ThRD that indicates the promising possibilities of US in the early diagnosis of respiratory problems in MND patients.

Disclosure: Nothing to disclosure.

Figure 1 – Examination of the diaphragm function (from left to right: position of the US sensor, measuring the thickness and amplitude of the diaphragm movement)

Results: US in MND patients revealed significant decrease in thickness of the diaphragm (ThD) and amplitude of diaphragm movement (ADM) during quiet and deep breathing on both sides (U, $p<0.05$), reduction of the intercostals spaces size (IcS) during quiet and deep breathing on both sides (U, $p<0.05$), reduction of the respiratory mobility of the kidneys (RMK) during quiet and deep breathing on both sides (U, $p<0.05$), decrease of the thickening ratio of the diaphragm (ThRD) Left (U, $p <0.05$) (Table 1).

EPO-355

Evaluation of a clinically-validated web-based analysis MRI platform to provide biomarkers in ALS

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Background and aims: Studies in ALS showed that diffusion tensor imaging (DTI) allows to detect white matter alterations within the cerebral cortico-spinal tract considered as a proxy of upper motor neuron involvement. We aimed to test whether DTI metrics can discriminate patients with ALS from normal controls with a clinically-validated and CE marked web-based MRI analysis platform.

Methods: 3T-MRI DTI acquisitions were performed in 24 ALS patients and 22 sex-and age-matched controls. Images were processed by the platform. Outputs were the Mean diffusivity (MD) and Fractional Anisotropy (FA) in regions selected to encompass the corticospinal tract: the posterior limb of internal capsule (PLIC) and cerebral peduncle (CP). The primary objective was to test whether DTI-metrics were different in ALS patients compared to controls. Secondary objectives were to test whether DTI metrics changes correlated with functional severity (ALSFRS-R) and were abnormal in the subgroup of patients without upper motor neuron (UMN) clinical signs.

Results: MD in the PLIC and the CP were increased in ALS patients compared to controls. Decrease of FA did not reach statistical significance. MD in the PLIC was correlated with the ALSFRS-R score. Compared to controls, MD in the CP was increased in the subgroup of patients without clinical UMN signs.

Conclusion: This study shows that a clinically-validated MRI platform can provide DTI metrics proxies of upper motoneuron degeneration in ALS patients even without clinical signs. This tool could be transferred in a clinical setting for diagnosis, decision-making and clinical trials recruitment.

Disclosure: No institutional nor commercial support was obtained.

EPO-356

Acetylcholinesterase activity does not change in the plasma of patients with amyotrophic lateral sclerosis

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Background and aims: It is believed that the acetylcholinesterase (AChE) activity changes in blood plasma in ALS. In some studies, increased activity of AChE was shown (Rasool et al., 1983), but another study showed the opposite results (Niebroj-Dobosz, Hausmanowa-Petrusewicz 1989). Skeletal muscle biopsies of ALS patients also showed a decrease in AChE activity (Fernandes et al 1986). Since then, additional studies of AChE activity in ALS patients have not been conducted. Recent reviews on AChE and neuromuscular synapse degeneration in ALS (Campanari et al., 2016; Verma et al., 2022) also pay attention to altered AChE activity in plasma and suggest that AChE can be considered as a diagnostic biomarker. Given the conflicting results of previous studies, we decided to recheck these data.

Methods: 17 patients with ALS were examined (31 to 71 y.o.). 9 patients with ALS mimics served as disease controls (DC, 33 to 61 y.o.). 15 healthy persons served as normal controls (NC, 36 to 72 y.o.). Fasting blood was taken and plasma was separated by centrifugation. AChE activity was measured by Ellman's method. All values were presented as mean ± SEM. The Mann-Whitney U test was used to evaluate statistical significance.

Results: AChE activity in ALS group was 0.53 ± 0.07 U/mg protein plasma. In DC and NC groups AChE activity was 0.69 ± 0.1 and 0.65 ± 0.12 respectively. No statistical significance between groups was found.
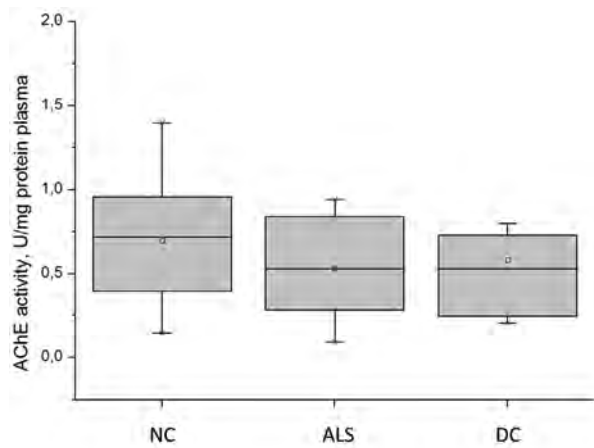
AChE activity in blood plasma of patients with ALS, disease and normal controls

Conclusion: No alterations in plasma AChE activity in ALS patients were found, therefore AChE cannot be considered as a diagnostic biomarker for ALS.

Disclosure: This study is a part of A.N. Khabibrakhmanov's Ph.D. research work

EPO-357

Nusinersen treatment in a wide severity spectrum of SMA in long-term observation – real-world experiences

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Background and aims: Nusinersen is the first modifying therapy approved for Spinal Muscular Atrophy (SMA). The objective of the study was to assess effectiveness and safety of nusinersen in long-term observation in wide spectrum of SMA patients in two centers in Poland.

Methods: We studied 120 genetically confirmed patients (adults and older children, 5–66y.) with SMA treated with nusinersen. The motor functions were assessed with Hammersmith Functional Rating Scale Expanded (HFMSE, applied to 6 SMA2, 61 SMA3 and 6 SMA4 patients) or Children's Hospital of Philadelphia Infant Test of Neuromuscular Disorders (CHOP-INTEND, applied to 12 SMA1, 15 SMA2 and 20 SMA3 patients). We included patients with clinical data available at least at baseline (D1-beginning of treatment) and 6 months (D180). The longest observation was 780 days (D780).

Results: The median of age at first administration of nusinersen was 31.5 y. In 67 patients with SMA3-4 we observed significant increase in HFMSE from D1 to D180 (median change +3, $p<0.0000$), D300 (+3.5, $p<0.0000$), D420 (+5, $p<0.0000$), D540 (+4, $p<0.0000$), D660(+7, $p<0.0000$) , D780 (+7.5, $p<0.0000$). In 12 adults with SMA1, CHOP-INTEND improved from D1 to D300 (median change +5, $p=0.04$), D420 (+6, $p=0.02$), D540 (+7, $p=0.2$), D660 (+8 $p= 0.01$), D780 (+11, $p=0.01$). Similar trends were found in all other groups of patients. No serious adverse event was observed during the treatment. The most common adverse event was post-dural puncture headache (19%).

Conclusion: Our data provide further evidence of nusinersen safety and effectiveness in long duration treatment in adults and older children regardless type and severity of SMA.

EPO-358

Salivary gland Radiotherapy for Sialorrhea in Amyotrophic Lateral Sclerosis patients: a real life study.

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Background and aims: To evaluate the efficacy and safety of radiotherapy (RT) of the primary salivary glands in ALS patients with refractory sialorrhea.

Methods: 212 patients treated between 2010 and 2020 were retrospectively analyzed. RT efficacy was assessed using the 9-item Sialorrhea Scoring Scale (SSS).

Results: At the end of RT, all but 1 patient had an improvement in SSS. Patients treated with 20Gy versus 10Gy were more likely to have a complete response. There was no > grade 1 toxicities.

Conclusion: RT is an effective and safe treatment for ALS patients with sialorrhea.

Disclosure: Nothing to disclose.

EPO-359

Muscle ultrasound in the Diagnosis of Amyotrophic Lateral Sclerosis (ALS)

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Background and aims: ALS is a progressive neurodegenerative disease with involvement of the upper and lower motor neurons. By Awaji criteria fasciculation potentials is a sign of acute denervation as evidence of LMN dysfunction. Muscle ultrasound (US) can detect fasciculations (Fs) and their distribution.
Objective: To explore the possibilities of muscle US for identification of Fs and their distribution for diagnosis of suspected ALS.

Methods: were investigated 208 ALS patients (age – 57[49;63]; M/F ratio – 123/85; ALS duration –18 mon). The diagnosis of ALS was based on the revised El Escorial criteria endorsed by Awaji consensus group criteria. The control group consisted of 45 healthy individuals. The groups were matched by age and sex. The muscle US were conducted in both groups by created protocol.

Results: Detecting of Fs were observed during muscle US in 204 (98.1%) ALS patients and 5 control cases (χ^2=28,1; p<0,001). The Sensitivity (Se) and Specificity (Sp) were established by ROC analysis: Se-100 (95% CI: 98.2–100); Sp -87.8 (95% CI: 73.8–95.9); AUC values -0.939 (p<0.0001). Detecting of Fs generalization (involved 3–4 regions (bulbar, cervical, thoracic and lumbosacral) were observed during muscle US in all 204 (98.1%) ALS patients and was out of control. Se -98,99 (95% CI: 96,4–99,9); Sp -100 (95% CI: 91.4–100.0); AUC values -0.995 (p<0.0001).

Conclusion: Muscle US diagnostics of Fs generalization has high Sensitivity and Specificity in ALS patients. Combination of clinical examination and muscle US increase ALS diagnostic sensitivity with followed by EMG study.

Disclosure: Nothing to disclose.

EPO-360

Upper motor neuron signs in primary lateral sclerosis

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Background and aims: Upper motor neuron (UMN) signs characterize primary lateral sclerosis (PLS). We aimed to study the spectrum of UMN signs in PLS.

Methods: We retrospectively analysed the frequency of different UMN signs in patients with PLS at first visit in our clinic, including tendon reflexes (limbs and jaw), spasticity of limbs and tongue, plantar response and Hoffman sign. We compared subgroups according to onset region and disease duration until diagnosis.

Results: We included 34 patients with probable and definitive PLS, 20 (58.8%) women, with a median disease duration until diagnosis of 39.5 months (interquartile range, 25–78.3). Overall, hyperreflexia of upper (88%) and lower (94%) limbs and lower limbs spasticity (79%) were the most common findings. In the lower limb-spinal onset subgroup (n=25), hyperreflexia of upper (88%) and lower (96%) limbs and lower limbs spasticity (92%) were the most common signs. In the upper limb-spinal onset subgroup (n=3), hyperreflexia of upper limbs and Hoffman sign were present in all. In the bulbar-onset subgroup (n=6), hyperreflexia of lower limbs (100%), tongue spasticity (83%) and abnormal jaw jerk reflex (67%) were the most common signs. The subgroup with shorter disease duration included more bulbar-onset patients (4 versus 2) and had a tendency (not statistically significant) to more frequent tongue spasticity (53% versus 29%) and abnormal jaw jerk (65% versus 35%).

Conclusion: The distribution of UMN signs is dependent on onset region and disease duration. Overall, limbs hyperreflexia and lower limbs spasticity are common markers that should guide clinical diagnosis.

Disclosure: Nothing to disclose.

EPO-361

Wasted Leg Syndrome: an atypical slow-progressive form of lower motor neuron disease

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Background and aims: Focal lower limb amyotrophy is a rare motor neuron disease (MND) phenotype, designated as "wasted-leg syndrome", more frequently described in Asians. It mainly affects younger males, being characterized by a slow progression of muscle wasting and weakness restricted to one leg. We propose that a particular phenotype is thigh weakness.

Methods: Retrospective and descriptive analysis of 4 patients with thigh weakness followed in our unit in the 1997–2021 period.

Results: All patients were males, mean age at onset of 48.3±9.7. Two patients were of Indian origin and two were Europeans. In all of them weakness was restricted to thigh unilaterally (right side in 3 cases). Both Indian patients progressed to the contralateral proximal lower limb after 3 months and 6 years, respectively. However, none of them showed a relevant functional deterioration (stable ALSFRS-R) over a follow-up period of 12.1±6.7 years. No upper limb, bulbar or respiratory involvement was observed. No sensory loss or pyramidal signs were detected. Nerve conduction studies were normal, but needle electromyography revealed chronic loss of motor units in proximal lower limb muscles, bilaterally. CSF analysis and spine MR imaging were unremarkable. One Indian patient was diagnosed with CADASIL later.

Conclusion: This is the first description of thigh weakness phenotype of wasted-leg syndrome, and including 2 Caucasians. Although all patients presented with unilateral weakness, slow progression to the contralateral proximal lower limb was observed in two patients. This enlarges the spectrum of benign MND phenotypes.

Disclosure: None of the authors has any conflict of interest to disclose.

Movement disorders 3

EPO-362

Correlates of Psychological Distress in Patients with Parkinson's Disease During the COVID-19 Outbreak

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Background and aims: Following the severe consequences of the COVID-19 outbreak, on March 9, 2020, the Italian government implemented extraordinary measures to limit viral transmission, including restrictive quarantine measures. This resulted in a rapid and profound change of people's daily lives. We assessed the psychological impact of the 40-day quarantine in a large cohort of patients with Parkinson's disease (PD) and their caregivers. Moreover, we analyzed whether prelockdown clinical features may predispose to this subjective response.

Methods: The study sample was recruited from an ongoing longitudinal study. Therefore, an extensive prelockdown motor, non-motor and cognitive evaluation were performed. From this cohort, we selected a subset of 94 patients with PD. After 40 days of lockdown, the Impact of Event Scale-Revised, the Kessler Psychological Distress Scale, and the 12-item Zarit Burden Inventory were obtained from PD patients and their caregivers by email. A multivariate regression analysis was performed to determine whether prelockdown clinical features were associated with the psychological impact of lockdown.

Results: Regression analyses showed that prelockdown levels of anxiety, treatment-related motor complications, patients' quality of life, and lockdown hours per day were significantly associated with psychological impact measures of the 40-day quarantine. We also showed that caregiver burden was correlated with overall patient autonomy and attention/memory impairment.

Conclusion: We identified specific PD motor and nonmotor features potentially predisposing to higher psychological impact of stressful situations, such as quarantine. This may help guide postpandemic interventions and preventive strategies to avoid further impairment of psychological well-being in patients with PD.

Disclosure: Nothing to disclose.

EPO-363

Pharmacokinetics–pharmacodynamics of levodopa/carbidopa following subcutaneous infusion with ND0612

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Background and aims: ND0612 is an investigational subcutaneous delivery system providing minimally invasive, continuous infusion of liquid levodopa/carbidopa under development for potential sustained relief of motor fluctuations in patients with Parkinson's disease (PD). The aim of this pharmacokinetic study was to evaluate the pharmacokinetic–pharmacodynamic relationships between levodopa plasma exposure and motor response in patients with PD treated with ND0612 and adjunct oral PD medication.

Methods: Seventeen PD patients (Hoehn & Yahr score of ≤3 during ON & ≥2 hours daily OFF-time at baseline) who had completed at least 1-year of open-label treatment with ND0612 (16-hour or 24-hour infusion regimens) were included in this study. In parallel to the pharmacokinetic parameters (assessed over 24 hours), the pharmacodynamic response was assessed using the treatment response scale (TRS) and patient ON/OFF diaries (30-minute intervals over 24 hours).

Results: In general, increasing plasma concentrations of levodopa were associated with higher TRS scores and more ON-time. In the 16-hour regimen, the first morning hours were characterized by a higher proportion of lower TRS scores as expected due to the low levodopa plasma concentrations, until reaching stable, clinically relevant levodopa levels. Levodopa pharmacokinetics and the pharmacodynamic response as assessed by the TRS were correlated.

Conclusion: The results of this study support the translation of stable levodopa pharmacokinetics, as provided by continuous infusion with ND0612, into stable and improved motor responses in PD patients experiencing motor fluctuations.

Disclosure: Funded by NeuroDerm.

EPO-364

Initial and residual symptoms of Wilson's disease: could we predict the clinical course of the disease?

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Background and aims: Wilson disease (WD) is an autosomal recessive disorder that leads to copper accumulation and deposition in different organs with highly variable clinical presentation. The aim of this study was to describe neurological symptoms present initially before diagnosis was made and during the course of the disease and after the years of treatment. We tried to establish whether the presence of certain symptoms in the beginning may be the possible predictor of the outcome.

Methods: Our study included 40 WD patients who were regularly monitored and treated at the Clinic of Neurology, University Clinical Center of Serbia. The data were collected from medical reports, patient's interview and neurological examination.

Results: The main clinical and demographic data are presented in the Table 1. Severity of the disease was examined using the Global Assessment Scale for WD (GAS). The predominant symptoms, both initially and years after treatment initiation, were speech problems, tremor, clumsiness, gait disturbance and drooling. However, patients had significantly improved over time achieving average residual GAS of 7.50±7.65 in comparison with GAS before treatment initiation 20.12±9.25 (p 0.001). The linear regression shown that the presence of dystonia initially is a predictor of worse residual GAS, while the predictors of severity of residual dystonia were gender and age at treatment initiation.

	Mean value with SD (minimum and maximum)
Current age *	45,17±12,14 (27-77)
Age at the disease onset *	26,92±8,59 (11-50)
Age at the time of diagnosis *	29,52±9,18 (15-53)
Latency to diagnosis *	2,59±4,47 (8-19)
Age at treatment initiation *	29,92±8,97 (15-53)
Latency to treatment initiation *	2,99±4,17 (0-19)
Disease duration *	15,65±11,28 (0-44)
Treatment duration *	15,25±11,24 (0-44)

*years

Table 1: Clinical and demographic data of WD patients

N=40	Initial symptoms	Residual symptoms	P (<0.05)
Speech problems ∞	36 (90%)	28 (70%)	**0.02**
Tremor ∞	36 (90%)	27 (67.5%)	**0.01**
Clumsiness ∞	27 (67.5%)	14 (35%)	**0.00**
Gait disturbance ∞	25 (62.5%)	14 (35%)	**0.01**
Drooling ∞	24 (60%)	17 (42.5%)	0.12
Slowness of movement ∞	21 (52.5%)	14 (35%)	0.11
Postural disturbance ∞	18 (45%)	9 (22.5%)	**0.03**
Work impairment ∞	17 (43.6%)	8 (20%)	**0.03**
Swallowing difficulties ∞	17 (42.5%)	15 (37.5%)	0.65

∞ number of patients with percentage in brackets

Table 2: Initial and residual symptoms of WD patients

Conclusion: During the course of the disease, frequency and presence of observed neurological symptoms remained the same, while its severity diminished resulting in improvement of GAS score. The presence of dystonia initially was a predictor of worse outcome.

Disclosure: Nothing to disclose.

EPO-365

Factors Influencing Research Participation in Huntington's Disease: Clues from Southern and Eastern Europe

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Background and aims: Effective therapies for Huntington's disease (HD) are much dependent on how HD families engage in research. The European Huntington Association (EHA) aimed to determine which factors affect the willingness of persons at risk for HD (HDRisk) and persons with premanifest HD (PreHD) to participate in studies and check for differences across European regions.

Methods: The EHA created two online surveys to assess the perceptions about research participation among persons with HDrisk and PreHD in Spain and Russia. The two countries were compared on questions about research experience and knowledge, sources of research information, the importance of reasons for getting involved and not getting involved in studies, and factors preventing and facilitating study participation.

Results: 128 persons from Spain (SPHD) and 59 persons from Russia (RUHD) completed the surveys. While the overall motivation of the two groups to engage in studies was high, they both had reduced experience and knowledge about research. Nevertheless, the SPHD had greater rate of study participation. Interestingly, altruistic reasons were more important for SPHD research involvement, whereas individual benefits and access to care were more important for RUHD research involvement. Additionally, the SPHD reported closer contact with healthcare professionals.
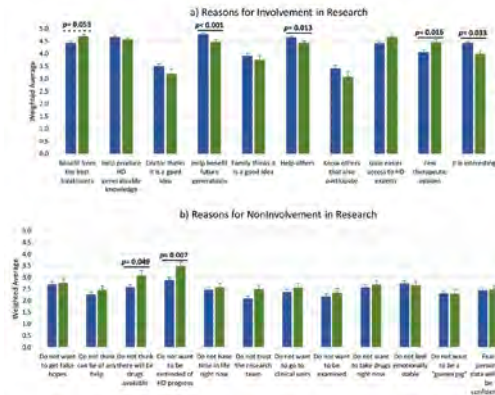
Figure 1 - Reasons for Involvement and Noninvolvment in Research

Experience, Knowledge, and Information about HD Research			
	Spain n= 128	Russia n= 59	Chi-Square Spain vs Russia
	%	%	χ2 (p-value)
Previous HD Research Experience			
Yes	22.7	6.8	7.005 (0.008)**
No	77.3	93.2	
Knowledge about HD Research			
Not Good	14.1	22	1.856 (0.173)
Should be Better	46.1	30.5	4.050 (0.044)*
Satisfactory	12.5	15.3	0.265 (0.607)
Good	24.2	25.4	0.032 (0.859)
Excellent	3.1	5.1	0.430 (0.512)
Do not want to know about HD research	0	1.7	2.181 (0.140)
Sources of Information about HD Research			
Internet	64.1	74.6	2.031 (0.154)
Television	2.3	6.8	2.205 (0.138)
Press/Newsletters/Flyers/Booklets	18	3.4	7.411 (0.006)**
HD Associations and/or Support Groups	53.1	40.7	2.503 (0.114)
Health Care Professionals	39.8	10.2	16.782 (< 0.001)
Family Members	28.1	23.7	0.398 (0.528)
Not interested in HD research information	0	5.1	6.615 (0.010)*

Table 1 – * statistically significant p≤ 0.05 ** statistically significant p≤ 0.01.

Table 1 - Previous Experience, Level of Knowledge and Sources of Information about HD Research

Factors Influencing Research Participation			
	Spain n= 128	Russia n= 59	Chi-Square Spain vs Russia
	%	%	χ2 (p-value)
Factors Preventing Participation			
I would have to travel to the study site	28.9	20.3	1.533 (0.216)
I would not have family support	2.3	1.7	0.081 (0.776)
I would have personal expenses	25.8	39	3.355 (0.067)
I would have to do motor exams	2.3	1.7	0.081 (0.776)
I would have to find someone to take care of my sick parent	10.2	8.5	0.131 (0.717)
I would have to skip work days/hours	43	25.4	5.308 (0.021)*
I would have to be involved in the study for a long time	14.8	8.5	1.464 (0.226)
I would have to go through invasive procedures	26.6	32.2	0.633 (0.426)
I would have to do cognitive assessments	3.1	3.4	0.009 (0.924)
I would have to find someone to take care of my children	10.9	11.9	0.035 (0.852)
I would have to rethink my decisions about family planning	12.5	13.6	0.041 (0.840)
None of the above	31.3	30.5	0.010 (0.919)
Factors Facilitating Participation			
I would have assistance from a patient advocate	16.4	15.3	0.040 (0.842)
I would have family support	31.3	28.8	0.113 (0.737)
The researcher is my doctor/my family member doctor	21.1	8.5	4.534 (0.033)*
My personal expenses would be reimbursed	24.2	45.8	8.761 (0.003)**
I would get the chance to meet other HD families	32.8	25.4	1.040 (0.308)
I would gain easier access to treatments and health professionals	69.5	74.6	0.500 (0.479)
I would have psychological and social care available	58.6	59.3	0.009 (0.925)
I would not have to go through invasive procedures	28.1	25.4	0.149 (0.700)
I know and trust the study team	40.6	42.4	0.051 (0.821)
I would have regular feedback about my health condition	58.6	66.1	0.957 (0.328)
None of the above	3.9	3.4	0.030 (0.863)

Table 2 – p≤ 0.05 ** statistically significant p≤ 0.01.

Table 2 - Factors Influencing Research Participation

Conclusion: Distinct HD communities show high motivation to take part in studies, despite limited research experience and literacy. This motivation is influenced by factors that seem to derive from uneven access to care and research across Europe. Our findings highlight the relevance of planning country-specific interventions to support an informed participation of HD families in research.

EPO-366

Frequency of diagnosed comorbid conditions amongst myasthenia gravis patients: Analysis of real-world data

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Background and aims: Myasthenia gravis (MG) is a rare, chronic condition, manifesting as muscle weakness and fatigue, substantially impairing patients' capacity to perform daily activities. MG patients are at higher risk of developing comorbidities including conditions secondary to and/or worsened by long-term use of immunosuppressant therapies (corticosteroids, non-steroidal immunosuppressants). Our aim was to describe the frequency of comorbidities in a real-world population of MG patients.

Methods: Data were drawn from the Adelphi MG Disease Specific Programme™, a cross-sectional study of physicians and MG patients across 5 European countries and the US in 2020. Physicians reported patient demographics and clinical characteristics, including comorbidities and treatment history. Descriptive statistics are reported.

Results: 242 physicians provided data for 1,234 MG patients. Patients were 50.2% female and 84.5% Caucasian, with mean age of 54.2 (SD±16.3) and BMI of 25.4kg/m^2 (SD±4.1). Comorbidities were present in 69.0% of patients [Table 1]. Cardiovascular conditions were present in 42.5%, including hypertension (28.1%) and dyslipidaemia (17.3%). Psychiatric/neurological conditions were present in 26.7%, including anxiety (17.8%) and depression (16.0%). Of the 1,234 patients, 43.1% were currently or had previously been prescribed corticosteroids as MG treatment. Corticosteroid-naïve patients had a mean of 1.4 (SD±1.58) diagnosed comorbidities, and patients who had ever received corticosteroids had a mean of 1.8 (SD±1.78).

	All Patients (n=1234)	Corticosteroid naïve (n=702)	Received corticosteroids currently or previously (n=532)
Number of current concomitant conditions, mean (SD)	1.6 (1.68)	1.4 (1.58)	1.8 (1.78)
Current concomitant conditions, n (%)			
None	383 (31.0)	244 (34.8)	139 (26.1)
Hypertension	347 (28.1)	182 (25.9)	165 (31.0)
Anxiety	220 (17.8)	102 (14.5)	118 (22.2)
Dyslipidaemia	214 (17.3)	114 (16.2)	100 (18.8)
Depression	197 (16.0)	95 (13.5)	102 (19.2)
Diabetes without chronic complications	129 (10.5)	73 (10.4)	56 (10.5)
Obesity	99 (8.0)	49 (7.0)	50 (9.4)
Chronic pulmonary disease	73 (5.9)	33 (4.7)	40 (7.5)
Osteoporosis	63 (5.1)	29 (4.1)	34 (6.4)
Peripheral vascular disease	56 (4.5)	35 (5.0)	21 (3.9)
Rheumatologic disease	50 (4.1)	24 (3.4)	26 (4.9)
Mild liver disease	46 (3.7)	22 (3.1)	24 (4.5)
Hashimoto's thyroiditis	44 (3.6)	20 (2.8)	24 (4.5)
Peptic Ulcer Disease	42 (3.4)	21 (3.0)	21 (3.9)
Renal disease	41 (3.3)	20 (2.8)	21 (3.9)
Congestive heart failure	40 (3.2)	19 (2.7)	21 (3.9)
Cerebrovascular disease	40 (3.2)	16 (2.3)	24 (4.5)
Myocardial infarction	35 (2.8)	18 (2.6)	17 (3.2)
Hyperthyroidism	27 (2.2)	16 (2.3)	11 (2.1)
Diabetes with chronic complications	24 (1.9)	11 (1.6)	13 (2.4)
Any malignancy, including leukemia and lymphoma	16 (1.3)	7 (1.0)	9 (1.7)
Other thyroid abnormality	14 (1.1)	10 (1.4)	4 (0.8)
Hemiplegia or paraplegia	11 (0.9)	5 (0.7)	6 (1.1)
Dementia	10 (0.8)	7 (1.0)	3 (0.6)
Moderate or severe liver disease	7 (0.6)	4 (0.6)	3 (0.6)
Systemic lupus erythematosus (SLE)	5 (0.4)	2 (0.3)	3 (0.6)
Metastatic solid tumor	4 (0.3)	2 (0.3)	2 (0.4)
AIDS/HIV	3 (0.2)	1 (0.1)	2 (0.4)
Healthcare associated infection (HCAI)	3 (0.2)	3 (0.4)	0 (0.0)
Other(s)	64 (5.2)	30 (4.3)	34 (6.4)

Table 1. Comorbidities present for MG patients

Conclusion: More than two thirds of patients had comorbidities, many of which can be secondary to and/or exacerbated by corticosteroid treatment. Cardiovascular and psychiatric/neurologic comorbidities were the most commonly reported. These findings highlight the need for physicians to carefully consider comorbidities when making MG treatment decisions.

EPO-367

Impact of generalised myasthenia gravis on activities of daily living and employment for patients and caregivers

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Background and aims: Generalised myasthenia gravis (gMG) is a rare chronic disease, causing debilitating muscle weakness. Patients with gMG experience difficulties in performing activities of daily living (ADLs), thus requiring caregiver assistance. Our aim was to describe disease impact on gMG patients and their caregivers.

Methods: Data were drawn from the Adelphi Myasthenia Gravis (MG) Disease Specific Programme™, a cross-sectional survey of physicians and MG patients across 5 European countries and the US in 2020. Physicians completed patient record forms reporting patient caregiver status and assisted activities. Patients filled in self-completion form including the Work Productivity and Activity Impairment (WPAI:SHP) instrument. Descriptive statistics are reported.

Results: Physicians provided data for 119 gMG patients requiring a caregiver who had completed the WPAI. Mean age was 57.5 (SD±13.4) years and 56% were male. Patients reported 55% of their daily activities had been impaired by their condition in the past week. 84% of patients received care from non-professional caregivers [Table 1], with a mean of 27.2 (SD±30.2) hours of care per week. The main non-professional caregiver was partner/spouse for most patients (82%). 42% of non-professional caregivers' employment was affected by disease [Table 2]. Caregiver assistance was commonly required for walking (50%), shopping (45%) and emotional support (41%) [Table 3].

Top 10 activities requiring caregiver assistance, n (%)	All patients (n=119)
Walking	60 (50)
Help with shopping	54 (45)
Emotional support	49 (41)
Travelling out of home	41 (36)
Help with preparing meals/cooking food	38 (32)
Motivation to engage in daily activities	38 (32)
Getting washed and dressed	27 (23)
Help planning and organising daily activities	20 (17)
Help with going to the toilet	19 (16)
Help gardening	18 (15)

Table 3. Physician-reported daily activities requiring caregiver assistance for gMG patients

Conclusion: Patients were moderately impaired in performing daily activities, many requiring caregiver assistance for daily tasks. Non-professional caregivers often altered working patterns to care for patients due to required hours of care. This highlights the substantial impact of gMG on patients and caregivers and considerable indirect economic burden.

Disclosure: This study was supported by Alexion Pharmaceuticals. All authors contributed to the development of the abstract and maintained control over the final content.

	All patients (n=119)
Caregiver status, n (%)	
Non-professional caregiver only	100 (84)
Professional caregiver only	15 (13)
Both non-professional and professional caregivers	4 (3)
Main non-professional caregiver relationship to patient, n (%)	**(n=102)**
Partner/spouse	84 (82)
Child	5 (5)
Other family member/friend/non-professional	13 (13)

Table 1. Physician-reported caregiver status for gMG patients and relationship to patient

Caregiver's change to employment due to caring for the gMG patient, n (%)	All patients with non-professional caregiver (n=93)
No change	54 (58)
Reduce working hours	21 (23)
Stop working	13 (14)
Change type of work	3 (3)
Work unsociable hours (e.g., night shifts)	2 (2)

Table 2. Physician-reported impact on employment for non-professional caregiver

EPO-368

Proprioception might be more disrupted in PSP than in PD: a posturography study

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Background and aims: Differential diagnosis of Parkinson´s disease (PD) and progressive supranuclear palsy (PSP) might be difficult due to the shared clinical signs. They might both present with deficits in postural control, even though, in the case of PSP, it is typically earlier in the disease course. The pathophysiology of balance difficulties remains elusive.

Methods: We performed standard posturography in patients with PD (n=9,) and PSP (n=11) with a history of at least one fall in the previous 3 months with matched disease durations. The posturographic protocol consisted of quiet standing with eyes opened, eyes closed, galvanic stimulation, vibration stimulation of the Achilles tendon. Each trial lasted 50 seconds, the stimulation (vibration, galvanic) was applied between 10–20th second, if applicable. Amplitude and velocity of postural response (separately medio-lateral, anterior-posterior direction), root mean square and line integral. All patients were recorded in the best ON state with the absence of interfering dyskinesia.

Results: A statistically significant difference in postural response was found between PD and PSP in the trial with the vibration stimulation of Achilles tendon. The difference was observed after the onset of stimulation (10–20th second) and reflected in the root mean square and LI (p=0.038) with smaller postural responses in PSP. There was no other difference in the rest of the posturographic parameters.

Conclusion: The underlying deficit in postural control might be different in PD and PSP, possibly due to the more pronounced deficit of the proprioceptive system in PSP patients. This might be also discriminative in the differential diagnosis.

Disclosure: Nothing to disclose.

EPO-369

Long-term non-motor effects of Opicapone in Parkinson's disease

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Background and aims: Opicapone is a long-acting, third-generation COMT-inhibitor, indicated as adjunctive treatment for motor fluctuations in Parkinson's Disease. Evidence from the OptiPark study suggests that opicapone leads to a short-term (3 months) beneficial effect on non-motor symptoms (NMS) in people with Parkinson's (PwP). We investigated real-life, long-term NMS effects of opicapone in PwP compared to those of standard care without opicapone.

Methods: In this retrospective data analysis, pre- and post-opicapone initiation data were collected from the Non-motor-International-Longitudinal study (NILS) and the OpiSleep study at King's College Hospital (London, UK). Thirteen PwP patients were included with a post-opicapone assessment after an average of five months. A matched control group of 13 PwP patients treated with standard care without opicapone and with a similar follow-up period was identified from the NILS database (table 1). The primary outcome was to assess pre- and post-opicapone initiation differences in the NMS scale (NMSS) total score. Secondary outcomes included differences in the individual NMSS domains and SCOPA-motor total scores at follow-up. Data were summarised descriptively, and changes in outcomes tested using the Wilcoxon signed-rank test. Benjamini-Hochberg procedure was used to correct for multiple testing.

TABLE 1: Baseline clinical features of active (opicapone) and control group (standard care without opicapone)

	PwP without Opicapone (N=13)	PwP with Opicapone (N=13)	p1	p2
Age (yrs)	59.6±10.1	58.8±10.9	0.801	0.915
Sex (M/F)	9/4	9/4	1.000	1.000
HY	3 (2-3)	2 (1-3)	0.661	0.881
Disease duration (yrs)	6.5±4.1	7.2±3.6	0.545	0.872
LEDD	845.0±343.6	684.2±220.3	0.153	0.408
SCOPA-motor total	17.5±6.6	15.0±9.6	0.479	0.855
NMSS total	67.5±38.6	61.0±43.3	0.762	0.915
NMSS cardiovascular/falls	1.5±2.8	1.5±2.8	0.920	0.981
NMSS sleep/fatigue	15.5±11.0	13.0±11.7	0.614	0.881
NMSS mood/apathy	8.6±8.6	18.1±13.0	0.050	0.304
NMSS perceptual/hallucinations	2.6±3.8	0.5±1.7	0.101	0.404
NMSS attention/memory	5.1±6.0	8.2±9.1	0.479	0.855
NMSS gastrointestinal	7.5±5.8	2.5±2.8	0.022	0.304
NMSS urinary	10.1±7.5	8.5±12.1	0.264	0.603
NMSS sexual	5.5±5.0	2.4±4.6	0.057	0.304
NMSS miscellaneous	11.2±8.7	6.3±5.9	0.139	0.408

Data are presented as mean ± standard deviation, median (25th and 75th percentiles) or absolute number as appropriate. Differences between groups were tested using Mann-Whitney-U test or Pearson Chi-square where appropriate (p < 0.05 was considered significant). Abbreviations: F, female; HY, Hoehn and Yahr; LEDD, Levodopa equivalent daily dose; M, male; N, number NMSS, nonmotor symptom scale; PwP, people with Parkinson's; p1, uncorrected p-value; p2, p-value corrected for multiple testing using Benjamini-Hochberg procedure; SCOPA, SCales for Outcomes in PArkinson's disease; Yrs, years.

Results: Introduction of opicapone led to a significant reduction in NMSS total scores (p=0.037; table 2). No significant changes were observed for secondary outcomes in the two groups

TABLE 2: Pre and post outcomes in the active (opicapone) and comparative group (standard care without opicapone)

	PwP without Opicapone (N=13)				PwP with Opicapone (N=13)			
	BL	FU	p1	p2	BL	FU	p1	p2
Primary outcome								
NMSS total	61.0±43.3	38.1±31.4	**0.037**	-	67.5±38.6	62.9±49.1	0.421	-
Secondary outcomes								
LEDD	684.2±220.3	931.8±274.8	**0.003**	**0.033**	845.0±343.6	806.5±318.0	0.594	0.653
SCOPA-motor total	15.0±9.6	17.6±11.2	0.196	0.539	17.5±6.6	20.2±8.3	0.463	0.653
NMSS cardiovascular/falls	1.5±2.8	0.9±1.9	0.528	0.645	1.5±2.8	3.9±5.0	0.150	0.550
NMSS sleep/fatigue	13.0±11.7	9.2±7.8	0.114	0.418	15.5±11.0	11.8±9.6	0.124	0.550
NMSS mood/apathy	18.1±13.0	8.5±8.8	**0.012**	0.066	8.6±10.3	11.4±17.1	0.541	0.653
NMSS perceptual/hallucinations	0.5±1.7	1.4±3.8	0.655	0.721	2.6±3.8	1.9±4.4	0.527	0.653
NMSS attention/memory	8.2±9.1	6.5±7.6	0.284	0.580	5.1±6.0	3.4±4.7	0.439	0.653
NMSS gastrointestinal	2.5±2.8	2.6±4.1	1.000	1.000	7.5±5.8	4.7±4.9	0.070	0.550
NMSS urinary	8.5±12.1	6.6±7.3	0.422	0.580	10.1±7.5	9.9±9.5	0.906	0.906
NMSS sexual	2.4±4.6	2.1±3.7	0.416	0.580	5.5±5.0	6.2±6.8	0.443	0.653
NMSS miscellaneous	6.3±5.9	5.8±8.3	0.400	0.580	11.2±8.7	9.8±7.8	0.359	0.653

Data are presented as mean ± standard deviation. Wilcoxon signed-rank test for within-group changes. p < 0.05 was considered significant. Abbreviations: BL, Baseline; FU, Follow Up; N, number; NMSS, nonmotor symptom scale; PwP, people with Parkinson's; p1: uncorrected p-value; p2: p-value corrected for multiple testing using Benjamini-Hochberg procedure; SCOPA, SCales for Outcomes in PArkinson's disease

Conclusion: Opicapone use reduces NMS burden in the long-term compared to standard clinical care without opicapone and NMS outcome-based studies are encouraged.
Disclosure: The OpiSleep study is an IIS partly funded by Bial.

EPO-370

A longitudinal evaluation of the peripheral immune phenotype in a cohort of Parkinson's disease patients

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Background and aims: Pathophysiology of Parkinson's disease (PD) is complex and multifactorial. Recently, the role of immune system has been identified as crucial. Indeed, PD patients display a pro-inflammatory peripheral immune phenotype but less is known about the trend of immunological parameters during disease decourse. The aim is to evaluate the suitable modifications of immunological parameters in a through characterized population of Italian PD patients

Methods: From 2014, drug naïve PD patients underwent a peripheral blood withdrawal annually, evaluating lymphocytes sub-populations and transcription factors (TF). Patients were excluded in presence of immune disease or immunomodulant/depressant treatment Clinical and demographic parameters were monitored.

Results: 49 PD patients (33 male, mean age 68±8.4) with at least one follow-up visit were included. Th1 lymphocytes were higher after 2 and 4 years (p=0.03 and p=0.0006) while Th2 and Th17 were persistently reduced both as percentage and total count. Dealing with TF, STAT1 presented constantly significanlty increased levels (V0: $1.61*10{-4}±0.0001$; V1 $2.39*10{-4}±0.0001$; V2: $2.38*10{-4}±5*10{-5}$; V3: $2.86*10{-4}±0.0001$; respectively p=0.01; p=0.006; p<0.0001) while STAT6 levels were reduced. Total number of Treg was reduced in V3 and V4 and both activated and resting subsets. Accordingly, FOXP3 levels were significantly reduced at V4 compared to baseline.

Conclusion: This is the first longitudinal study evaluating peripheral immune system in PD. Our data, though preliminary, indicate that the pro-inflammatory phenotype represents and early phenomenon in the disease decourse. Accordingly, immunotherapy in PD, which is under investigation, should be started soon in the disease history in order to act as disease modifier.

Disclosure: The authors have nothing to disclose.

EPO-371

Functional MRI and gait analysis characteristics in patients with idiopathic rem sleep behavior disorder

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Background and aims: Clinical, gait analysis, and MRI features might predict the conversion from idiopathic REM sleep behavioral disorder (iRBD) to clinically manifested alpha-synucleinopathies. The aims of this study were to assess gait analysis, neurological, neuropsychological and resting-state functional MRI (RS-fMRI) functional connectivity (FC) characteristics in iRBD patients and to study the correlations between clinical features and RS-fMRI alterations.

Methods: Ten patients with a polysomnography-confirmed iRBD underwent clinical, cognitive, and RS-fMRI evaluations. Gait analysis was performed using a stereophotogrammetric system to assess asymmetry of spatio-temporal gait parameters during a four-meter walking test with and without a cognitive dual-task. Ten age/sex-matched healthy controls underwent neuropsychological evaluation and RS-fMRI.

Results: IRBD patients showed mild asymmetry of spatio-temporal gait parameters, particularly during dual-task gait. IRBD patients showed an increased FC in the right executive control, sensorimotor and dorsal default mode networks compared to healthy controls. Basal ganglia and cerebellar networks showed reduced FC. Correlation analyses showed that an increased asymmetry in the lower limb swing time during gait correlated with an increased FC in the right executive control network, whereas an increased asymmetry of lower limb stride length during dual-task gait correlated with an increased FC in the sensorimotor network.

Conclusion: This study suggested that RS-fMRI and gait analysis characteristics could be promising biomarkers for early alpha-synucleinopathy detection and prediction. The collection of longitudinal data in a larger sample will allow the assessment of conversion from iRBD to parkinsonian syndromes and to test a multifactorial prediction model combining fMRI, gait analysis, clinical and neuropsychological data.

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EPO-372

Emotion Recognition in Multiple System Atrophy – an Eye-Tracking Study

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Background and aims: Multiple System Atrophy (MSA) is a rare neurodegenerative disease. The lack of emotion recognition in idiopathic Parkinson's disease has been previously described, however the knowledge in MSA patients is lacking. This study aims to provide insights into emotion processing in patients with MSA compared to healthy controls (HCs) by using two different Eye-Tracking paradigms.

Methods: We included 14 patients with MSA-P and 15 matched HCs. Every participant underwent Montreal cognitive assessment (MoCA), Hospital Anxiety and Depression Scale (HADS-D) and Toronto Alexithymia Scale (TAS-20). Emotion recognition was carried out on an Eye-Tracking device (Tobii TX 300). The modified Geneva Emotion Recognition Test (GERT) showed 24 short videos and the static test 63 faces of people expressing different emotions. Total-fixation-duration (TFD), fixation-count (FC) and time-to-first-fixation (TTFF) were calculated on predefined areas of interest (AOI).

Results: No demographic differences were detected. MSA-P patients scored higher on HADS (p<0.001). Both groups performed similar at the GERT and static test (p>0.1). We observed significant differences for FC face and body at GERT (p<0.001). For static testing, TTFF face was shorter in MSA-P (p=0.021) and contrarily longer at TTFF eyes (p=0.019). FC face scored higher and FC eyes lower (p<0.001) in MSA-P. TFD of the eyes was shorter (p=0.016) in MSA-P and longer at the nose region (p<0.001).

Conclusion: Although MSA-P patients recognized emotions as well as HCs, there are differences regarding the gaze behaviour. MSA-P patients tend to avoid direct eye contact with lower FCs and a shorter TFD in the eye region compared to HCs.

Disclosure: Nothing to disclose.

EPO-373

Descriptive case studies of patients in their fifth consecutive year of treatment with ND0612

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Background and aims: ND0612 is in development as a continuous subcutaneous (SC) levodopa/carbidopa delivery system for patients with Parkinson's disease (PD) experiencing motor fluctuations. Primary data from the BeyoND safety study showed that ND0612 is generally safe up to 1 year of treatment. Here we describe the long-term experience of three individual patients receiving ND0612 treatment in the ongoing BeyoND study.

Methods: We report three individual cases (2M/1F) from Israel and the USA. Eligible patients (aged ≥30 years) had a diagnosis of PD (Hoehn & Yahr Stage ≤3) and were experiencing ≥2 hours of OFF time/day despite receiving ≥4 levodopa doses/day and ≥1 other PD medication.

Results: All three cases received continuous ND0612 for 24-hours/day. These patients were aged 61–68 years old, Hoehn and Yahr Stage 2–3, and experiencing motor fluctuations for 1–7 years. All three patients showed relevant reductions from baseline in OFF time and increases in ON time without troublesome dyskinesia, which were maintained until last date of efficacy follow-up. All three patients experienced infusion site reactions, mainly nodules and bruising, which were mild or moderate and well tolerated. One patient had a serious infusion site infection which was managed successfully with antibiotics and abscess drainage. This patient decided to continue ND0612 treatment because of its favorable effect on motor fluctuations and gait.

Conclusion: Continuing into their fifth year of treatment, these patients exemplify the favorable long-term benefit/risk profile of ND0612 and will serve to inform future patient selection and education.

Disclosure: Funded by NeuroDerm.

EPO-374

Retinal thickness in Essential Tremor and early Parkinson's Disease: exploring diagnostic insights

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Background and aims: Essential Tremor (ET) represents a broad phenotypically heterogeneous neurodegenerative condition, often encompassing subtle clinical aspects overlapping with early stages of Parkinson's Disease (PD). Moreover, longstanding ET demonstrated a higher risk of developing PD, especially with a Tremor-Dominant phenotype. Therefore, in some conditions, a differential diagnostic approach between ET and early-PD could be challenging. Optical Coherence Tomography (OCT) has been recognized as a reliable tool to assess retina as a proxy of neurodegeneration. We aimed to explore the possible role of retinal assessment in a differential diagnostic setting in ET through a standardized OCT protocol.

Methods: Macular layers and peripapillary retinal nerve fiber layer (RNFL) thickness among ET, early-PD and Healthy Controls (HCs) were assessed using OCT. Exclusion criteria were glaucoma, concurrent retinal disease, ocular trauma, cataract, high intraocular pression, systemic disease impairing visual system (diabetes, uncontrolled hypertension/hypotension, cardiovascular diseases) and other neurological diseases.

Results: 42 eyes from 23 ET, 41 eyes from 21 early-PD and 33 eyes from 17 HCs were analysed. Macular RNFL, Ganglion Cell Layer, Inner Plexiform Layer and Inner Nuclear Layer were thinner in PD as compared with ET and even more in HCs. No significant adjunctive data were reported considering ET in comparison to different PD phenotypes. Peripapillary temporal quadrant thinning was demonstrated in ET in respect with HCs.

Table 1. Demographical and clinical characteristics. Multivariate analysis.

	PD N= 21 (41 eyes)	ET N= 23 (42 eyes)	HCs N= 17 (33 eyes)	ANOVA p-value
Sex (M)	12 (57.1%)	14 (60.9%)	9 (52.9%)	0.886
Age	61.5 ± 6.5	72.3 ± 6.5	65.1 ± 10.7	<0.001
Age at onset	59.3 ± 7.0	58.8 ± 18.4	/	0.898
Disease Duration (years)	2.3 ± 1.2	13.6 ± 15.4	/	0.002
UPDRS-III	25.0 ± 6.9	14.9 ± 10.0	2.7 ± 1.8	<0.001
TETRAS-performance total	/	21.3 ± 9.1	/	/
MMSE	27.0 ± 2.7	28.3 ± 2.0	27.0 ± 2.3	0.184
Hypertension (%)	13 (61.9)	18 (78.3)	4 (23.5)	0.001
OCT PARAMETERS				
RNFL (μm)	13.4 ± 1.9	15.0 ± 1.6	17.8 ± 2.2	<0.001
GCL (μm)	16.1 ± 3.2	17.6 ± 3.4	21.4 ± 2.2	<0.001
IPL (μm)	21.4 ± 2.9	22.1 ± 3.3	24.2 ± 2.1	<0.001
INL (μm)	20.7 ± 5.5	23.5 ± 5.1	28.2 ± 4.5	<0.001
OPL (μm)	28.5 ± 6.3	27.9 ± 5.1	31.2 ± 4.8	0.030
ONL (μm)	86.1 ± 12.6	87.3 ± 9.9	97.7 ± 7.7	<0.001
RPE (μm)	15.6 ± 1.6	15.7 ± 1.6	16.3 ± 1.7	0.168
ON (μm)	92.8 ± 9.4	95.5 ± 10.0	101.1 ± 7.9	0.004
ON SUPERIOR (μm)	112.8 ± 16.5	114.0 ± 11.2	120.6 ± 9.6	0.026
ON TEMPORAL (μm)	70.5 ± 9.8	72.7 ± 7.4	78.3 ± 7.8	<0.001
ON INFERIOR (μm)	120.2 ± 15.0	115.5 ± 11.5	119.4 ± 9.2	0.189
ON NASAL (μm)	73.0 ±10.2	75.3 ± 9.4	80.9 ± 8.2	0.002

	MULTIVARIATE ANALYSIS			
	ET vs HC		ET vs PD	
OCT PARAMETERS	AdjOR* (95% CI)	p-value	AdjOR* (95% CI)	p-value
RNFL (μm)	0.51 (0.33 – 0.78)	0.002	3.17 (1.74 – 5.77)	<0.001
GCL (μm)	0.49 (0.33 – 0.74)	0.001	1.30 (1.04 – 1.60)	0.017
IPL (μm)	0.82 (0.63 – 1.07)	0.153	1.40 (1.08 – 1.82)	0.010
INL (μm)	0.84 (0.72 – 0.98)	0.031	1.15 (1.00 – 1.31)	0.042
OPL (μm)	0.88 (0.75 – 1.02)	0.104	1.00 (0.91 – 1.10)	0.998
ONL (μm)	0.92 (0.85 – 0.99)	0.038	1.03 (0.98 – 1.08)	0.284
RPE (μm)	0.91 (0.61 – 1.36)	0.641	1.06 (0.72 – 1.54)	0.771
ON (μm)	0.96 (0.87 – 1.03)	0.261	1.05 (0.99 – 1.11)	0.128
ON SUPERIOR (μm)	0.95 (0.89 – 1.02)	0.206	1.02 (0.98 – 1.06)	0.338
ON TEMPORAL (μm)	0.88 (0.81 – 0.97)	0.007	1.03 (0.96 – 1.10)	0.441
ON INFERIOR (μm)	0.99 (0.93 – 1.05)	0.736	1.00 (0.95 – 1.04)	0.820
ON NASAL (μm)	0.96 (0.89 – 1.03)	0.285	1.06 (1.00 – 1.13)	0.052

Table 1 legend. * Adjusted by Age, Sex and Hypertension. PD: Parkinson's Disease. ET: Essential Tremor. HCs: Healthy Controls. UPDRS-III: Unified Parkinson's Disease Rating Scale - Part III. TETRAS: The Essential Tremor Rating Assessment Scale. MMSE: Mini Mental State Examination. RNFL: Retinal Nerve Fiber Layer. GCL: Ganglion Cell Layer. IPL: Inner Plexiform Layer. INL: Inner Nuclear Layer. OPL: Outer Plexiform Layer. ONL: Outer Nuclear Layer. RPE: Retinal Pigment Epithelium. ON: Optic Nerve.

Figure 1. Macular and Peripapillary Retinal Thickness differences among groups.
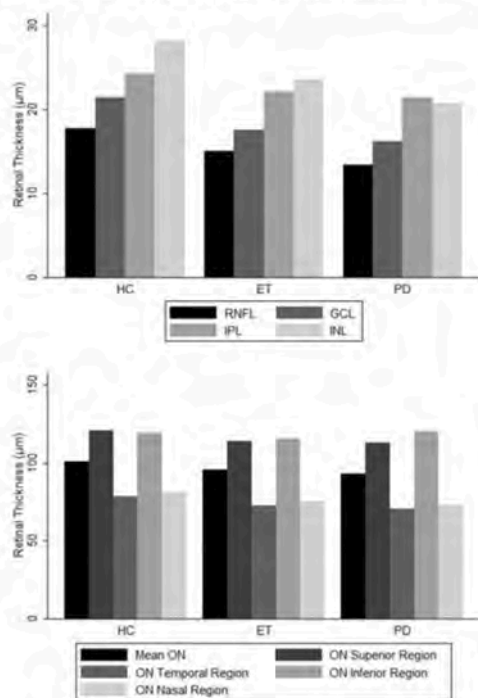
Conclusion: In early-PD and ET macular inner retina was thinner than HC, and values of ET were between PD and HC. These findings suggest a possible OCT role in a differential diagnostic setting.

Disclosure: Authors have nothing to report.

Movement disorders 4

EPO-375

Freezing gait in Parkinson's disease: the relationship between visual dysfunction and cognitive and structural disorders

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Background and aims: Freezing of gait (FOG) is a complex disorder of sensorimotor integration with involving motor, cognitive and sensory systems. The fact that visual input may cause freezing episodes in Parkinson's disease (PD), as well as help overcoming them, indicates visual system contribution to the FOG pathogenesis. We investigated the cognitive and structural features of PD patients with FOG in relation to visual impairments.

Methods: 27 PD-with-FOG patients, who were matched for age and PD severity with 30 PD-without-FOG patients, Methods were examined: 1) Neuropsychological tests including cognitive and visual attention assessment; 2) Freezing of Gait Questionnaire (FOG-Q); 3) Contrast sensitivity (CS) and visual field examination with total visual sensitivity (TVS) estimation; 4) Voxel-based morphometry (VBM).

Results: 1. Differences were found between groups by TVS and CS at low spatial frequencies, disease duration, motor symptoms, TMT and FAB (table). 2. The FOG+group showed reduced gray matter volume in the cuneus, lingual gyrus, posterior cingulate cortex, superior parietal lobe, supplementary motor area and middle frontal cortex compared with the FOG-group. 3. A decrease in CS and TVS had strong correlation with a decrease in gray matter volume at the lingual gyrus and the superior parietal lobe; moderate correlation with FOG-Q score and FAB, and; weak correlation with TUG, TPCT and MMSE.

Demographic and Disease Characteristics	FOG+ group (n = 27)	FOG- group (n = 30)
	Median (IQR)	
Age (years)	63 (57 – 68)	60 (55 – 67)
H & Y stage	2.5 (2–3)	2.5 (2.0–2.5)
Disease duration (years)	9 (6 – 14)	6 (5 – 12)*
UPDRS (part I)	18 (16 - 25)	17 (16 – 22)
UPDRS (part III)	38 (28 - 49)	31 (25 – 42)*
Timed Up and Go Test (TUG) (seconds)	14 (9 – 19)	11 (7 -16)*
MMSE	28 (26 – 29)	29 (27 - 30)
TPCT	9 (7 – 9)	9 (8 – 9)
FAB	14 (12 – 15)	16 (14 – 17)*
Trails Making Test Part A (seconds)	67 (57 – 80)	58 (51 – 75)*
Trails Making Test Part B (seconds)	162 (141 – 224)	119 (103 – 158)*
FOG-Q	14 (7–18)	0 (0–1)*
Peripheral Visual Field Thresholds (60-4-SITA algorithm) - total visual sensitivity	980 (849 – 1213)	1117 (1009 – 1338)*
Contrast sensitivity (white-black / red-black /green-black / blue-black)		
Spatial frequency	1 cycle / °	36 (32-42)/ 34 (26-40)/ 32 (27-38)/ 28 (24- 34)	42 (38-44)•/ 40 (36-42)•/ 38 (36-46)•/ 36 (32-42)•
	4 cycle / °	44 (40-50)/ 42 (38-48)/ 41 (36-47)/ 38 (34-44)	48 (48-52)/ 48 (42-50)•/ 46 (38-50)/ 42 (40-48)•
	8 cycle / °	46 (38-48)/ 40 (36-46)/ 39 (34-46)/ 34 (28-38)	48 (42-50) /44 (44-46)/ 42 (36-48)/ 38 (32-42)

* - Statistically significant difference (p < 0.05) between FOG+ group and FOG- group (Mann–Whitney test);
H&Y stage - Hoehn & Yahr stage; UPDRS - Unified Parkinson's Disease Rating Scale; MMSE - mini mental state evaluation; FAB - frontal assessment battery; TPCT - ten-point clock test.

Table: Demographic and clinical characteristics of PD patients with and without FOG

Conclusion: Our results confirm that in addition to motor symptoms, the PD-related visual disorders have a significant contribution to the development of FOG. Visual information is particularly important for the organization of proper sensorimotor integration in order to initiate and maintain posture and walking function.

Disclosure: Nothing to disclose.

EPO-376

Painless legs moving toes (PoLMT) associated with hyperthyroidism: A case report

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Background and aims: Moving toes syndrome is a rare movement disorder characterized by repetitive movements of the toes. Its etiology and physiopathology are unclear. Here we describe a patient with painless repetitive movements of the left toes, who was found to have hyperthyroidism.

Methods: A 51-year-old male presented with a 5-months history with involuntary movements of his left toes without experience of any accompanying pain. His past medical history was insignificant for any trauma or medication use. His family history was unremarkable for any neurological disease. On examination, he had involuntary movements of his left toes, predominantly of the fifth toe. The movements were irregular, with different frequency and amplitude, and of adducting pattern of the fifth toe. They persisted during rest, sleep and activity, and could be voluntarily suppressed for a brief time. The rest of examination was normal. His brain and spine magnetic resonance imaging, nerve conduction studies resulted normal. On further workup thyroid stimulating hormone level resulted very low with high level of T3 and T4. Thyroid gland echography was significant for multinodular goiter.

Results: He was diagnosed with hyperthyroidism and was started on unimazole, propranolol, clonazepam. After 2 months his thyroid function was improved, and mild response to clonazepam was noted.

Conclusion: PoLMT is a variant of painful legs and moving toes syndrome. There are cases in the literature that describe this syndrome in association with neuropathy, spinal cord trauma, Wilson's disease, stroke and endocrinopathies such as Hashimoto's disease. We believe that this patient clinical manifestation is due to hyperthyroidism.

Disclosure: Nothing to disclose.

EPO-377

OCEAN Study in Parkinson's: Status Update of a Randomised Double-Blind Placebo-Controlled Trial of Opicapone

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Background and aims: Opicapone (OPC) proved effective for the treatment of end-of-dose motor fluctuations (MF) in patients with Parkinson's disease (PD). End-of-dose MF and associated pain are commonly reported in patients with PD and have a negative impact on patients' quality of life. This study aims to evaluate if treatment with OPC can improve MF-related pain.

Methods: The OCEAN study is a double-blind, randomised, placebo-controlled trial that aims to recruit ~140 patients (≥30 years old) with idiopathic PD, who were treated with 3−8 daily oral doses of L-dopa/DDCI and experienced pain associated with end-of-dose MF. Patients will be randomised (1:1) to OPC 50 mg once daily or placebo during a 24-week follow-up period (Figure).

Figure. Study design (a) and timeline of study assessments (b). *V2 is divided into V2a and V2b. If ON/OFF diary entries are non-compliant at V2a, the patient will be re-trained on correct use of the diary and visit V2b will be postponed for 3–4 days. If diary completion is satisfactory at V2a, V2b is performed immediately on the same day.
AE, adverse event; EDV, early discontinuation visit; CGI-C, Clinicians' Global Impression of Change; DDCI, dopa decarboxylase inhibitor; EMD, early morning dystonia; EDV, early discontinuation visit; KPPS, King's Parkinson's Disease Pain Scale; L-dopa, levodopa; MDS-NMS, Movement Disorder Society-Non-Motor Scale; MDS-UPDRS, Movement Disorder Society-Unified Parkinson's Disease Rating Scale; PDQ-8, Parkinson's Disease Questionnaire 8-item; PDSS-2, Parkinson's Disease Sleep Scale 2; PFS-16, Parkinson's Disease Fatigue Scale 16-item; PGI-C, Patients' Global Impression of Change; R, randomisation; V, visit.
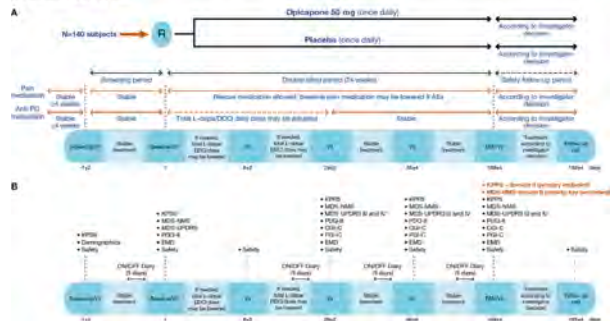
Results: The primary endpoint is change from baseline in domain 3 (fluctuation-related pain) of the King's-Parkinson's-Disease-Pain-Scale (KPPS). Secondary endpoints include tolerability, motor and non-motor symptoms (KPSS, Movement Disorder Society-Non-Motor Symptoms, Parkinson's Disease Questionnaire-8, Hauser's home diary), and Clinician and Patient Clinical Global Impression of Change. The study received approval in Germany, Italy, Portugal, Spain and the UK. Six sites are actively recruiting and 37 site-initiation-visits have been performed. As of December 2021, 14 patients have been randomised and at least 2 have completed the study.

Conclusion: This study will evaluate the benefit of OPC 50 mg once daily as adjunctive therapy to L-dopa/DDCI on MF-related pain in patients with PD.

Disclosure: Supported by Bial.

EPO-378

Open-Label, Single-Arm, Exploratory Trial of Opicapone: Status Update of the OASIS (OPICAPONE IN SLEEP DISORDER) Study

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Background and aims: Non-motor symptoms have a substantial impact on health-related quality of life and are reported in ~90% of patients with idiopathic Parkinson's Disease (PD). End-of-dose motor fluctuations (MF) and associated sleep disorders are commonly observed in PD patients receiving levodopa (L-dopa)/DOPA decarboxylase inhibitors (DDCI). Opicapone (OPC) proved effective in reducing end-of-dose MF in patients with PD. This study aims to evaluate the effects of OPC treatment on sleep disorders in patients with PD and 'wearing-off'.

Methods: OASIS is an open-label, exploratory trial aiming to recruit ~30 patients (aged ≥30 years) with idiopathic PD, treated with 3−8 daily doses of L-dopa/DDCI, with 'wearing-off' and sleep disorders. Patients will receive OPC 50 mg once daily during a 6-week evaluation period (Figure).

Figure. Overall OASIS study design. *0–5 days prior V2b / If the patient completed the diary satisfactorily, it should be immediately continued with V2b, on the same day. **Objective measurement of Motor symptoms (AX3 device). CGI-C, Clinicians' Global Impression of Change; DDCI, dopa decarboxylase inhibitor; EDV, early discontinuation visit; EMD, early morning dystonia; L-dopa, levodopa; MDS-NMS, Movement Disorder Society-Non-Motor Scale; MDS-UPDRS, Movement Disorder Society-Unified Parkinson's Disease Rating Scale; PDQ-8, Parkinson's Disease Questionnaire 8-item; PDSS-2, Parkinson's Disease Sleep Scale 2; PFS-16, Parkinson's Disease Fatigue Scale 16-item; PGI-C, Patients' Global Impression of Change; V, visit
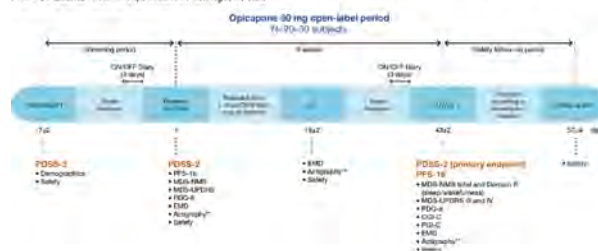
Results: The primary endpoint is change from baseline in total score of Parkinson's Disease Sleep Scale-2. Secondary endpoints include tolerability, motor and non-motor assessments (Movement Disorder Society-Non-Motor Symptoms Scale, Parkinson's Disease Questionnaire-8, Parkinson's Fatigue Scale, ON/OFF home diary), and Clinician and Patient Global Impression of Change. The study has been approved in Germany and Portugal. As of December 2021, 4 patients have been randomised.

Conclusion: This exploratory study will provide preliminary data on the potential benefit of OPC 50 mg once daily as adjunctive therapy to L-dopa/DDCI on PD-associated sleep disorders.

Disclosure: Supported by Bial.

EPO-379

Dual target deep brain stimulation for clinically complex tremor disorders: a single centre prospective study

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Background and aims: The ventral intermediate (ViM) nucleus of the thalamus is the traditional Deep Brain Stimulation's (DBS) target for tremor. The posterior subthalamic nucleus (pSTN) including the caudal Zona Incerta (cZI) has also been demonstrated to be an effective target. Here, we presented a case series of patients with refractory complex tremor treated with dual targeting DBS of ViM and pSTN/cZI.

Methods: Eight contacts VerciseTM Boston scientific DBS lead was utilised in all cases; pulse generator was either Vercise IPG or Gevia IPG Boston Scientific. 55 patients with complex tremor were consecutively recruited from the DBS clinics at the Walton Centre NHS Foundation Trust.

Results: 50 patients had bilateral VIM and pSTN/cZI DBS and five unilateral DBS of the same targets. The EuroQol-5D (EQ-5D) average score improved from 0.585 (SD±0.220) to 0.661 (SD±0.187) (13%) at the six-month follow up post-DBS . This improvement was sustained at five years follow up. The Fahn-Tolosa tremor rating scale scores showed an average improvement from 53.44 (SD±12.73) to 33.27 (SD±17.87) six months post-implantation (37.74%). Sustained improvement was demonstrated at five year follow up.

Conclusion: Overall, this study indicated that that dual target stimulation of VIM and pSTN/cZI is an effective target for complex refractory tremor.

Disclosure: Nothing to disclose.

EPO-380

OnabotulinumtoxinA treatment and physician and patient satisfaction in patients with spastic hemiparesis from ASPIRE

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Background and aims: Clinical presentations of spastic hemiparesis are common and likely require treatment to multiple muscles across both the upper limb (UL) and lower limb (LL). We examined onabotulinumtoxinA utilisation and physician and patient satisfaction in patients with UL and LL spasticity from the Adult Spasticity International Registry (ASPIRE) study.

Methods: 2-year, multicentre, observational registry (NCT01930786). Adults with spasticity were treated with onabotulinumtoxinA at the physician's discretion. OnabotulinumtoxinA utilisation and safety data were collected at each treatment session. Patient and physician treatment satisfaction were collected after each treatment. Patients with spastic hemiparesis included those who received ≥1 UL treatment and ≥1 LL treatment during the 2-year study.

Results: Of 730 patients, 284 were defined as hemiparetic, with 275 treated for the UL and LL at the same treatment session. Hemiparetic patients were on average 53.2 years old and 51.3% male. Clenched fist was the most common UL presentation (n=219) and equinovarus foot was the most common LL presentation (n=238). Patients and physicians were consistently satisfied with the management of symptoms and duration of effect over repeated treatment sessions (Figures 1 and 2). Ninety-four patients (34.2%) reported 293 non-serious adverse events (AEs); 3 serious AEs in 2 patients (0.7%) were considered treatment-related.

Figure 1. Patient satisfaction with onabotulinumtoxinA
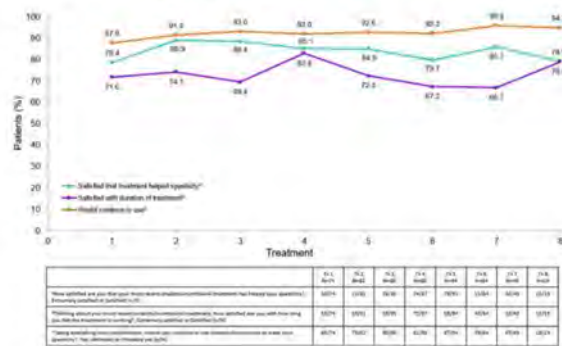
a,b Patient satisfaction question scores were rated on a 5-point scale where 1 was extremely satisfied, 2 was satisfied, 3 was neither satisfied nor dissatisfied, 4 was dissatisfied, and 5 was extremely dissatisfied. c Score for patient continuation of onabotulinumtoxinA to manage spasticity was rated on a 5-point scale where 1 was yes, definitely, 2 was probably yes, 3 was undecided, 4 was probably not, and 5 was definitely not.

Figure 2. Physician satisfaction with onabotulinumtoxinA
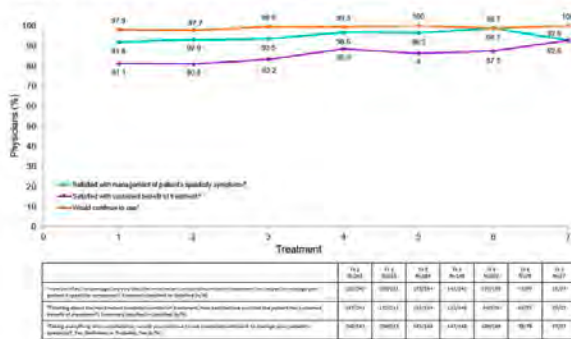
a,b Physician satisfaction question scores were rated on a 5-point scale where 1 was extremely satisfied, 2 was satisfied, 3 was neither satisfied nor dissatisfied, 4 was dissatisfied, and 5 was extremely dissatisfied. c Score for physicians to continue to use onabotulinumtoxinA to manage their patient's spasticity was rated on a 5-point scale where 1 was yes, definitely, 2 was probably yes, 3 was undecided, 4 was probably not, and 5 was definitely not.

Conclusion: ASPIRE provides real-world evidence on the use of onabotulinumtoxinA to treat patients with spastic hemiparesis, with the majority of patients and physicians reporting treatment satisfaction.

Disclosure: This study was supported by Allergan (prior to its acquisition by AbbVie).

EPO-381

The effect of a exercise on exosomal alpha-synuclein level and nonmotor symptoms in idiopathic Parkinson's disease

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Background and aims: We've investigated the effect of the Multi-Model exercise program (MEP) on functional mobility, motor, non-motor symptoms, quality of life and its correlation with serum exosomal alpha-synuclein (ExS) level in idiopathic Parkinson's patients (İPD).

Methods: A 12-week MEP, including spinal flexibility, balance, coordination and postural control, was applied to 26 patients and we record Plasma and ExS levels ,UPDRS ,HYR ,Frontal behavioural battery,Verbal Fluency Test, Abstraction Skill test, Clock Drawing Test, HADS, PDQ-39,NMSQ-TR, Epworth Sleepiness Score, Brief Pain Index Form, RLS Severity Rating Scale, Tinetti walking and balance and fall efficiency scale.

Results: We have detected a significant increment in both motor, nonmotor, cognitive and mood parameters. In addition, Exosomal alpha-synuclein (p=0.159) level decreased after MEP, but it was not found to be statistically significant. A moderate positive correlation was found between total alpha-synuclein (p<0.05, r:0.55) and short-term memory scores.
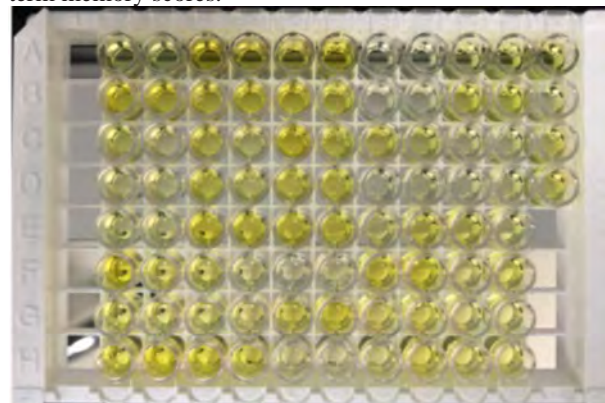
Colorimetric ELİSA Test Results

Conclusion: In this study, significant improvement was observed in both motor and non-motor symptoms after MEP. However, no significant decrease in exosomal alpha-synuclein level was achieved. Herein, it was thought that the main reason was due to the relatively small size of the group. Since exosomal alpha-synuclein is closely related to clinical severity, age and cognitive function, it raises great hopes for being a clinical biomarker. It is a great advantage that it can be looked at in the serum directly from the brain.

Disclosure: We need more Long term and randomise case-control studies for detect their relationship with exercise.

EPO-382

Projecting the Subthalamic Nuclei by using MER Data Recording through Deep Brain Stimulation

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Background and aims: Micro Electrode Recording (or Microrecording "M.E.R") is the technique of interleaving a microminiatured tiny but very high-impedance electrode into the brain parenchyma and acquiring extemporaneous and induced neural activity which sequences and angles the form of both single-neuron activity "S.N.A" (i.e.,"spiking") and local field potential ("L.F.P") activity.

Methods: 16 patients underwent bilateral S.T.N-D.B.S. Concurrent M.E.R signal recording was done in a Ben's-gun pattern setup in locally anesthetized Parkinson subjects (patients) with a 5 core-pentode (5 microelectrodes in an array). Using spikes and circumstantial (or contextual) background activity dissimilar parameters plus their phantom estimates in various-frequency-bands which include low-frequency(θ:2Hz–7Hz), α:Hz–12Hz, β:13Hz–20Hz (sub-divided as low-β) and superior β:21Hz–30Hz and γ:31Hz-49Hz were computed.

Results: The optimal lead implantation through the highest ideal medical effect/side-effect ratio accorded to the highest spike-rate(S.R) in 86% of the implantation. The amplitude mean-background activity in low-slung βfrequency-range(FR) was analogous to right depth in 86% and right-hemisphere position in 95% of the implantation. Intraoperative-MER-technique can be applied for planning S.T.N and intraoperative outcomes for embedding electrodes with a high accuracy. Spiking and background activity in the β-limit are highly likely objective parameters for the delineation of the correct-site anatomically.

Conclusion: MER confirms presence of abnormal STN neurons. Certainly, M.E.R can corroborate and pinpoint the lead-position of microelectrodes plus strengthen the confidence of the neurosurgeons that they are in the right-target. Availability of MER results in a vast data vis-à-vis functioning on neurons positioned-deep in the brain may further help in untying esoteric of brain.

Disclosure: Nothing to disclose.

EPO-383

A systematic Review on Deep Brain Stimulation for Atypical Parkinsonism

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Background and aims: Atypical Parkinsonisms (APs), including multiple system atrophy (MSA), progressive supranuclear palsy (PSP), corticobasal degeneration (CBD), and dementia with Lewy bodies (DLB), are neurodegenerative disease characterized by parkinsonism plus specific clinical features. Currently, no effective treatment is available. Deep Brain Stimulation (DBS) is an effective and relatively safe treatment for Parkinson disease (PD) patients presenting suboptimal control of motor symptoms despite best medical therapy. Although its effectiveness in PD fed expectations for the treatment of APs, DBS is still not recommended for APs based on expert consensus and lack of clinical trials. In this systematic review, we analyzed current evidence on safety and efficacy of DBS in APs, discussing clinical indications, stimulation settings, and ethical issues.

Methods: Following PRISMA guidelines for systematic review, we searched PubMed for studies prior to March 1, 2021 reporting the safety and efficacy outcomes of DBS in patients with PSP, MSA, DLB, and CBD.

Results: We identified 25 studies for a total of 66 reported patients with APs treated with DBS: 31 PSP, 22 MSA, 12 DLB, 1 unspecified (Table 1, Table 2, and Table 3).

Summary of literature data on people with PSP treated with Deep Brain Stimulation

Summary of literature data on people with MSA treated with Deep Brain Stimulation

[b] If many follow-ups were present in the article, we reported the first and the last one.

nbM = Nucleus basalis of Meynert; PSA = Posterior Subthalamic Area; MDS-UPDRS = Movement Disorders Society Unified Parkinson's Disease Rating Scale; NPI = Neuropsychiatric Inventory Questionnaire; FCRST = Free and Cued Selective Reminding Test; NR = Not reported in the respective study.

[*] Patient with atypical parkinsonism not better specified.

Summary of literature data on people with DLB treated with Deep Brain Stimulation

Conclusion: Several limitations undermine the possibility of drawing robust conclusions. However, some interesting insights emerge, such as the relative safety of DBS in PSP and DLB, and the possible positive effect on specific symptoms. Advances in DBS technology and APs pathogenesis comprehension, paired with further research to identify the most suitable targets and stimulation parameters, might lead to more efficacious applications of DBS in these conditions.

Disclosure: Nothing to disclose.

EPO-384

Young-onset Parkinsonism and neuropathy in FIG4 gene mutations

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Background and aims: Young-onset Parkinsonism (YOP) and peripheral neuropathy (PN) have been mostly described in patients bearing pathogenic variants in PARK2 or POLG. Biallellic mutations in FIG4 were originally described in Charcot-Marie-Tooth disease 4J (CMT4J), and more recently Yunis-Varon syndrome and Parkinsonism+CMT4J. We aim to describe a patient with YOP and PN, with compound heterozygous mutations in FIG4.

Methods: Descriptive analysis of clinical, imaging, electrophysiological, genetic findings.

Results: A 39-year-old male, born of nonconsanguineous parents, came to our attention for a one-year history of hands rest tremor and gait impairment. He described pes cavus and hammertoes since childhood and no family history of neurological disorders. On examination there was facial hypomimia, left predominant rest and re-emergent postural tremor, cogwheel rigidity and bradykinesia. Additionally, he had decreased vibration sensation, difficulties in walking on heels and bilaterally decreased arm swing. Brain MRI disclosed small pallidal hypointensities; DaTSCAN a marked bilateral presynaptic dopaminergic deficit. Electromyography revealed a sensory-motor polyneuropathy with severe distal-to-proximal axonal loss and demyelinating features in some slightly preserved nerves. NGS panel, based in WES, for 1410 genes related with neurological disorders, identified two variants in FIG4 gene [(NM_014845.5) – c.122T>C (p.(Ile41Thr)) and (NM_014845.5) – c.1519dup (p.(Tyr507Leufs*10))]. He is currently under levodopa/rotigotine with a good response.

Conclusion: To our knowledge this is the sixth reported patient with Parkinsonism and PN with FIG4 mutations. The majority had young-onset and, the ones who were treated, clinical improvement under antiparkinsonian drugs. NGS sequencing techniques have greatly contributed to the characterization of YOP and expansion of the classical genotype-phenotype correlations.

Disclosure: Nothing to disclose.

EPO-385

Inhibitors of vesicular monoamine transporter type 2 (VMAT2) and the risk of anxiety and depression: meta-analysis

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Background and aims: Inhibitors of vesicular monoamine transporter type 2 (VMAT2 inhibitors) such as tetrabenazine, deutetrabenazine and valbenazine are used in treatment of hyperkinetic movement disorders with FDA-approval for tardive dyskinesia and Huntington's disease. We have conducted a meta-analysis of randomized placebo controlled, double-blind studies to investigate the prevalence of anxiety, depression and suicidal ideation related to the use of VMAT2 inhibitors.

Methods: We searched PubMED and EMBASE for randomized, double-blind, placebo controlled trials of VMAT2 inhibitors. We conducted a random-effects meta-analysis of logit event rates to estimate the risk of anxiety, depression and suicidal ideation in VMAT2 inhibitors as a class and among individual VMAT2 inhibitor medications.

Results: After reviewing eight eligible studies, we observed much lower rates of depression and suicidal adverse events for both VMAT2 inhibitors and placebo then we expected. Our results do not show a significant relationship between VMAT2 inhibitors and suicide, depression, or anxiety-related adverse events. However, the database was too weak to reach statistical power.

Conclusion: The preliminary results of our study indicate that VMAT2 inhibitors are not related to increased risk of depression, suicidal ideation and anxiety, but further studies are needed. It is difficult to generate conclusions from this meta-analysis because many of the included studies did not analyze or report on all of the adverse events we were studying.

Disclosure: Nothing to disclose.

EPO-386

Quantitative Measurement of Iron in NBIA patients with Quantitative Susceptibility Mapping and Clinical Evaluation

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Background and aims: Neurodegeneration with brain iron deposition (NBIA) is a group of inherited diseases in which iron deposition usually occurs in the basal ganglia (BG) in the brain, and presents predominantly extrapyramidal symptomatology, although it has heterogeneous clinical manifestations. The aim of this study is to measure the iron in BG with a sensitive method and to reveal the relationship between the amount of iron accumulation and some of the clinical features (age of onset, subtypes, and course of the disease).

Methods: Patients genetically diagnosed with NBIA (n = 16, 9 PKAN, 3 MPAN, 2 PLAN, 2 Kufor Rakeb) and age- and sex-matched healthy controls were included. 3 Tesla Magnetic Resonance Imaging (MR) including T1, T2 and SWI sequences was performed on all of them. Quantitative iron content in all BG nuclei was evaluated by the QSM method. In addition, the BFM dystonia scale (BFMS) was used to determine clinical severity.
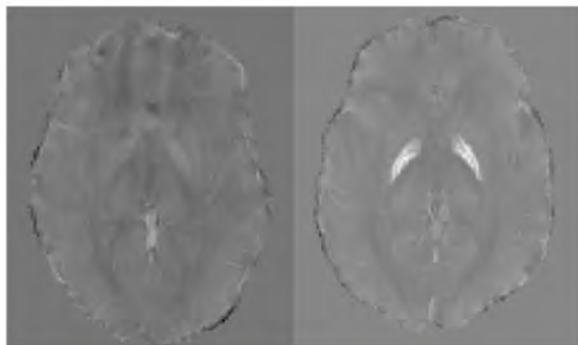
Figure 1: QSM of healthy control vs PKAN patient

Results: The most iron accumulation was found in the GP. Compared to the healthy controls, PKAN patients had in GP, and MPANs in GP and SN with 2.5 times more iron. There was no significant relationship in terms of iron accumulation between the age of onset, gender, and clinical severity.

Conclusion: Iron deposition in the GP seems to play a key role in the pathology of NBIA. However, there may not be a predictable relationship between various clinical features and iron quantification.

Disclosure: Nothing to disclose.

EPO-387

Exploratory analysis of factors driving QoL in people with Parkinson's disease using Adelphi Real World's DSP™ dataset

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Background and aims: Parkinson's disease (PD) is known to impact QoL in people living with the condition. This exploratory analysis aimed to identify symptoms, side-effects, and activities of daily living (ADLs) with the greatest impact on QoL as measured by the EuroQol 5-dimensions (EQ-5D) utility score, visual analog scale (EQ-VAS), and 39-item Parkinson's Disease Questionnaire (PDQ-39).

Methods: The Adelphi Real World Parkinson's Disease Specific Programme (DSP) is a physician- and patient-completed survey, gathering data on symptoms, side-effects, and QoL using the EQ-5D, EQ-VAS and PDQ-39. This analysis used the German dataset from 2019. Symptoms and ADLs were identified to align with items of the Movement Disorder Society Unified Parkinson's Disease Rating Scale (MDS-UPDRS) and side-effects included in the DSP. A Least Absolute Shrinkage and Selection Operator (LASSO) regression analysis was employed to generate a statistical model that selected and estimated coefficients for the variables most closely associated with QoL.

Results: In total, 392 PD patients were included. A subgroup analysis was completed for patients rated at their most recent consultations to be Hoehn & Yahr stages 1–3 (n=301). PD's impacts on hygiene, performing hobbies and activities, and dressing were identified as the major drivers of poor QoL for all measures. OFF time, tremor on action, rigidity, and lack of facial expression were the most frequently identified symptoms driving poorer QoL. The most frequent side-effect driver of poor QoL was hallucinations.

Conclusion: In PD patients, QoL scores are heavily dependent on patients' ability to conduct ADLs, with some motor symptoms also playing a role.

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MS and related disorders 3

EPO-388

The contribution of spinal cord atrophy in the assessment of processing speed performance in Multiple Sclerosis

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Background and aims: In multiple sclerosis (MS), cognitive decline is probably related to the neurodegenerative component of the disease and is associated with brain atrophy, a marker of neuroaxonal damage. However, it is unknown whether cognitive disability prediction can be improved by adding measures of spinal cord (SC) atrophy. We aimed to assess the usefulness of combining SC and brain Gray Matter (GM) volume to explain the frequent impairment observed in processing speed in MS.
Methods: We included 186 patients from Hospital Clinic Barcelona and 67 from University of Naples with available processing speed assessment by Symbol Digit Modalities Test (SDMT). SDMT was obtained regularly for a mean follow-up period of 5 years. Participants had a baseline brain MRI including upper cervical SC segments. Normalized brain GM volume was estimated with SIENAx. Mean Upper Cervical Cord Area (MUCCA) was measured at C2-C3 using the SC toolbox. Lasso regression was used to explain the role of MUCCA in the SDMT performance.
Results: Patients were mainly female (64%), with a mean age of 50 (SD11) years, and relapsing-remitting course (75%). Mean SDMT at baseline and follow-up was 46 (SD13) and 40 (SD14), respectively. When MUCCA was added to GM volume, the model showed a relative improvement of 13% (r^2=0.35) to explain baseline SDMT performance. MUCCA also improved the predictive value of GM volume by 3.3% (r^2=0.31) in the evolution of SDMT.
Conclusion: The combined assessment of MUCCA and brain GM volume helps to describe the behavior of cognitive performance, and provides a more comprehensive evaluation of neuroaxonal damage in MS.
Disclosure: Authors have nothing to disclose related to the present abstract

EPO-389

Effect of ocrelizumab on humoral and cellular immunity in multiple sclerosis and its clinical correlates

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Background and aims: We aim to evaluate immunological effects of anti-CD20 monoclonal antibody ocrelizumab in multiple sclerosis (MS), in particular: (1) changes in total lymphocyte count, lymphocyte subpopulations, neutrophils and immunoglobulins when compared with pre-infusion assessment; (2) any further changes after the first infusion; and (3) possible clinical correlates.
Methods: This real-world observational cohort study has been conducted on prospectively collected data from 2018 to 2021, including MS patients treated with ocrelizumab for at least 2 years (5 infusions). We performed clinical consultations and collected blood samples every three months, and used flow cytometry in the peripheral blood to count total lymphocytes and lymphocytes expressing different phenotypic markers (CD4, CD8, CD19, CD20, CD27, CD3-CD27, CD19-CD27), and nephelometry for serum immunoglobulins.
Results: We recruited 78 MS patients (47.8±10.5; females 48.7%) commencing on ocrelizumab from 2018, with 36.5±6.8 months of follow-up. Over the follow-up, when compared with pre-infusion values we observed reduction of total, CD19 and CD20 lymphocyte counts; however, after the first infusion, their levels remained substantially stable. Over time we observed a progressive reduction of CD8 lymphocytes, while no changes were observed for CD4, CD27, CD3-CD27, CD19-CD27. After the first infusion, we observed reduction in IgG, which further decreased during the follow-up. The probability of EDSS progression was associated with higher CD8 lymphocyte.
Conclusion: Ocrelizumab exerts wide range effects on both humoral and cellular immune response, mostly occurring from the very first infusion. The effect on CD8 cytotoxic lymphocytes was related to the effect on disability progression.
Disclosure: The authors have nothing to disclose.

EPO-390

Effect of ocrelizumab treatment on retinal atrophy: preliminary results from a single-center observational study

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Background and aims: We aim to investigate the effect of Ocrelizumab (OCR) treatment on retinal thinning in patients with relapsing-remitting (RR-) and progressive (P-) multiple sclerosis (MS) and whether rates of peripapillary retinal nerve fiber layer (pRNFL) and ganglion cell+inner plexiform layer (GCIPL) atrophy differ according to treatment response.

Methods: All subjects underwent spectral-domain optical coherence tomography (Spectralis, Heidelberg Engineering) scans at baseline and at 2-years follow-up. Demographic characteristics and effectiveness outcomes throughout follow-up were collected. NEDA3 status was defined as absence of relapses, disability worsening, MRI activity. Eyes with previous optic neuritis were excluded.

Results: We included 33 MS patients [17 RR-MS and 16 P-MS; females: 58%; mean age and disease duration:42.7±11.8 and 9.9±10.3 years; median EDSS: 3.5 (1–6.5)]. No significant differences were observed between baseline and follow-up pRNFL (95.34±9.71 vs 93.07±9.42 μm respectively; p=0.68) and GCIPL (79.97±9.21 vs 79.96±9.22 μm, respectively; p=0.21) thickness. Retinal thinning was similar between RR-MS (pRNFL:- 3.8±7.6 μm; GCIPL: 0.008±3.8 μm) and P-MS patients (pRNFL: -0.5±2.5 μm; GCIPL :-0.03±5.8 μm) (p=0.29 and p=0.52, respectively). While no GCIPL atrophy was observed in patients achieving NEDA3 status during follow-up (baseline vs follow-up thickness: +1.5±6.2 μm), a reduction in GCIPL thinning was observed in patients who lost NEDA3 (baseline vs follow-up thickness: -1.3±2.8 μm; p=0.003).

Conclusion: The overall stability of pRNFL and GCIPL thickness over 2-years follow-up suggests a neuroprotective effect of OCR treatment in RR-MS and P-MS patients. A more pronounced retinal thinning was observed in patients loosing NEDA3 throughout follow-up. Our findings support the role of GCIPL in monitoring treatment response, though should be confirmed by larger studies.

Disclosure: MC,EM,GB,NB,GN,SM,LG,EC,CL:no disclosures. AU:fees from Biogen, Roche, Teva, Merck, Genzyme, Novartis. AL:compensation from Novartis, Sanofi, Biogen, Merck, Roche, Teva; MI:fees from Roche, Genzyme, Merck, Biogen, Novartis.

EPO-391

Disability Improvements With Ublituximab in Relapsing Multiple Sclerosis: Pooled Post Hoc Analyses of ULTIMATE I and II

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Background and aims: Ublituximab, a novel monoclonal antibody targeting a unique epitope of CD20, is glycoengineered for enhanced antibody-dependent cellular cytotoxicity and is administered in 1-hour maintenance infusions after the first infusion. In a prespecified pooled tertiary analysis of the ULTIMATE studies in relapsing multiple sclerosis, ublituximab significantly increased the proportion of patients with 12-week and 24-week confirmed disability improvement (CDI).

Methods: The Phase 3 ULTIMATE I (n=549) and II (n=545) studies evaluated ublituximab (n=543) 450 mg intravenous infusion every 24 weeks or teriflunomide (n=546) 14 mg oral once daily for 96 weeks. Sustained CDI and Expanded Disability Status Scale (EDSS) score improvements (unconfirmed) were evaluated in pooled post hoc analyses.

Results: Among ublituximab patients with 12-week CDI (n=65), 95% sustained the improvement through study end. 12-week CDI was significantly improved with ublituximab versus teriflunomide, regardless of having received prior disease-modifying therapy (p<0.01 for treatment naive and previously treated) (Figure 1). Patients on ublituximab (12.9%) were more likely to have >1 EDSS improvement than patients on teriflunomide (7.0%) (p<0.01) (Figure 2). Significant EDSS improvements of 1.0 and 1.5 steps were seen at Weeks 60, 72, 84, and 96 for ublituximab versus teriflunomide (baseline EDSS score ≥2.0) (Figure 3).
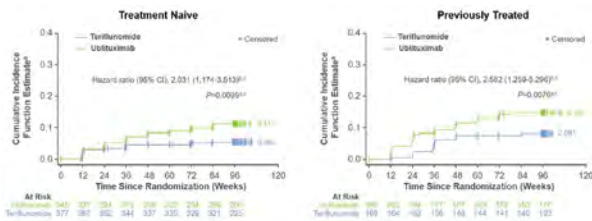
Figure 1: Time to 12-Week CDI by Prior Treatment
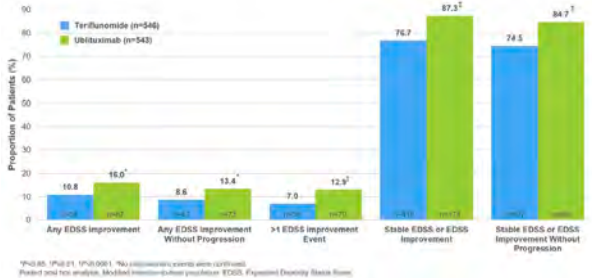
Figure 2: EDSS Improvement[a]
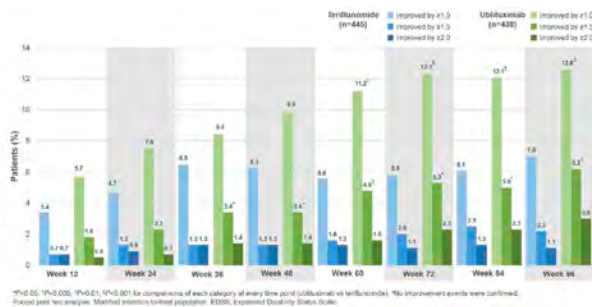
Figure 3: EDSS Improvement (Baseline EDSS Score ≥2.0)[a]

Conclusion: Evaluations of EDSS score improvements during treatment showed a consistent and significant benefit for ublituximab versus teriflunomide. Along with prespecified 12- and 24-week CDI analyses, pooled post hoc evaluations of sustained 12-week CDI and EDSS score provide further evidence of clinically meaningful disability improvement with ublituximab in ULTIMATE I and II.

Disclosure: Authors have received compensation from Pharma companies for speaking, consulting and contracted research.

EPO-392

Treatment patterns prior to and post cladribine in patients with multiple sclerosis

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Background and aims: Cladribine is a disease-modifying drug (DMD) EMA-approved (2017) for the treatment of highly active relapsing multiple sclerosis (RMS). The aim of this study was to identify and characterise treatment switches and disease activity in cladribine-treated patients with MS (PwMS) over time.

Methods: We analysed cladribine-treated RMS patients from the German MS Register during 2017–2021 regarding pre-treatments, switch reasons, efficacy (annualised relapse rate [ARR], expanded disability status scale [EDSS], magnetic resonance imaging [MRI] activity [gd+/new T2 lesions]) and follow-up treatments.

Results: Data of a total of 390 cladribine patients were analysed, of which 26.9% (n=105) were therapy-naïve before initiating cladribine and 7.4% (n=29) had previously received therapy but had been off treatment for ≥1 year. Moreover, 27.7% (n=108) switched from high-efficacy treatments and 36.4%(n=142) from first-line treatments within one year. Most common switch reasons were insufficient efficacy (53.4%) and adverse events (27.1%). During four-year observation, both proportion of patients with MRI activity and ARR were highest in the year prior to therapy start with cladribine (MRI: 44% active, ARR=0.35), and decreased subsequently over time (MRI: ≤17% active, ARR≤0.18). Insufficient efficacy (73.9%) was reported as the most frequent reason for atypical cladribine cessation by a subset of 23 PwMS with available data. Patients who started another DMD after cladribine cessation (n=30) mostly switched to ocrelizumab (60.0%).

Treatment length (years)	≤1	1-2	2-3	≥3	p-value	N
	N=148	N=140	N=83	N=19		
Sex: female	106 (71.6%)	99 (70.7%)	65 (78.3%)	15 (78.9%)	0.56	390
Age at first symptoms	30.8 (10.8)	30.9 (10.1)	31.4 (10.9)	30.1 (9.4)	0.96	366
Age at diagnosis	33.0 (11.2)	32.7 (9.9)	33.1 (10.9)	32.8 (9.9)	0.99	371
Time to diagnosis (years)	0.88 (2.39)	1.68 (3.88)	1.02 (2.09)	1.27 (2.03)	0.33	220
Previous therapy:						390
Switch from high-efficacy treatment	47 (31.8%)	34 (24.3%)	29 (34.9%)	12 (63.2%)		
Switch from first-line treatment	57 (38.5%)	60 (42.9%)	36 (43.4%)	4 (21.1%)		
Therapy-naïve	43 (29.1%)	41 (29.3%)	18 (21.7%)	3 (15.8%)		
Other (e.g. study medication)	1 (0.7%)	5 (3.6%)	0 (0.0%)	0 (0.0%)		
EDSS at initiation of cladribine	2.0 [1.5;3.5]	3.0 [2.0;4.0]	2.0 [1.5;3.5]	2.5 [1.5;4.0]	0.18	246
EDSS after 12 months		2.5 [1.5;3.5]	2.0 [1.5;4.0]	3.0 [2.0;5.0]	0.56	161
EDSS after 24 months			3.0 [1.5;4.0]	3.0 [1.5;4.5]	0.72	87
EDSS at last follow-up	2.0 [1.5;4.0]	3.0 [2.0;4.0]	2.5 [1.5;4.0]	2.5 [2.0;6.0]	0.10	376

Table: Characteristics of PwMS treated with cladribine (N=390) stratified by treatment length (actual duration as per prescribing information/last follow-up). Percentages, mean (standard deviation) or IQR (median [Q25;Q75]) are given.

Figure 1: Distribution of EDSS differences at 2 years (±90 days) after treatment start of cladribine towards baseline EDSS.

Mean EDSS difference after:
1 year (N=148): 0.03
2 years (N=89): 0.19
3 years (N=45): 0.01

Figure 2: Annualized relapse rates (ARR) prior and post to cladribine (CT) initiation. Number of relapses and cumulative follow-up times in years (cum. FU) are given.
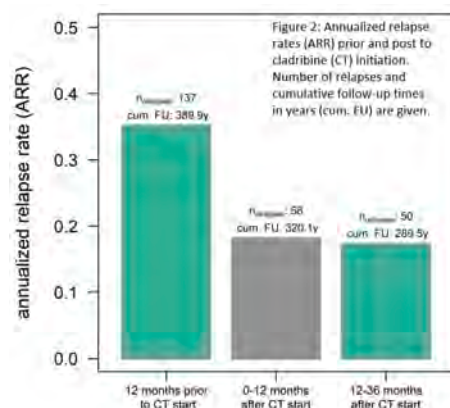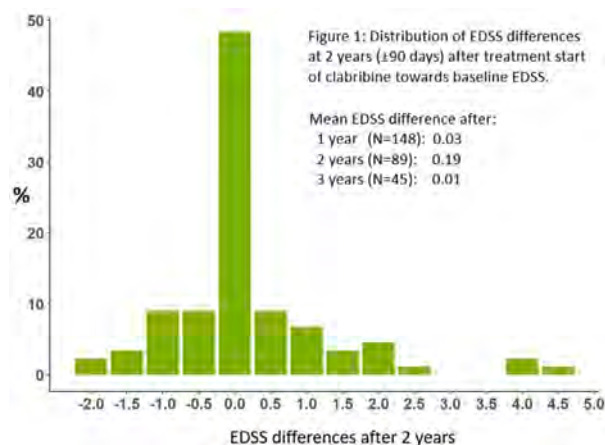
Conclusion: Our data show a long-lasting and prompt efficacy of cladribine regarding both, disease activity and progression. Non-responders were identified early in the treatment cycle and switched accordingly.

Disclosure: The authors have received speaking fees, travel support, honoraria from advisory boards, and/or financial support for research activities from pharmaceutical companies. None resulted in a conflict of interest.

EPO-393

Cost-analysis of subcutaneous versus intravenous administration for natalizumab in Multiple Sclerosis in Spain

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Background and aims: A subcutaneous (SC) formulation of natalizumab has been recently authorized. This study aimed to assess implications for Multiple Sclerosis patients and Spanish healthcare system associated with SC versus intravenous (IV) natalizumab therapy.

Methods: A cost-analysis was developed to estimate SC (not yet-marketed)- and IV- natalizumab annual-cost. A national expert-panel involving neurologists, pharmacists and nurses provided according to natalizumab experience (IV) or estimated (SC) resource-consumption for drug- and patient-preparation, administration, and documentation, considering patient-route-care. One hour of observation was applied to first 6- (SC) or 12- (IV) doses, and 5 min for successive doses. Hospital-day facilities at a reference-hospital were considered for IV administrations and the first 6 SC injections. For successive SC injections, either reference-hospital or regional-hospital, in consultation facilities were considered. Productivity-time associated to travel (28 min to reference-hospital, 12 min to regional-hospital), and waiting-time pre- and post-treatment (SC: 15 min, IV: 25 min) were assessed for patients and for caregivers (accompanying 20% of SC and 35% of IV administrations). National salaries for healthcare-professionals were used for cost-estimation (€, year 2021).

Results: At years 1&2, total time and cost-saving (excluding drug-acquisition-cost)/patient driven by saving on administration, patient- and caregiver-productivity for SC at reference-hospital versus IV at reference-hospital were 116h (54.6%) and €3,682.42 (66.2%). In case of SC at regional-hospital were 129h (60.6%) and €3,883.47 (69.8%).

Conclusion: Natalizumab SC was associated with cost-savings for healthcare system by avoiding drug-preparation, reducing administration-time and freeing up infusion-suite-capacity. Additional cost-savings could be derived with regional-hospital-administration of natalizumab SC by reducing productivity loss.

Disclosure: This analysis was supported by Biogen Spain S.L.U. LG and IT are Biogen employees. MG, NE and IO are PORIB employees. TASC group members have received compensation for serving on activities with pharmaceutical companies including Biogen.

EPO-394

Ublituximab Efficacy Outcomes in Relapsing Multiple Sclerosis Patient Subgroups in the ULTIMATE I and II Studies

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Background and aims: Ublituximab is a novel monoclonal antibody targeting a unique epitope of CD20. Ublituximab is glycoengineered for enhanced antibody-dependent cellular cytotoxicity and is administered in 1-hour maintenance infusions after the first infusion. In ULTIMATE I and II, ublituximab significantly improved annualized relapse rate (ARR), number of gadolinium-enhancing (Gd+) T1 lesions and new/enlarging T2 lesions, and proportion of patients achieving no evidence of disease activity (NEDA) versus teriflunomide in patients with relapsing multiple sclerosis (RMS).

Methods: The Phase 3 ULTIMATE I (N=549) and II (N=545) studies evaluated ublituximab 450 mg intravenous infusion every 24 weeks or teriflunomide 14 mg oral once daily for 96 weeks in patients with RMS. Pooled post hoc analyses evaluated efficacy based on prespecified subgroups, including: sex (male or female), age (<38 or ≥38 years), Expanded Disability Status Scale (EDSS) score (≤3.5 or ≥4.0), number of relapses in prior 2 years (≤1, 2, or ≥3), prior disease-modifying therapy (yes or no), and baseline number of Gd+ lesions (0 or ≥1).

Results: A statistically significant benefit with ublituximab versus teriflunomide was observed for ARR (Figure 1), number of Gd+ T1 lesions (p<0.0001 for all; Figure 2), number of new/enlarging T2 lesions (p<0.0001 for all), as well as NEDA (24–96 weeks re-baselined; p<0.0001 for all; Figure 3) among nearly all evaluated subgroups.
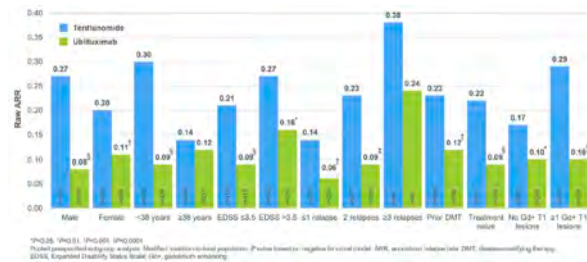
Figure 1: ARR by Subpopulation
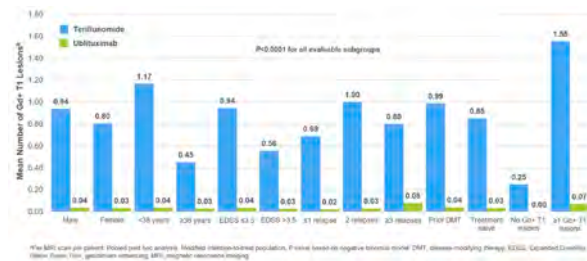
Figure 2. Gd+ T1 Lesions by Subpopulation
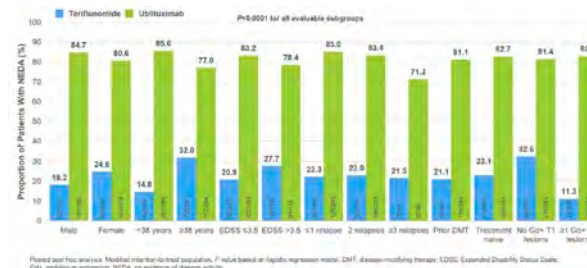
Figure 3. NEDA by Subpopulation (Week 24 to Week 96, With Re-baselining at Week 24)

Conclusion: Ublituximab was superior to teriflunomide in key efficacy measures across multiple demographic and disease characteristic subpopulations.

Disclosure: Authors have received compensation from Pharma companies for speaking, consulting and contracted research.

EPO-395

Repeated confirmed disability progressions analyses of the OPERA and ORATORIO studies and their open-label extensions

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Background and aims: Time-to-first event analyses neglect information about subsequent progression; repeated event analyses provide more comprehensive assessments of long-term disability trajectories. This analysis assessed the rate of repeated 48-week (48W) confirmed disability progressions (CDP) during OPERA (NCT01247324/NCT01412333) and ORATORIO (NCT01194570) and their open-label extensions (OLE).

Methods: In the double-blind period (DBP) patients were randomised to ocrelizumab (OCR) or placebo (PBO; ORATORIO)/interferon-beta 1a (IFN; OPERA) for ≥120/96 weeks. OLE patients continued OCR (OCR-OCR) or switched to OCR (PBO-OCR)/(IFN-OCR). Repeated 48W-CDP rates were defined as for prior first CDP event analyses, then Expanded Disability Status Scale (EDSS), Nine-Hole Peg Test (9HPT) or Timed 25-Foot Walk Test (T25FW) following rebaselining after the respective initial progression of the previous event.

Results: In primary progressive multiple sclerosis (PPMS), after 7 years, continuous OCR treatment reduced the rate of repeated 48W-CDP-EDSS, repeated 48W-CDP-9HPT and repeated 48W-CDP-T25FW vs PBO-OCR (24%, 36%, 27%; Table 1). Annualised repeated event rate ratios (ARER: 48W-CDP-EDSS) for OCR-OCR/PBO-OCR were: 0.52 at Week (W) 48, 0.64 at W144, 1.24 at W240 and 1.04 at W384 (Table 2); CDP trajectories were similar for 48W-CDP-9HPT and 48W-CDP-T25FW. In relapsing MS (RMS), after 7 years, continuous OCR reduced the rate of repeated 48W-CDP-EDSS vs IFN-OCR by 26% (Table 1). ARER: 48W-CDP-EDSS for OCR-OCR/IFN-OCR was: 0.41 at W48 DBP, 0.45 at W96 DBP, 0.84 at OLE W48 and 0.92 at OLE W288 (Table 2).

ORATORIO: OCR-OCR vs PBO-OCR	Rate ratio	95% CI	P-value
Repeated 48W-CDP-EDSS	0.76	0.62–0.92	0.005
Repeated 48W-CDP-9HPT	0.64	0.47–0.86	0.005
Repeated 48W-CDP-T25FW	0.73	0.59–0.90	0.003
OPERA: OCR-OCR vs IFN-OCR	**Rate ratio**	**95% CI**	**P-value**
Repeated 48W-CDP-EDSS	0.74	0.58–0.95	0.017

9HPT, Nine-Hole Peg Test; CDP, confirmed disability progression; EDSS, Expanded Disability Status Scale; IFN, interferon; OCR, ocrelizumab; PBO, placebo; T25FW, Timed 25-Foot Walk Test; W, week. Clinical cut-off date: 27 November 2020.

Table 1: Rate ratio for repeated: 48W-CDP-EDSS, 48W-CDP-9HPT and 48W-CDP-T25FW, after 7 years in patients from ORATORIO and OPERA studies

ORATORIO: OCR-OCR/PBO-OCR (48W-CDP-EDSS)	ARER (95% CI)	P-value	OPERA: OCR-OCR/IFN-OCR (48W-CDP-EDSS)	ARER (95% CI)	P-value
W48 (DBP)	0.52 (0.33–0.64)	0.008	W48 (DBP)	0.41 (0.21–0.79)	0.007
W144 (ECP start)	0.64 (0.44–0.94)	0.022	W96 (DBP end/OLE start)	0.45 (0.26–0.78)	0.004
W240 (ECP end/OLE start)	1.24 (0.71–2.17)	0.451	W48 OLE	0.84 (0.43–1.64)	0.610
W384 (OLE)	1.04 (0.45–2.42)	0.919	W288 OLE	0.92 (0.44–1.94)	0.833

ARER, annualised repeated event rate ratio; CDP, confirmed disability progression; DBP, double-blind period; ECP, extended controlled period; EDSS, Expanded Disability Status Scale; IFN, interferon; OCR, ocrelizumab; OLE, open-label extension; PBO, placebo; W, week. Clinical cut-off date: 27 November 2020.

Table 2: Annualised repeated event rate ratios: 48W-CDP-EDSS, after 7 years in patients from ORATORIO (DBP, ECP, OLE) and OPERA (DBP, OLE) studies

Conclusion: Repeated CDP analyses better capture treatment effects after first disability progression events, providing further insights into the longer trajectory of disease progression and response to treatment.

Disclosure: Sponsored by F. Hoffmann-La Roche Ltd; writing and editorial assistance was provided by Articulate Science, UK.

EPO-396

A long term post-marketing observational monocentric study of a population of patients treated with Dimethyl Fumarate

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Background and aims: To date, long-term data of efficacy and safety of Dimethyl Fumarate (DMF) in relapsing-remitting multiple sclerosis patients (RR-MS) in real-world practice are poor. The aim of this study was to analyze long-term effectiveness and safety of DMF in RR-MS and to identifying predictive factors of efficacy

Methods: 838 patients who started DMF between January 2014 and July 2020 at San Raffaele Hospital MS Center were included with a mean follow-up of 39.5 months(±25.2). We analyzed the results for protocol.

Results: Basal characteristics are shown in Table 1. 40% were naïve, 37% switched from first-line treatment for intolerance and 16% for inefficacy, 7% switched from second-lines treatment. 30% discontinued DMF. ARR decreased from 0.63 at baseline to 0.12 and 0.05 at first and second year respectively(p<0.0001) and then remained low for over 5 years. 72% and 84% of patients were relapse free and progression free at 5 years respectively. T1-gadolinium-enhancing lesions decreased from 0.39 at baseline to 0.25 and to 0.10 at first and second year respectively(p<0.0001) and then remained low. Predictive factors of discontinuation for inefficacy were age, ARR in previous year, MRI activity at baseline, disease activity at rebaseline. 2017 was a watershed for a better patient's selection with a decrease of efficacy discontinuation rate from 19.2% to 8% (Figure1). The incidence/type of adverse events were in line with the known safety profile of DMF (Table 2).

Table 1

Table 2

Figure 1

Conclusion: Our data confirm long-term safety and efficacy of DMF. DMF can be considered as initial treatment for patients with low/moderate activity and without negative predictive factors

Disclosure: All the authors do not have disclosures related to this manuscript.

EPO-397

Beyond steady-state amyloid PET to detect demyelination in multiple sclerosis (MS)

M. Pardini [1], A. Chincarini [2], L. Roccatagliata [1], A. Donniaquio [3], I. Donegani [3], R. Gianeri [2], F. Sensi [2], G. Novi [4], A. Laroni [1], A. Murialdo [4], G. Ribizzi [4], A. Uccelli [1], M. Inglese [1], F. Nobili [1], S. Morbelli [1]

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Background and aims: Quantification of myelin loss in multiple sclerosis (MS) remains challenging. Based on the proposed amyloid PET tracers affinity to myelin, we evaluated the value of early PET dynamic images followed by late acquisition to elucidate the biologic underpinnings of amyloid PET in MS.

Methods: 95 white matter lesions in eleven MS patients (6 PPMS, 5 RRMS, age 43.2±10.8 years) were assessed using 3T MRI. Baseline [18F]Florbetaben PET (early dynamic acquisition of the first 30 minutes and late steady state acquisition 90–110 minutes p.i.) data were analyzed. After PET normalization on the cerebellum, SUVratio in the individual lesions and in the contralateral normal appearing white matter (NAWM) was measured in late and early PET images. Early frames were submitted to a principal component analysis (PCA). Late lesional and NAWM SUVr and PCA scores, were compared and correlated among themselves and with T1/T2 ratio, a proxy measure of myelin loss, by means of linear regression and Bland-Altmann plot.

Results: Two PCAs explained 90% of variance of early dynamic tracer profile. PCA1 corresponded to a positive and constant vector, while PCA2 loads showed a descending trend overtime. Late SUVratio and early PCA2 were significantly lower in lesions compared to NAWM (p<0.001). Both in lesions and in NAWM, late static SUVratio and PCA2 (but not PCA1) correlated with and T1/T2 ratio values (all p<0.001), while PCA1 did not.

Conclusion: AMY-PET tracer kinetic over time might open a further window on the capability of - amyloid PET to assess myelin changes in MS lesions.

Disclosure: The work was supported by a grant from the Italian Ministry of Health (RIcerca Finalizzata, RF-2018-12366238).

EPO-398

Abstract withdrawn.

EPO-399

Improved Quality of Life With Ublituximab in the ULTIMATE I and II Studies in Relapsing Multiple Sclerosis

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Background and aims: Ublituximab, a novel monoclonal antibody targeting a unique epitope on the CD20 antigen, is glycoengineered for enhanced antibody-dependent cellular cytotoxicity and is administered in 1-hour maintenance infusions after the first infusion. In ULTIMATE I and II, ublituximab significantly improved relapse rates compared with teriflunomide in patients with relapsing multiple sclerosis (RMS).

Methods: The Phase 3 ULTIMATE I (N=549) and II (n=545) studies evaluated ublituximab 450 mg intravenous infusion every 24 weeks (following Day 1 infusion of 150 mg) or teriflunomide 14 mg oral once daily for 96 weeks in patients with RMS. Multiple Sclerosis Quality of Life-54 (MSQOL-54) assessments, inclusive of Short Form-36 (SF-36), were tertiary endpoints of the individual studies. Post hoc pooled analyses of the change from baseline were conducted for Weeks 24, 48, and 96 and evaluated based on all postbaseline timepoints using mixed-model repeated measures (ublituximab, n=543; teriflunomide, n=546).

Results: At all postbaseline timepoints, statistically significant improvements favoring ublituximab were seen in overall quality of life, physical and mental health composites, role limitations (physical), physical health, changes in health, and energy (Figure 1), and in SF-36 physical component summary, physical functioning, and role-physical (Table 1).
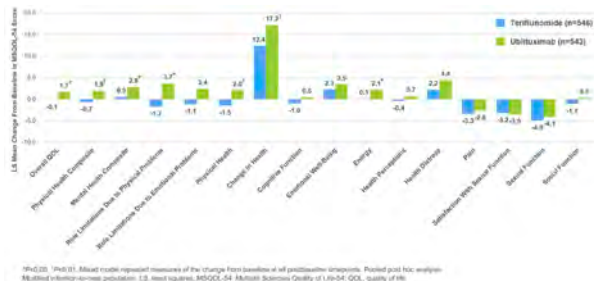
Figure 1. Change in MSQOL-54 Scores From Baseline to Week 96

Table 1. Change in SF-36 Scores From Baseline to Week 96

Conclusion: Ublituximab provided significant improvement over teriflunomide in multiple measures of quality of life and physical functioning at 96 weeks in ULTIMATE I and II.

Disclosure: Authors have received compensation from Pharma companies for speaking, consulting and contracted research.

EPO-400

The real-world effectiveness of ocrelizumab for treating patients with MS: 1-year data from the MuSicalE study

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Background and aims: Real-world experience with ocrelizumab is rapidly-growing, with approximately 225,000 patients with multiple sclerosis (PwMS) treated globally; however, evidence of the efficacy-safety profile in clinical practice remains limited. MuSicalE (NCT03593590) is a study designed to assess the real-world effectiveness and safety of ocrelizumab over 4 years.

Methods: PwMS initiating ocrelizumab per local label (25 countries) were included. The primary endpoint was change in SymptoMScreen, key secondary outcomes included Expanded Disability Status Scale (EDSS), relapse rate, MS Impact Scale (MSIS-29), Fatigue Scale for Motor and Cognitive Functions (FSMC), ABILHAND-56 and 12-item MS Walking Scale. Here, we report interim results from the 1-year follow-up.

Results: A total of 1,720 patients were enrolled, of which 1,059 reached the 1-year follow-up. SymptoMScreen scores showed slight improvements in daily functioning across all cohorts (relapsing-remitting MS, 21.8 to 20.2; secondary progressive [SP]MS, 28.2 to 27.4; primary progressive MS, 27.6 to 26.9). Similar improvements were observed across other patient reported outcomes, except for the SPMS cohort, where worsening in fatigue (FSMC, 65.3 to 67.6) and psychological well-being (MSIS-29 psychological, 42.3 to 44.0) were observed. For most patients (90.0%), EDSS remained stable or improved; no relapses were reported in 91.4% of relapsing PwMS. Adverse events (AEs) and serious AEs were reported in 44.8% and 3.5% of patients, respectively. Four fatalities (ocrelizumab-unrelated) were reported.
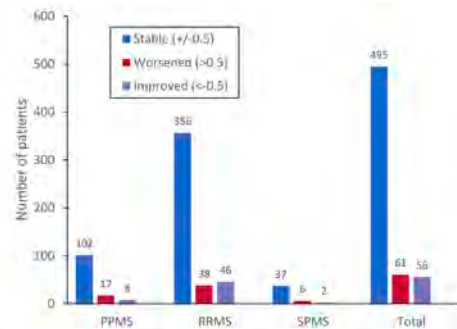
Figure 1. Absolute changes in EDSS at Year 1

Table 1. Baseline characteristics for all enrolled patients and patients with 1 year of follow-up

Conclusion: In this large, global, real-world cohort, 1-year treatment with ocrelizumab was associated with low levels of disease progression and activity, stabilisation and potential improvement in daily functioning, and a safety profile in line with clinical trials.

Disclosure: This study was sponsored by F. Hoffmann-La Roche Ltd; writing and editorial assistance was provided by Articulate Science, UK.

MS and related disorders 4

EPO-401

Cancer risk of immunosuppressive treatment in multiple sclerosis patients

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Background and aims: Our aim is to study if patients treated with an immunosuppressive drug (Fingolimod) are at risk of a higher cumulative incidence of secondary malignancies.

Methods: Retrospective cohort study of all patients treated with Fingolimod (FTY) in a tertiary hospital Data collected were demographic and clinical features as well as treatment duration on FTY were collected and cancer incidence was compared with cumulative incidence data in general population.

Results: 255 MS patients on FTY were included. Mean age at diagnosis was 29 years old with 73-month average before treatment discontinuation. 15 women and 4 men developed cancer with a cumulative incidence of 7.45 % Duration of treatment with FTY before malignancy was 83 months Most frequent malignancy in women was gynecological and in men were prostate and lymphoma The relative risk of cancer comparing the accumulated malignancy rate was 2.8 without statistically significant differences
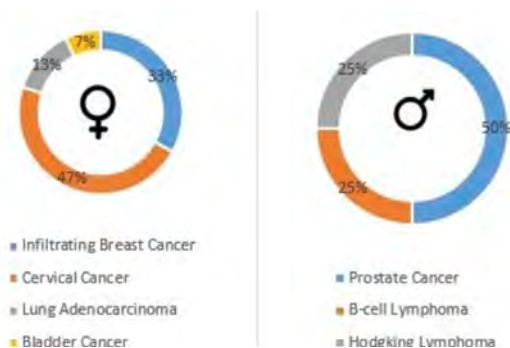
Conclusion: Cancer comorbidity in our FTY cohort was higher than expected in general population with a relative risk up to 2.8 Multicenter studies on long-term outcomes are needed to confirm or rule out these data but a close follow-up for patients on immunosuppressive disease modifying therapies, especially those on FTY is recommended.

Disclosure: E.M Alba-Suárez, J. Díaz-Díaz and I. Gómez-Estevez ,M. Luque-Alarcón, J.M. Martinez-Sesmero, J.A. Peña Pedrosa have nothing to disclose. C. Oreja-Guevara has received speaker and consultation fees from Biogen Idec, B.

EPO-402

Tailoring Rituximab according to memory B-cell vs B-cell monitoring in Neuromyelitis Optica Spectrum Disorder and MOGAD

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Background and aims: To evaluate the effect of a RTX personalized treatment approach based on memory B-cell vs B-cell monitoring on efficacy and infusion rates in neuromielitis optica spectrum disorder (NMOSD) and MOG associated antibody diseases (MOGAD).

Methods: This is a retrospective, uncontrolled, single center study performed at the Regional Reference Centre for Multiple Sclerosis (C.RE.S.M.), San Luigi University Hospital, Orbassano, Italy. All patients were treated with RTX induction, followed by maintenance infusion at the dosage of 1000 mg: initially according to B-cell CD19+ monitoring (>0.1% of lymphocytes), and subsequently according to memory B-cell (CD27+) repopulation (>0.05% of lymphocytes for the first 2 years, and subsequently >0.1%). Disease activity was assessed as clinical and/or MRI activity.

Results: 19 patients were included in the analysis. Median follow-up was 5.01 years [range 2.73-7.41]. Annualized relapse rate (ARR) was 2.37 [Standard deviation (SD), 1.34] in the year before RTX start and decreased to 0.68 (SD 0.88) in the subsequent years after RTX initiation. ARR did not differ before and after CD27 monitoring start. Median inter-dose time was 8.80 [range 5.78–14.23] before CD27 monitoring and 14.00 months [range 8.56–31.60] after CD27 monitoring (Wilcoxon Test Z -3.82; p<0.001). No severe adverse events were observed during treatment.

Conclusion: Our findings suggest that, compared to CD19+ monitoring, memory B-cell based RTX reinfusion regimen is able to reduce the number of RTX reinfusions with comparable efficacy and safety profile.

Disclosure: Dr Nicolo Bruschi has nothing to disclose. Fundings to report: none.

EPO-403

Risk factors for serious infections in patients with MS receiving long-term ocrelizumab treatment: Multivariate analyses

T. Derfuss [1], R. Bermel [2], C. Lin [3], S. Hauser [4], L. Kappos [5], T. Vollmer [6], G. Comi [7], G. Giovannoni [8], H. Hartung [9], J. Wang [3], N. Jessop [10], C. Chognot [10], L. Craveiro [10], A. Bar-Or [11]

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Background and aims: Serious infections (SIs) are reported infrequently in patients with multiple sclerosis (MS) treated with ocrelizumab (OCR), and incidence rates remain stable over time. However, little is known about the risk factors associated with SIs in patients continuously treated with OCR over the longer term.

Methods: Demographics (age, sex, body mass index [BMI], geographic region), disease characteristics (disability level, disease duration, relapses, treatment history), comorbidities and OCR-related covariates (immunoglobulin [Ig]G and IgM levels, treatment duration) were included in a multivariate Poisson Generalized Estimating Equation model. Separate models were built for patients with relapsing MS (RMS) and primary progressive MS (PPMS) who received >=1 dose of OCR during the Phase III OPERA (NCT01247324/NCT01412333) and ORATORIO (NCT01194570) trials and associated open-label extensions.

Results: As of January 2020, 2,092 patients had received OCR treatment for a median (max) time of 5.57 (8.7) years (Table 1). In patients with RMS, having >=2 comorbidities was associated with a significantly higher risk of SIs (Table 2); diabetes, renal and urinary tract disorders and depression showed the highest risk (univariate analyses). In patients with PPMS, an Expanded Disability Status Scale score >6.0 presented a six-fold increased risk of SIs; BMI>25kg/m^2 and low IgM levels (<0.4g/L) were also statistically significant risk factors (Table 3). In both RMS and PPMS, there was no increased risk associated with longer treatment duration.

Characteristic	OPERA (N=1,448)	ORATORIO (N=644)
Patient years	7,862.2	3,562.0
Median time on treatment, years (range)	5.53 (0.0–8.2)	6.43 (0.1–8.7)
Age at baseline, mean (SD) years	38.1 (9.3)	45.8 (8.1)
Age at CCOD, mean (SD) years	44.6 (9.2)	52.6 (7.8)
<40, n (%)	448 (30.9)	43 (6.7)
40–59, n (%)	919 (63.5)	454 (70.5)
>=60, n (%)	81 (5.6)	147 (22.8)
Sex, n (%)		
Female	949 (65.5)	320 (49.7)
BMI at baseline, mean (SD) kg/m²	26.2 (6.1)	25.0 (4.9)
Underweight <18.5 (%)	56 (3.9)	27 (4.2)
Normal weight 18.5–<25 (%)	677 (46.8)	345 (53.6)
Overweight 25–<30 (%)	389 (26.9)	174 (27.0)
Obese >=30 (%)	312 (21.5)	96 (14.9)
Unknown (%)	14 (1.0)	2 (0.3)
Subregion, n (%)		
Europe, Canada, Australia, South America	1,090 (75.3)	558 (86.6)
USA	358 (24.7)	86 (13.4)
EDSS at OCR start[b], mean (SD)	2.74 (1.37)	4.81 (1.28)
<3.0, n (%)	810 (55.9)	12 (1.9)
3.0–6.0, n (%)	625 (43.2)	529 (82.1)
>6.0, n (%)	13 (0.9)	102 (15.8)
Missing, n (%)	0	1 (0.2)
Disease duration since symptom onset, n (%)		
<5 years	658 (45.4)	190 (29.5)
5–10 years	405 (28.0)	288 (44.7)
>10 years	385 (26.6)	147 (22.8)
Missing	0	19 (3.0)
Number of relapses in year before OCR start, mean (SD)	0.09 (0.35)	0.01 (0.09)
Previous DMTs, n (%)		
0	1,065 (73.5)	569 (88.4)
1	345 (23.8)	63 (9.8)
>=2	38 (2.6)	12 (1.9)
Comorbidities at last known follow-up, n (%)		
Rheumatological and auto-immune disorders	38 (2.6)	20 (3.1)
Cardiovascular disorders	234 (16.2)	168 (26.1)
Cerebrovascular disorders	3 (0.2)	3 (0.5)
Chronic pulmonary disorders	108 (7.5)	36 (5.6)
Depression	401 (27.7)	185 (28.7)
Diabetes	38 (2.6)	36 (5.6)
Malignancies	2 (0.1)	3 (0.5)
Gastrointestinal and Liver disorders	37 (2.6)	24 (3.7)
Previous infections	481 (33.2)	224 (34.8)
Renal and urinary tract disorders	219 (15.1)	150 (23.3)
Number of comorbidities at last known follow-up, n (%)		
None	534 (36.9)	202 (31.4)
1	462 (31.9)	171 (26.6)
>=2	452 (31.2)	271 (42.1)

[a]CCOD, 3 January 2020; [b]Last valid assessment prior to the OCR treatment in DBP and in OLE for patients originally randomised to OCR arm and for switchers, respectively.
BMI, body mass index; CCOD, clinical cut-off date; DBP, double-blind period; DMT, disease-modifying therapy; EDSS, Expanded Disability Status Scale; OCR, ocrelizumab; OLE, open-label extension.

Table 1 - Demographic and clinical characteristics of patients from OPERA and ORATORIO included in the analysis at baseline and CCOD

Covariate	Serious infections			
	RR	Lower 95% CI	Upper 95% CI	p-value
Male (vs female)	1.0823	0.6961	1.6827	0.7253
>=45 years old at infusion start (vs <45)	0.8612	0.5326	1.3925	0.5422
BMI (vs 18.5–25 kg/m²)				
<18.5	2.0059	0.7401	5.4364	0.1712
>25	0.9942	0.6218	1.5898	0.9808
USA patients (vs ROW)	1.0057	0.5860	1.7259	0.9836
Number of comorbidities (vs 0)				
1	1.5878	0.9109	2.7676	0.1030
>=2	**2.2425**	**1.2084**	**4.1615**	**0.0105**
EDSS (vs <3)				
3–6	1.0896	0.6758	1.7568	0.7248
>6	2.0297	0.5877	7.0103	0.2630
>10 years disease duration (vs <=10)	1.3053	0.8096	2.1043	0.2742
Relapse ≤1 year prior to OCR start (vs no relapse)	1.5256	0.9275	2.5094	0.0962
Relapse during treatment (vs no relapse)	1.2073	0.4375	3.3315	0.7161
Prior DMT treatment (vs none)	1.4014	0.8553	2.2962	0.1805
IFN β-1a treatment arm (vs OCR treatment arm)	0.9129	0.5624	1.4819	0.7124
IgM <0.4 g/L (vs >=0.4)	0.8401	0.5302	1.3310	0.4581
IgG <LLN (vs >=LLN)	1.8590	0.8098	4.2675	0.1437
Time on OCR (per year)	0.9199	0.8241	1.0268	0.1365

BMI, body mass index; CI, confidence interval; DMT, disease-modifying therapy; EDSS, Expanded Disability Status Scale; IFN, interferon; Ig, immunoglobulin; LLN, lower limit of normal; OCR, ocrelizumab; RMS, relapsing multiple sclerosis; ROW, rest of world; RR, rate ratio.

Table 2 - Multivariate model for risk of infections and serious infections in OPERA (RMS)

Table 3 – Multivariate model for risk of infections and serious infections in ORATORIO (PPMS)

Covariate	Serious infections			
	RR	Lower 95% CI	Upper 95% CI	p-value
Male (vs female)	1.2187	0.7551	1.9668	0.4181
>=50 years old at OCR start (vs <50)	1.1643	0.7549	1.7958	0.4913
BMI (vs 18.5–25 kg/m²)				
<18.5	1.6487	0.3312	8.2080	0.5415
>25	**1.8980**	**1.2360**	**2.9144**	**0.0034**
USA patients (vs ROW)	1.5042	0.8587	2.6347	0.1535
Number of comorbidities (vs 0)				
1	0.9043	0.4751	1.7212	0.7594
>=2	1.3705	0.8052	2.3327	0.2454
EDSS (vs <3)				
3–6	1.8268	0.7009	4.7615	0.2177
>6	**6.0775**	**2.2616**	**16.3316**	**0.0003**
>6 years disease duration (vs <=6)	1.1080	0.6338	1.9370	0.7190
Prior DMT treatment (vs none)	0.9343	0.4979	1.7534	0.8325
Placebo treatment arm (vs OCR treatment arm)	1.8218	0.9441	3.5155	0.0737
IgM <0.4 g/L (vs >=0.4)	**1.6373**	**1.0509**	**2.5512**	**0.0293**
IgG <LLN (vs >=LLN)	1.2953	0.6245	2.6869	0.4870
Time on OCR (per year)	1.0251	0.9222	1.1395	0.6463

BMI, body mass index; CI, confidence interval; DMT, disease-modifying therapy; EDSS, Expanded Disability Status Scale; Ig, immunoglobulin; LLN, lower limit of normal; OCR, ocrelizumab; PPMS, primary progressive multiple sclerosis; ROW, rest of world; RR, rate ratio.

Table 3 - Multivariate model for risk of infections and serious infection in ORATORIO (PPMS)

Conclusion: No association between ocrelizumab treatment duration and risk of SIs was noted with long-term treatment. Addressing potentially modifiable risk factors, such as comorbidities and BMI, may reduce the risk of SIs.

Disclosure: Sponsored by F. Hoffmann-La Roche Ltd; writing and editorial assistance was provided by Articulate Science, UK.

EPO-404

Tocilizumab Desensitization in Neuromyelitis Optica Spectrum Disorder

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Background and aims: Tocilizumab is a humanized anti-human IL-6 receptor monoclonal antibody, used with good efficacy and safety profiles in Neuromyelitis Optica Spectrum Disorder (NMOSD). The most common adverse reactions to Tocilizumab are infections and gastrointestinal symptoms. However, hypersensitivity reactions are also described and in the majority of cases they are mild, but anaphylactic, life-threatening reactions can occur as well, leading to discontinuation of the treatment.

Methods: N/A

Results: A 50-year-old woman, with past history of hypothyroidism and no known allergies, was diagnosed with NMOSD with anti-Aquaporin-4 antibodies after presenting with a longitudinally extensive C6-D10 myelitis. She initiated tocilizumab and completed 5 treatments without problems. On the 6th treatment, after 15-30 minutes infusion was started, the patient presented with erythematous, papular, large, very itchy skin lesions on the heels, which then generalized to the entire integument and with associated hypotension. One month later, tocilizumab was administered slowing down the infusion rate and with premedication, including antihistamines and steroids, with the same reaction. Therapy was switched to Rituximab but urticariforme rash was observed. Allergy tests for tocilizumab revealed a positive intradermal test. The patient was initiated with a rapid intravenous desensitization to tocilizumab procedure and a 12-steps protocol was performed, reaching a cumulative dose of 400mg. The patient remains clinically stable, without relapses or clinical worsening.

Hypersensitivity reaction to tocilizumab

Conclusion: Desensitization protocols allow for a safe readministration of drugs after Type I hypersensitivity reactions (IgE-mediated). Desensitization is a promising method for NMOSD patients with tocilizumab hypersensitivity and can be used in selected patients, without loss of treatment efficacy.

Disclosure: Nothing to disclose.

EPO-405

Ocrelizumab dosing delay in multiple sclerosis during SARS-CoV-2 pandemic: the San Raffaele Hospital experience.

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Background and aims: During COVID-19 pandemic second line disease modifying therapies (DMTs) for multiple sclerosis (MS), have been frequently postponed because of the epidemiological situation and the lack of safety information. We retrospectively assessed clinical implications of Ocrelizumab dosing delay in the MS cohort of the San Raffaele Hospital, in Milan (Italy).

Methods: Data from 90 MS patients (65 RRMS, 25 PPMS) with Ocrelizumab dosing delay have been retrospectively obtained: in particular MS history, neurological examinations, white blood cells count (particularly lymphocyte subsets) and neuroradiological data have been collected.

Results: Enrolled patients have been followed up for a mean of 9.5 ± 2.8 months after Ocrelizumab dosing delay (mean dosing interval 7.67 ± 0.79 months). None of our 65 RRMS patients had clinical relapses, nor rapid disability worsening has been experienced by the PPMS cohort. Pre-infusion CD19+/CD20+ lymphocyte subset was available in 75/90 patients, with 18/75 patients showing significant B cells repopulation (defined as CD19+/CD20+ $\geq 1.0\%$). MRI data were available in 47/90 patients, with 5/47 patients showing evidence of neuroradiological disease activity (mild in all reported cases and in the absence of any correlation with B cells repopulation).

Conclusion: Our data suggest Ocrelizumab dosing delay is generally safe in MS patients. Experiences during COVID-19 pandemic could be a starting point towards a more personalized scheduling of Ocrelizumab therapy

Disclosure: The present work is the result of a spontaneous research initiative in the absence of any relevant specific conflict of interest.

EPO-406

Comparison of late-onset and early-onset people with multiple sclerosis based on cognitive and physical assessments

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Background and aims: Late-onset multiple sclerosis (LOMS) and early-onset multiple sclerosis (EOMS) are less common, and their prognosis can be different. The aim was to assess and compare cognitive functions between patients with LOMS and EOMS.

Methods: Patients with LOMS (initial age≥50 years) (n=32) and age-, gender-, and type of MS-matched patients with EOMS (initial age between 15–18 years) (n=125) were assessed with the Brief International Cognitive Assessment for Multiple Sclerosis (BICAMS) battery which included the Symbol Digit Modalities Test (SDMT), the California Verbal Learning Test-2 (CVLT2) and the Brief Visuospatial Memory Test-Revised (BVMT-R). The upper extremity function was assessed using the 9 Hole Peg Test (9DPT), Timed 25-Foot Walk Test (T25FW), and Timed up Go (TUG) was used to assess lower extremity function were evaluated.

Results: There was no significant difference in disease duration between the two groups. The EDSS score and age were higher in the LOMS group (2.90±2.07 and 60.25±5.42, respectively) compared with EOMS (1.33±1.83 and 25.76±8.98, respectively). Covariates included age and the EDSS score. There was no significant difference between the groups regarding T25FW, TUG, 9HPT, and BICAMS (p>0.05).

Conclusion: The cognitive, upper, and lower extremity functions were similar in the two groups. Considering that distribution of gender and the disease durations were similar; these results suggest that the prognosis of EOMS may be worse than expected.

Disclosure: Nothing to disclose.

EPO-407

Predictive factors of conversion of clinically isolated syndrome to clinically definite multiple sclerosis

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Background and aims: Clinically isolated syndrome (CIS) is a term that describes a first clinical episode with features suggestive of multiple sclerosis (MS). After the second clinical relapse, the patient fulfils the criteria of clinically definitive MS (CDMS). The study aimed to determine predictive factors of conversion of CIS to CDMS.

Methods: The study analyzed the clinical, radiological and electrophysiological findings at the time of CIS first diagnosis in a group of patients observed at University Hospital MS centre for CIS (47 patients, 31 women, age 36 ± 9) or CDMS (122 patients, 91 women, age 33 ± 9). The CDMS group of patients was divided according to the clinical course into individuals who converted in CDMS early (within two years after CIS), in the medium-term (2 – 5 years) or late (after more than five years).

Results: A comparison of all evaluated parameters between CIS and CDMS groups are shown in Table 1. Significant differences between CDMS subgroups are summarized in Table 2. The evaluated groups did not differ in terms of demographic characteristics. Compared to the CIS, patients with CDMS had more oligoclonal bands and significantly frequent intramedullary demyelinating lesions. In addition, patients with CDMS exhibited a higher incidence of visual evoked potentials abnormalities.

		CIS n = 47	CDMS n = 122	p-value
Age		37 (22–59)	33 (15–60)	0,092
Sex	Male	16 (34 %)	31 (25 %)	0,262
	Female	31 (66 %)	91 (75 %)	
McDonald criteria 2010 fulfilling: **				
	Yes	7 (15 %)	16 (13 %)	0,797
	No	37 (79 %)	96 (79 %)	
McDonald criteria 2017 fulfilling: †				
	Yes	34 (72 %)	89 (73 %)	0,687
	No	10 (21 %)	22 (18 %)	
Cerebrospinal fluid				
Oligoclonal bands		6 (0–24)	10 (0–26)	**0,042**
Magnetic resonance (MRI) lesions				
Supratentorial	Yes	43 (91 %)	108 (89 %)	0,994
	No	4 (9 %)	14 (11 %)	
Infratentorial	Yes	18 (38 %)	57 (48 %)	0,244
	No	29 (62 %)	61 (52 %)	
Intramedullary	Yes	15 (32 %)	61 (52 %)	**0,021**
	No	32 (68 %)	57 (48 %)	
10> lesions	Yes	25 (57 %)	72 (62 %)	0,585
	No	19 (43 %)	45 (38 %)	
Evoked potentials (SSEP, BAEP, MEP)				
	Abnormal	5 (42 %)	33 (53 %)	0,463
	Normal	7 (58 %)	29 (47 %)	
Visually evoked potentials (VEP):				
	Abnormal	14 (54 %)	30 (37 %)	0,119
	Normal	12 (46 %)	52 (63 %)	
Conversion to CDMS (months)		-	15 (0,5–180)	-
MRI progression (months)		15 (0–113)	30 (0–177)	**0,049**

CIS - clinically isolated syndrome; CDMS - clinically definitive multiple sclerosis

** Polman et al. 2011; † Thompson et al. 2018

Table 1. Comparison of CIS and CDMS groups of patients

Table 2. Comparison of subgroups according to duration the second relapse

Conclusion: Identifying the above-mentioned risk factors will make it possible to identify patients at higher risk of a more severe course of the disease and thus indicates more frequent monitoring and early use of highly effective disease-modifying therapies.

Disclosure: The research was approved by the local ethics committees. There are no conflicts of interest to declare. Supported by the Ministry of Health of the CR – RVO (ref. FNBr, 65269705) and specific university research.

EPO-408

Autologous hematopoietic stem cell transplantation in multiple sclerosis: intermediate results

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Background and aims: High-dose chemotherapy (HDCT) with autologous hematopoietic stem cell transplantation (AHSCT) is a promising therapy of treatment-refractory multiple sclerosis (MS). The study aimed to refine this method, evaluate the efficacy and safety of treated patients.

Methods: We studied 10 patients (5 women and 5 men, aged from 29 to 57) with relapsing-remitting (RRMS; n=3; 30%), secondary progressive (n=6; 60%) and primary progressive MS (n=1; 10%). Four last patients were included in the study in Nov.-Dec. 2020 and their follow-up period is currently goes on up to 1 year. HDCT contains cyclophosphamide + rituximab chemotherapeutic regimen.

Results: There were no treatment-related mortality and uncontrolled complications. Positive dynamics of the average Expanded Disability Status Scale (EDSS) were found: EDSS before treatment - 5.9 points, 1 year after treatment - 5.3 points, 3 years after (only for 6 patients) - 5.3 points. In the period of one year after treatment, RRMS patients showed a more pronounced decrease of EDSS score, compared to patients with progressive MS (1.17 points versus 0.42). There was shown a positive effect on the quality of life and emotional status of patients. In the relatively short follow-up period after treatment, a stabilizing effect was revealed in 90% of cases, according to criteria No Evidence of Disease Activity-3. One secondary progressive patient showed signs of magnetic resonance activity with increased EDSS by 0.5
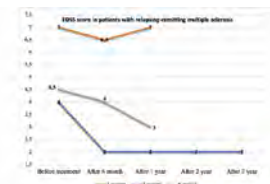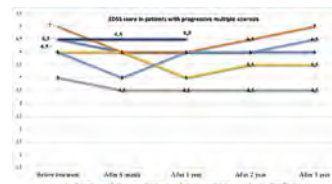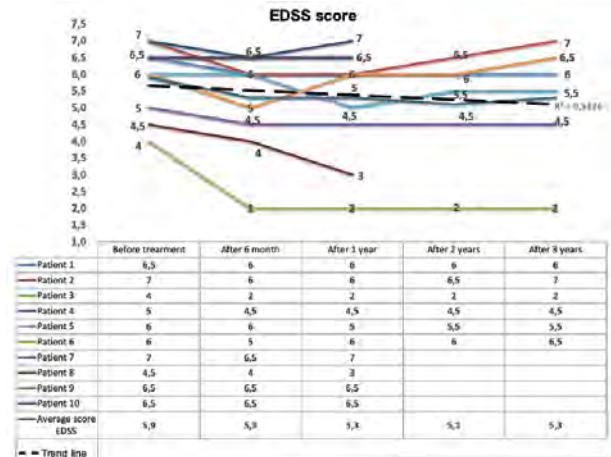
Conclusion: HDCT+ AHSCT is highly effective and safe enough method of therapy of treatment-refractory MS and showed more potential for patients with RRMS.

Disclosure: Clinical testing with support of the Ministry of Health of the Russian Federation.

EPO-409

The use of ocrelizumab in the Campania Region of Italy

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Background and aims: Ocrelizumab was the first disease-modifying treatment (DMT) approved for both relapsing and primary-progressive multiple sclerosis (MS). While different studies showed its clinical efficacy and safety, little is known about persistence, healthcare resource utilization and costs. We aim to describe ocrelizumab in a real-world setting, using routinely-collected healthcare data of the Campania Region (Italy).

Methods: We included people with MS who received first or switch DMT prescription from Jan 2018 to Dec 2020, and with at least 3-month follow-up (n=2,495). We used hospital discharge records and drug prescriptions to calculate persistence (time from first prescription to DMT discontinuation/switch), adherence (proportion of days covered(PDC)), annualized hospitalization rate (AHR, for MS-related hospital admissions), and DMT costs.

Results: Ocrelizumab was the most commonly-prescribed DMT (n=399; age=45.74±10.98 years; females=224), after dimethyl-fumarate (n=587) and fingolimod (n=401), and was most frequently prescribed to treatment naïve patients (n=104). The risk of discontinuation for ocrelizumab was lower than for other highly-active (HR=3.78 ;p=0.01), and platform DMTs (HR=7.59; p<0.01). PDC in ocrelizumab was similar to other highly-active (Coeff=0.01; p=0.31), but lower than platform DMTs (Coeff=0.09; p<0.01). AHR for ocrelizumab was similar to other highly-active (Coeff=0.01; p=0.51), and platform DMTs (Coeff=0.01; p=0.55). DMT monthly costs for ocrelizumab were lower than other highly-active (Coeff=92.30; p<0.01), but higher than platform DMTs (Coeff=-1,043.61;p<0.01).

Conclusion: Ocrelizumab was among most-frequently prescribed DMTs, especially to treatment-naïve patients, suggesting its relevance in addressing an unmet clinical need. Risk of discontinuation of ocrelizumab was lower than for other DMTs, confirming its favourable benefit-risk profile. Costs for ocrelizumab are lower than those associated to similarly effective DMTs, in absence of changes in healthcare resource utilization.

Disclosure: Nothing to disclose.

EPO-410

Blood pressure variability changes are more pronounced in secondary progressive multiple sclerosis

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Background and aims: Blood pressure variability (BPV) is a potential predictor of different forms of cardiovascular diseases, which are more prevalent in people with multiple sclerosis (pwMS) in comparison to healthy population. In order to evaluate changes in BPV parameters in pwMS, the aim of this study was to compare the BPV parameters in different forms of multiple sclerosis and healthy controls.

Methods: In 136 participants (46 with secondary progressive MS – SPMS, 52.3±9.5 years, 67.4% females; 46 with clinically isolated syndrome – CIS, 41.2±5.9, 65.2% females; and 44 healthy controls (HC) – HC, 51.7±9.1, 65.9% females) referred for testing of the autonomic nervous system, a semi-automated software made with MATLAB R2019b (The MathWorks, Inc.) was used for the evaluation of the BPV parameters (low frequency – LF, high frequency – HF, LF/HF ratio, normalized LF and HF values).

Results: For the supine position, there was statistically significant difference between the SPMS in comparison to CIS and HC for the LF, LF/HF, LFnu (SPMS<CIS and SPMS<HC) and HFnu (SPMS>CIS and SPMS>HC). For the tilted position, there was statistically significant difference between the SPMS in comparison to CIS and HC for LF (SPMS<CIS and SPMS<HC). There was no statistically significant difference between the CIS and HC groups in any of the conditions.
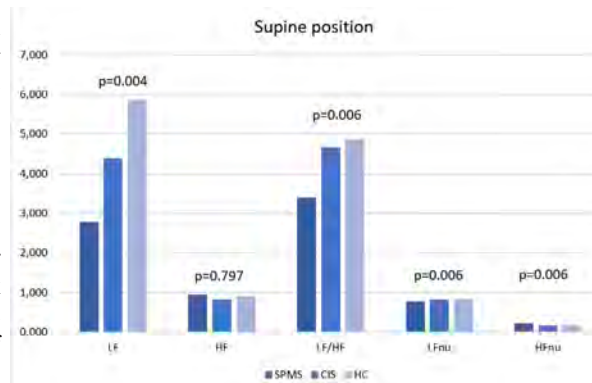
Figure 1: supine position
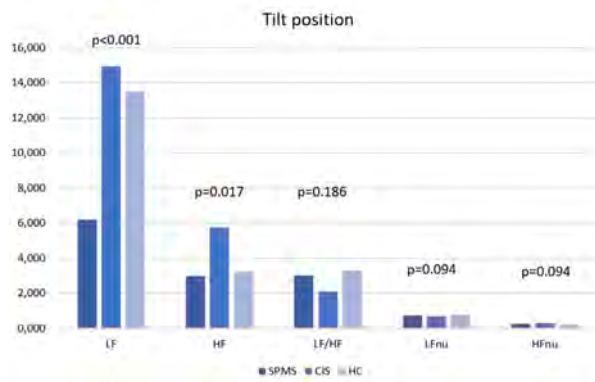
Figure 2: tilt position

Conclusion: There is a significant difference in BPV parameters in pwSPMS compared to pwCIS and HC. These findings may explain the increasing prevalence of cardiovascular comorbidities with advancing stages of MS.
Disclosure: Nothing to disclose.

EPO-411

Alemtuzumab-related lymphocytes subset dynamics and disease activity or autoimmune adverse event: real world evidence.

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Background and aims: Alemtuzumab is a monoclonal anti-CD52 antibody acting on B and T cells in highly active Multiple Sclerosis (MS). After the administration, reconstitution dynamic is different for B and T lymphocytes. We analyze the lymphocyte subsets changes after alemtuzumab administration in relation to disease activity and autoimmune adverse events.
Methods: This was a multicenter study involving MS patients treated with alemtuzumab as for clinical practice. Lymphocyte subset counts were assessed longitudinally using linear mixed models. Subset counts at baseline and during follow-up were correlated with relapse rate, adverse events or magnetic resonance (MRI) activity.
Results: We recruited 150 patients followed for a median of 2.7 ys (IQR:1.9-3.7). Total lymphocytes, CD4, CD8 and CD20 significantly decreased in all patients over 2 years (p<0.001). Dynamics of lymphocytes subset over follow up did not predict disease reactivation. Previous treatment with Fingolimod increase the risk of disease activity and adverse event (p=0.029). We found a higher probability of disease reactivation in male and in patients with over 3 active lesions at baseline. A total of 24 patients (16%) switched to another treatment. Higher EDSS at baseline and longer disease duration predict the switch to other treatments.
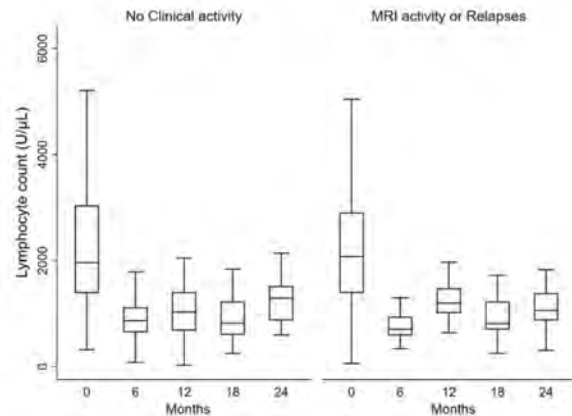
Lymphocytes dynamics in patients with or without clinical or instrumental activity
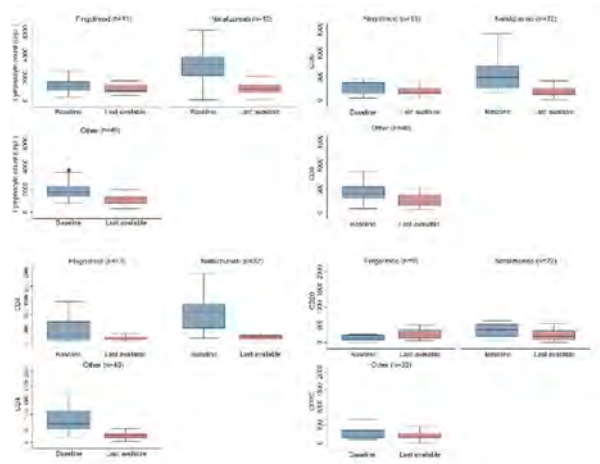
Boxplot of lymphocyte subset stratified for previous DMT at baseline and at the last available observation within 24 months. Data at 24 months were used if available, otherwise 18 months or 12 months were considered.

Conclusion: Our real-world study supports data from clinical trials in which lymphocytes subsets was not useful to predict disease activity or autoimmune disease during treatment. The early use of an induction therapy as alemtuzumab, in patients with lower EDSS and short history of disease could mitigate the risk of treatment failure.
Disclosure: Nothing to disclose.

EPO-412

Analysis of miRNA profiles in active and non-active multiple sclerosis patients

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Background and aims: Multiple sclerosis (MS) is a chronic, progressive neurological disorder. Given its marked clinical heterogeneity, MS is a typical condition where the identification of molecular markers predictive to disease outcome would be highly beneficial. Our aim is to identify miRNAs that may be relevant for MS disease activity.

Methods: Two cohort of treatment-naïve MS patients were studied: i) 67 MS patients recruited at the IRCCS San Raffaele Scientific Institute (Italy); ii) 86 MS patients recruited at the Centre Hospitalier Universitaire de Toulouse (France). At 2-year follow-up, patients were classified as NEDA (No Evidence of Disease Activity, defined as the absence of clinical relapses, MRI activity and confirmed disability progression assessed) or EDA (Evidence of Disease Activity). PBMCs were collected in absence of concomitant treatment and total RNA were extracted. MiRNA sequencing profiles were obtained (TruSeq® Small RNA Libraries Prep Kit). MiRNA-seq data were transformed into counts per transcript (Cutadapt, miRDeep2) and comparison between EDA and NEDA patients was performed (DESEq2).

Results: 76 miRNAs were found to be differentially expressed in the Italian cohort (p<0.05, adjPp<0.2). Among them, 5 were confirmed in the French cohort: hsa-miR-10400-5p, hsa-miR-5787, hsa-miR-1246, hsa-miR-664b-5p, hsa-miR-331-3p, all showing a higher expression in NEDA patients. Shared miRNA targets include genes involved in synaptic function and myelination (NEURL1, ARL8A, RNF40) as well as immune function (ADCY9, BCL9L, FURIN).

Conclusion: We identified 5 miRNAs potentially relevant for MS disease activity. Co-expression analyses with transcriptome profiles from the same samples are ongoing to define the involved molecular mechanisms.

Disclosure: FE received compensation (consulting or speaking activities) from Novartis, Sanofi Genzyme, Almirall and Merck-Serono. MF from Bayer, Biogen Idec, Merck-Serono, Novartis, Roche, Sanofi Genzyme, Takeda, and Teva Pharmaceutical Industries.

EPO-413

Real-world effectiveness and safety of teriflunomide in Chinese MS patients: a multi-center retrospective study

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Background and aims: Teriflunomide is a first-line oral immunomodulatory agent approved for the treatment of relapsing MS in China. We aim to investigate the effectiveness and safety of teriflunomide in multi-center real-world Chinese MS patients for the first time.

Methods: This retrospective study was conducted by four tertiary hospitals in different geographical regions of China. We collected the previous clinical data of patients treated with teriflunomide during Jan 1st, 2017 and Aug 31st, 2021. The change of annualized relapse rate(ARR) and expanded disability status scale(EDSS) in MS patients treated with teriflunomide for at least 6 months, the average duration of teriflunomide use and the safety of teriflunomide in overall MS population were evaluated.

Results: Of 315 patients (68.9% female) enrolled, 250 (79.4%) were treated with teriflunomide for at least 6 months. Median age at onset and disease duration were 30 and 3.3 years, respectively. The most common initial symptoms were limbs numbness (39.4%), limbs weakness (16.8%) and blurred vision (14.9%). Median duration of teriflunomide exposure was 12 months. After at least 6 months teriflunomide treatment, the ARR was significantly lower (0.23±0.47) at last follow-up visit compared to the pre-treatment (1.02±0.69) (p<0.005), with a 77.3% reduction. The EDSS score showed a reduction with a baseline of 2.01±1.56 to a post-treatment of 1.92±1.65. The most common adverse events (AEs) were alopecia (23.5%), abnormal liver function (7.0%), leukopenia (3.5%) and skin eruption (3.5%).

Conclusion: Teriflunomide is associated with a lower relapse and less disability accumulation in real-world relapsing MS of Chinese population. Also, teriflunomide was generally well tolerated.

Disclosure: Nothing to disclose.

Muscle and neuromuscular junction disorder 2

EPO-414

Clinical and morphological follow up in patients with riboflavin-responsive MADD

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Background and aims: Late onset MADD is an autosomal recessive disorder of fatty acid oxidation characterized by exercise intolerance, muscle weakness and lipids storage in myofibers. Most of MADD patients greatly benefit from riboflavin supplementation.

Methods: A retrospective study was conducted on patients with a diagnosis of vacuolar myopathy with lipid storage followed in our Neuromuscular Unit in the last 20 years. We selected 12 unrelated patients with diagnosis of MADD. Clinical features, blood tests including serum acylcarnitines, EMG and ENG and morphological studies were revised.

Results: At clinical evaluation at onset all our patients showed fatigue and muscle weakness; 4 patients showed difficulties in chewing, 4 patients complained of dysphagia, 2 patients had a dropped head, and a patient had an unexpected ataxia with numbness and dysesthesia. Laboratory blood tests revealed variable increase of serum CK (500 to 6,500). Plasma acylcarnitines profile at diagnosis evidenced increased levels of different chains intermediates. Muscle biopsies showed a vacuolar myopathy with variable increase of lipid content. Patients were treated with high doses of riboflavin (400 mg/die). Follow up was performed every six months to one year for over 10 years. Riboflavin administration determined a prompt recovery with no side effects. Muscular symptoms and laboratory abnormalities rapidly normalized

Conclusion: Our data confirmed that clinical features in MADD patients are extremely variable in terms of disease onset and symptoms. The favourable response to riboflavin supplementation strengthens the importance of an early diagnosis of these disorders among the spectrum of metabolic myopathies.

Disclosure: Nothing to disclose.

EPO-415

Malignancy and mitochondrial dysfunction: a case report and a review of the literature

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Background and aims: Mitochondrial dysfunction can lead to alterations in cellular gene expression with a consequent risk of developing cancer. There are indications that patients with a mitochondrial disorder (MD) develop malignomas or benign tumors more frequently than the general population. The most common of the malignancies was breast cancer, followed by dermatological, gynecological, and gastrointestinal malignancies.

Methods: Here we describe the case of a 75-year-old woman with MD presented with chronic progressive external ophthalmoplegia (PEO), exercise intolerance and mild proximal weakness since age of 40. Diagnosis of MD was reached at age 50. Muscle biopsy showed several ragged red fibers and cox negative fibers. LongPCR of mtDNA revealed the present of mtDNA multiple deletions (MDELs). Several years later genetic analysis for a nuclear genes associated with mtDNA MDELS showed the presence of two heterozygous variants in DGUOK gene (c.130G>A /c.704C>p. Glu44Lys / Thr235Arg.

Results: At age of 70 yrs she developed a mediastinal neoplasm incidentally diagnosed after a thoracic CT scan. Complete resection was carried out and morphological study confirmed the diagnosis of mediastinal epithelioid hemangioendothelioma (EHE), a ultra-rare vascular sarcoma, usually behaving as a low-grade malignancy. After five years of follow up she has a regular outcome.

Conclusion: Our report confirms that patients with mitochondrial may have a higher risk to develop a rare tumor although a clear relationship between mitochondrial dysfunction and tumorogenesis need deeper investigations

Disclosure: Nothing to disclose.

EPO-416

A single-center longitudinal and retrospective study of Dysphagia in 113 patients with myotonic dystrophy type 1 (DM1)

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Background and aims: Pneumonia is the main cause of death in DM1 and aspiration may play an important role. Yet dysphagia is a seldom complaint, is poorly studied in the initial stages of disease and information on progression is scanty in this disease. Our aim was to describe swallowing function and nutritional status of patients with DM1 at baseline and over time.

Methods: Dysphagia was assessed in 113 adult patients with DM1 using validated questionnaires and fiberoptic endoscopic evaluation (FEES) and correlated to demographic features, nutritional status and disability.

Results: At baseline FEES showed that out of 113 patients (mean age: 49 years [42.50–57.50], mean disease duration: 16.76 years [9.56–23.72] ; mean MIRS: 4 [3–4]) 27 (24%) had a normal swallowing function (Dysphagia Outcome Severity Scale (DOSS): 6–7), 81 (72%) had mild-moderate impairment (DOSS: 3–5) and 5 (4.5%) had severe impairment (DOSS: 1–2). Follow-up data available in 65 patients showed progression to a mild-moderate swallowing impairment in 8 of 16 with normal swallowing function at baseline, while only 3 of 45 (6%) with mild-moderate swallowing impairment at baseline showed progression to severe impairment.

Conclusion: Dysphagia had a high prevalence in our cohort and most of our patients showed mild-moderate swallowing impairment, but with scarce awareness and possible unexpected complications. Although the progression from mild-moderate to severe dysphagia appears to be slow, the progression from normal function to mild-moderate impairment in 50% of our patients in less than 3 years suggests that regular and sistematic swallowing assessments are highly recommended.

Disclosure: There are no financial conflicts of interest to disclose.

EPO-417

Muscle Biopsy and correlation with electromyography: analysis based on 10 years of experience in a tertiary center

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Background and aims: Electromyographic studies and muscle biopsy still play an important role in the diagnosis of neuromuscular diseases. However, there are few studies that explore the correlation between the findings of these techniques. With this study we aim to evaluate the correlation between electromyographic and histopathologic findings of the muscle biopsies performed in the last 10 years.

Methods: Retrospective study that includes patients, over 18 years, that underwent a muscle biopsy between 2010 and 2021 in the Hospital of the University of Coimbra, Portugal. Clinical, laboratorial, electromyographic and histopathologic data was collected. The histopathologic findings were divided in 10 parameters and the electromyographic results were divided in 5 parameters. Kendall's tau was used for correlation analysis using SPSS® v21.

Results: 104 patients met the inclusion criteria (55.8% females). The analysis found a statistically significative correlation between rapid recruitment and the presence of atrophic, necrotic and regenerating fibers and inflammation. Spontaneous discharges correlated with necrotic and regenerating fibers and inflammation. Increased turns correlated with atrophic fibers. Short-duration motor unit potentials correlated with necrotic and regenerating fibers and with inflammation.

Conclusion: The verification of a meaning correlation between specific parameters of the electromyographic and histopathologic findings may contribute for a better interpretation of electromyographic results in patients with neuromuscular diseases. Nonetheless, more thorough studies are needed in order to obtain solid conclusions.

Disclosure: Nothing to disclose.

EPO-418
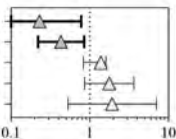
Clinical features of myasthenia gravis in adults based on age at onset

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Background and aims: Myasthenia gravis (MG) is an autoimmune disorder characterized by impaired neuromuscular transmission leading to skeletal muscle weakness in a specific distribution and fatigability. The aim is to analyze the weakness distribution in patients with early-onset MG (EOMG) and late-onset MG (LOMG).

Methods: This research retrospectively analyzed the medical data of 182 MG patients over 18 years old. We assessed the clinical features in patients with EOMG (the age at onset <50 years) and LOMG (after the age of 50).

Results: EOMG was in 128 patients (70%), LOMG was in 54 patients (30%). Ocular MG was 2.7 times more common among patients with LOMG (OR 2.68 [1.05; 6.88], p=0.035), which is almost equally common among men and women. EOMG was 2.8 times more common in women (OR 2.78 [1.43; 5.56], p=0.030) and was 2.7 times associated with generalized MG. Weakness affecting bulbar and limb skeletal muscle groups equally often developed in the EOMG and LOMG. Weakness in the ocular and facial muscles was more often detected with LOMG, respectively 4.3 and 2.3 times more often. Disease severity based on the Myasthenia Gravis Foundation of America (MGFA) class and the incidence of myasthenic crises was comparable in both groups of patients.

Factor	EOMG	LOMG	Odds Ratio [CI]
Ocular weakness	89	41	0,23 [0,07; 0,78]
Facial weakness	31	23	0,43 [0,22; 0,85]
Limb weakness	62	20	1,60 [0,83; 1,38]
Bulbar weakness	46	13	1,77 [0,86; 3,64]
Myasthenic crises	13	3	1,92 [0,53; 7,04]

Predictive role of clinical factors

Conclusion: EOMG is more common in women, LOMG has equal prevalence in men and women. The age of the disease onset determines certain weakness distribution, but does not determine the MG severity.
Disclosure: Nothing to disclose.

EPO-420

Utility of single fiber electromyography in the diagnostic evaluation of patients with isolated ocular symptoms

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Background and aims: Ptosis and diplopia are frequent presentation symptoms in the emergency rooms, ophthalmology and neurology clinics. Most of these cases are referred for single fiber electromyographic (SFEMG) examination to confirm or rule out ocular myasthenia gravis (OMG). The aim of this study is to investigate the clinical utility of SFEMG in the assessment of patients with ocular symptoms and signs.

Methods: The clinical and electrophysiological data of patients with isolated ocular symptoms, who were referred for SFEMG/jitter analysis to our laboratory for the last 3 years, were retrospectively reviewed.

Results: A total of 122 cases (78 female, 44 male) were included in the study. In retrospective review of the follow-up charts, 62.3% of them were found to have non-myasthenic disorders. Only 37.7% of the patients had the final diagnosis of OMG. The presence of both ptosis and diplopia, diurnal fluctuation and alternating patern were more likely to be indicative of OMG (p<0,001). SFEMG test was found to have a sensitivity of 80,4%, specificity of 90,8%, positive predictive value of 84.1%, and negative predictive value of 88.5%.

Conclusion: This study confirms the diagnostic utility of SFEMG in OMG, in concordance with the literature. However, it draws attention to the overutilization of the test and frequent misdiagnosis of OMG in clinical practice.
Disclosure: Authors have no financial disclosure.

EPO-421

Myasthenic storm severely breaking the heart, a case report

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Background and aims: Takotsubo cardiomyopathy is a grave clinical condition triggered by emotional or physical stress. Myasthenic crisis is a very rare cause of this condition due to the severe respiratory failure.

Methods: Here we report a case of myasthenia gravis presenting with respiratory failure and pulmonary edema.

Results: A 45 year-old women was who was previously diagnosed as a thymomatous myasthenia gravis presented with rapidly progressive dyspnea, nasal speech and ptosis after a 1-hour walk. She was immediately intubated. Her chest CT revealed significant pulmonary edema and cardiac evaluations showed severe left venticular dysfunction (Ejection Fraction (EF) of 10%) with normal serial cardiac enzymes. On ECG she had diffuse ST depression and T inversion. The patient experienced an episode of atrial tachycardia treated by amiodarone infusion and also an occasion of cardiac arrest returning back after 20 minutes CPR. IVIg and 1 mg/kg prednisolone were administered for the underlying myasthenic crisis and symptomatic treatments (forusmide, spironolactone and carvedilol) for pulmonary edema and cardiac failure. After 48 hours she was extubated and her follow up echocardiography showed marked improvement (EF: 45%). Takotsubo cardiomyopathy was considered and she was discharged after 25 days. Further outpatient follow up echocardiogram after 16 days was normal.

Conclusion: Acute cardiac failure can rarely be triggered by myasthenic crisis. The clinician must be aware of this condition to avoid administration of inappropriate drugs and unnecessary investigations.

Disclosure: Nothing to disclose.

EPO-422

Autophagic myopathy in carriers and patients with Huntington's disease

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Background and aims: Skeletal muscle wasting is one of the more severe clinical impairments in Huntington's disease (HD). Loss of muscle mass is accompanied with alteration in protein proteostasis. The aim of this study was to evaluate the activity of autophagy in skeletal muscles at pre-manifest and manifest stages of HD.

Methods: Muscle samples were taken from the middle of the belly of the right vastus lateralis muscle by a fine-needle biopsy technique using a 14G biopsy needle and a 14G puncture cannula after disinfection and local anesthesia. Muscle tissue of about 4–5 mg was transferred to the experiments. Muscle biopsies of seven control persons (four female, three male) aged 30–47 years, for pre-symptomatic HD (two female, two male) aged 21–26 years, and five manifest persons (three female, two male) aged 30–48 were analyzed. Expressions of huntingtin, K63-associated chains of ubiquitin, and the autophagy marker LC3B were determined using electrophoresis, immunoprecipitation and Western blot methods.

Results: Protein expressions of LC3B-I and -II in skeletal muscles were changed in HD patients in comparison with control. The LC3B-II/LC3B-I ratio was increased in manifest stage of HD that indicates the increase in autophagy activity in skeletal muscles of HD patients. At the same time, there was no changes in the expression of ubiquitylated proteins in HD. The impairment of the ubiquitin-proteasome system was reported to be compensated by activation of autophagy.

Conclusion: The alterations in autophagy in skeletal muscle were revealed in HD.

Disclosure: The authors declare no conflicts of interest.

EPO-423

Cascade apheresis as a monotherapy or in combination with IVIG in therapy of stiff-person syndrome

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Background and aims: Stiff-person syndrome (SPS) characterized by progressive fluctuating muscle stiffness, rigidity, and painful spasm. It is suspected an autoimmune component to the pathogenesis association with anti-glutamic acid decarboxylase antibodies. Pathogenetic therapy includes intravenous immune globulin (IVIG), therapeutic apheresis, or immunosuppressive agents. Cascade apheresis is semi-selective method to remove antibodies from the blood.

Methods: The study included 4 patients with SPS (women, range age 35–57). All of the patients have not diagnosed cancer or lymphoma. Patients were divided into two groups: 2 patients with monotherapy CA (3–5 sessions in a day); 2 patients combination CA+IVIG (IVIG 2 gm/kg per month). The effectiveness of the treatment evaluated by the Medical Research Council Weakness Scale (MRC) in musculus iliopsoas; the Modified Ashworth Scale (MAS) in musculus quadriceps femoris; the Visual Analogue Scale (VAS) and the Barthel index (BI) for disability before and after at least 2 sessions of CA.

Results: There has been an increase in muscle strength and reduction rigidity of 1 point by the MRC and MAS, also increases of 5 points by the BI in patients with CA alone. There has been an increase in muscle strength and reduction rigidity of 2 point by the MRC and MAS, also increases of 10 points by the BI in patients CA+IVIG.Two groups had reduction in VAS (≥50%).

Conclusion: In patients with SPS the combination CA+IVIG showed an advantage over CA alone by improving the clinical outcome of the disease and reducing the degree of disability in patients. Further study is needed to establish optimal therapy.

Disclosure: Nothing to disclose.

EPO-424

Delayed diagnosis of congenital myasthenic syndromes erroneously interpreted as mitochondrial myopathies

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Background and aims: Congenital myasthenic syndromes (CMS) are rare disorders. Both CMS and mitochondrial myopathies (MM) can present with ptosis, external ophthalmoplegia, and variable myopathy. We describe 3 cases of CMS diagnosed in adults, initially characterized as probable MM.

Methods: Description of 3 cases.

Results: All patients were male and presented with congenital external ophthalmoplegia and ptosis (case 1), bilateral ptosis (case 2) and ptosis with generalized hypotonia at birth (case 3). All three had proximal muscle weakness and exercise intolerance. After normal repetitive nerve stimulation (RNS) studies, a muscle biopsy (at a median age of 9 years old) was performed to rule out congenital muscle disorders. In all 3 cases, biopsy findings (cox-negative fibres or respiratory chain defects) pointed towards a MM. Subsequently, they were referred to our neuromuscular unit to confirm genetic diagnosis. However, at this time, fatigability was demonstrated and the RNS showed a decremental response in all 3 cases. Directed genetic studies revealed pathogenic variants in the MUSK, DOK7 and RAPSN genes. The median delay from symptom onset to final diagnosis of CMS was 29 years. Treatment resulted in functional improvement in all cases. Details of each case are found in table 1.

	Patient 1	Patient 2	Patient 3
Primary workup (performed at other medical centres)			
Sex	Male	Male	Male
Age of first symptoms	At birth	3–4	At birth/infancy
Signs and symptoms	Congenital external ophthalmoplegia and bilateral ptosis. Limb-girdle weakness at 30yo. Exercise intolerance.	Fixed palpebral ptosis, motor clumsiness and exercise intolerance	Generalized hypotonia, ptosis, episodes of respiratory insufficiency.
Blood analysis	CK: 400 U/L (34–171 U/L)	CK, aldolase, piruvate: Normal Lactate: 39,6 U/L (elevated)	CK: normal
EMG-ENG	Myopathic, abnormal jitter with normal RNS	Normal RNS in facial nerve.	Myopathic. Normal RNS
Muscle biopsy (age)	Fibers size variability. A total of 3 cytochrome c oxidase-negative fibres (<1% of total). No MRC defects. (48)	Fibers size variability, type I fibre predominance, isolated megamitochondria. No ragged red fibres. Complex I defect. (5)	1: MRC complex IV defect (3) 2: slight MRC complex I defect (12)
Secondary workup (performed at H12O specialized neuromuscular unit)			
Age	50	29	29
Signs and symptoms	Surgically corrected ptosis. Ophtalmoplegia. Axial weakness. Proximal fatigability	Surgically corrected ptosis, partial ophtalmoparesis, bilateral symmetrical facial weakness. Fatigability and proximal limb-girdle weakness	Fatigable asymmetrical ptosis, incomplete ophtalmoparesis, strabismus, and fatigable axial and proximal limb muscle weakness.
EMG-ENG	Pathological RNS in trapezius and ADM	Pathological RNS in trapezius, normal in ADM	Pathological RNS in trapezius
Altered gene Variant 1	MUSK (NM_005592.3) c.114T.A [p.(Asp38Glu)]→ Pathogenic	DOK7 (NM_173660.4) c.1120_1121insGCCT [p.(Ala378Sfs*29)]→ Pathogenic	RAPSN (NM_005055.4) c.1185del [p.(Thr396ProfsTer12)] → Pathogenic
Variant 2	c.251T.C [p.(Leu84Pro)]→ VUS	c.1373dupC [p.(Gln460Pfs*58)] → Pathogenic	c.264C>A [p.(Asn88Lys)]→ Pathogenic
Treatment	Ephedrine and 3,4-diamnipyridine	Salbutamol	Pyridostigmine and 3,4-diamnipyridine
Response	Improvement	Improvement	Improvement

CK: creatine kinase, EMG-ENG: electromyography-electroneurography, RNS: repetitive nerve stimulation, MRC: mitochondrial respiratory chain, H12O: Hospital 12 de Octubre, ADM: abductor digiti minimi, mtDNA: mitochondrial DNA, VUS: variant of unknown significance.

Table 1: Primary and secondary diagnostic work-up in the cases of congenital myasthenic syndrome initially diagnosed as probable mitochondrial myopathies

Conclusion: Early identification of CMS is important since medical treatment provides benefit. Their diagnosis can be challenging due to the phenotypic overlap with other myopathies. A high index of suspicion is necessary to guide the diagnostic strategy. In these cases, fatigability and fluctuations in symptoms were the key, despite the results of the biopsies

Disclosure: Authors have no conflicts of interest to disclose.

Neurogenetics 1

EPO-425

Clinical-genetic ALS and mutation in C9orf72 gene

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Background and aims: Amyotrophic lateral sclerosis (ALS) is a rare neurodegenerative disease characterized by progressive impairment of upper and lower motor neurons, leading to muscle weakness, disability, and death. The genetic background is proven in about 60% of familial cases and 5–10% of sporadic cases, with 35 genes and 2 gene loci being described. Among the genes with high epidemiological frequency, C9orf72 occupies the main place, mutations in which are found in about one third of familial cases. The aim of this study is to evaluate the frequency of mutations in the C9orf72 gene in Bulgarian patients and to describe the clinical features of the affected.

Methods: 171 samples were selected from patients with a clinical diagnosis of ALS, who underwent genetic testing and neurologic examination.

Results: In 7/171 samples (4.1%) we found expansions with over 145 GGGGCC repeats. No short expansions and border repeats (24–30 GGGGCC) were found. The analysis of the neurological status revealed the mean age at onset of 56,5 years (with the exception of one39-years-old case) and initial bulbar symptoms in five patients, initial involvement in the upper limb - in three, and initial involvement in the lower limb - also in three.

Conclusion: The obtained results enrich the global databases and reveal the clinical-genetic phenotype among Bulgarian ALS patients. These data would help identification of ALS patients and follow-up of their relatives.

Disclosure: Nothing to disclose.

EPO-426

Genotype-phenotype correlation in Italian patients affected by Tuberous Sclerosis

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Background and aims: Tuberous Sclerosis complex (TSC; MIM #191100, MIM #613254) is a rare autosomal dominant disorder characterized by the presence of widespread hamartomatous lesions in several organs. TSC is caused by mutations in either TSC1 or TSC2 genes leading to dysfunction of hamartin or tuberin, respectively. In this study, we investigated the clinical phenotypes and the genetic variants to evaluate the genotype-phenotype correlation in an Italian study cohort.

Methods: We conducted a retrospective study, including 41 familial/sporadic TSC patients, enrolled at Division of Neurology, Neurofibromatosis and Rare Diseases Center of AOU Luigi Vanvitelli and at Division of Pediatric Neurology of Santobono-Pausilipon Children's Hospital. All TSC patients were clinically evaluated according to NIH diagnostic criteria. TSC1 and TSC2 genetic testing by Targeted next-generation sequencing or multiplex ligation-dependent probe amplification (MLPA) and statistical analysis for genotype–phenotype correlations were performed.

Results: In our study the mutation detection rate was 93% (39/42), TSC2 or TSC1 variants were reported respectively in 25 and 14 TSC patients. 18% of identified mutation were novel. TSC1 mutations were associated with a less severe phenotype than TSC2. No retinal manifestations were detected in TSC1 patients.

Conclusion: Our findings offered an important contribution to identify further novel genotype–phenotype associations that may have a positive impact on patient follow-up.

Disclosure: The authors declare that the research was conduct in the absence of any commercial or financial relationship that could be construed as a potential conflict of interest.

EPO-427

Homocysteine dosage is always worthwhile: a common and an uncommon presentation of cblC deficiency

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Background and aims: CblC (Cobalamin C) deficiency is the most common genetic remethylation disorder and it is associated with heterogeneous neurological conditions.

Methods: We report two patients admitted simultaneously in our department that had been diagnosed with Methylmalonic Aciduria with Homocysteinuria CblC type (MAHCC).

Results: Patient 1: A 34 years-old woman was admitted in March 2021 because of a progressive sensory ataxia over the past year. MRI showed mild hyperintensity of the dorsal columns of cervical and dorsal spinal cord, evoked potentials revealed an impaired sensory and motor central conduction. Patient 2: A 36 years-old man was admitted for a slowly progressive cognitive decline, behavioural and personality changes and myoclonic epilepsy that began 18 years before. MRI revealed mild and diffuse brain atrophy and normal spinal cord. Both patients had normal B12 levels but increased plasmatic levels of Homocysteine and Methylmalonic Acid plasmatic levels Genetic testing revealed two pathogenetic variants of MMACHC gene, c. 566G>A and c. 666C>A, in patient 1. Patient 2 also had a compound heterozigosity of MMACHC, c.271dupA and c.482G>A. MAHC CblC type was diagnosed. Therapy with hydroxocobalamin and betaine led to partial clinical improvement in both patients.
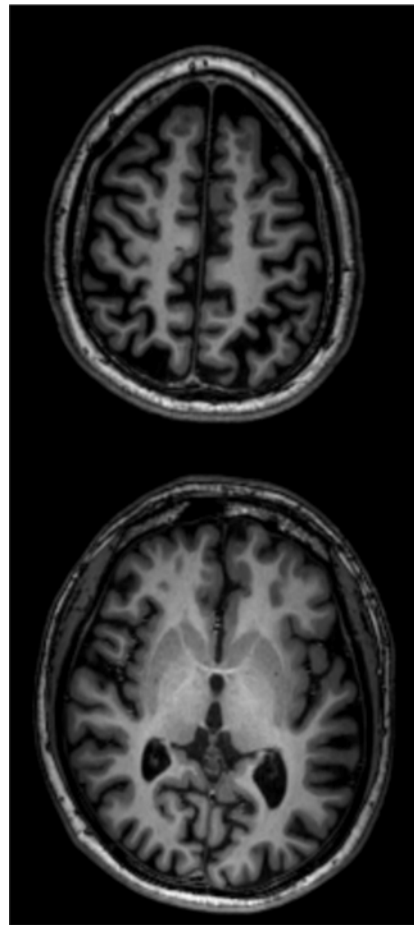
Patient 2

Conclusion: If not recognised and treated, CblC defiiency is associated with a severe and progressive disability. We want to highlight the heterogeneity of this genetic condition and to underline the value of plasmatic homocysteine as a screening test, eventually followed by dosage of plasmatic methylmalonic acid, for any subacute, young adult-onset neurological disorders to investigate uncommon B12 metabolism defects.

Disclosure: Nothing to disclose.

Patient 1

EPO-428

Hepcidin-Ferroportin axis in Friedreich´s ataxia

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Background and aims: Iron accumulation is advocated as key mechanism contributing to disease progression Friedreich´s Ataxia (FRDA), but clinical studies applying iron chelation were inconclusive. Cumulative evidence identified the hormone hepdicin (HAMP) as the main regulator of systemic iron metabolism. HAMP is synthetized by the liver and, in condition of iron excess, induces the degradation of ferroportin (FPN), the only cellular iron-exporting protein in the organism. The state of the HAMP-FPN axis in FRDA patients was not investigated up to date.
Methods: We measures systemic HAMP levels, iron and copper parameters, endogenous erythropoietin, erythroferrone as well as frataxin and FPN expression in PBMCs of FRDA patients, heterozygous relatives and matched controls. Moreover, we quantify iron content in liver, pancreas and spleen using standardized MRI techniques. Within April 2022, we plan to recruit 40 FRDAs and 40 heterozygous carriers.
Results: We currently recruited 27/40 FRDAs, 17/40 Carriers and 13/40 controls. In the preliminary analysis of iron parameters in whole blood/serum, patients displayed reduced iron levels and transferrin saturation compared to controls, while HAMP and ferritin values were comparable. FRDA patients displayed no absolute iron accumulation in the liver (values within the norm in all patients), yet a comparison with healthy controls is still missing. Two patients showed an excessive iron accumulation in the pancreas and in the spleen. PBMCs were isolated in all recruited subjects and will be analysed once the recruitment has been completed.
Conclusion: The completion of study investigations is awaited to elucidate the state of the HAMP-FPN axis in FRDA.
Disclosure: The present study is sponsored by the Friedreich´s Ataxia research Alliance (FARA).

EPO-429

Serum miRNA expression profiles in the Neurofibromatosis type 1 and related clinical complications in an Italian study

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Background and aims: MiRNAs are a class of short noncoding RNAs, involved in regulating gene expression post-transcriptionally. Several investigations have suggested their function as biomarkers in various human diseases. Its roles in mediating tumorigenesis remain largely unexplored in many disorders, including Neurofibromatosis type 1 (NF1, OMIM#162200), the most frequent tumour predisposition syndrome, caused by mutations in the NF1 gene. We aim to identify miRNA profiling in the NF1 and NF1-related clinical complications, and deregulated molecular pathways.
Methods: The study includes 128 familial/sporadic NF1 patients, enrolled at Division of Neurology of AOU Luigi Vanvitelli and diagnosed based on the NIH Consensus Conference criteria of 1988. Clinical subgroups have been classified: NF1 patients with classical phenotype (G1); NF1 patients with G1 features plus systemic complications (G2); NF1 patients with G1 features, multi-apparatus involvement and diagnosis of MPNST (G3); NF1 patients with G1 features, multi-apparatus involvement and neurological malignancies (G4); NF1 patients with G1 features, multi-apparatus involvement and other tumours (G5). For each clinical groups and controls 15 serum samples were pooled and RNA was analyzed through miRNA sequencing. Comparative analysis of deregulated miRNA were studied.
Results: Differential miRNA signatures were identified and qPCR validation is ongoing. Deregulated miRNAs are mainly involved in the tumorigenesis, cell cycle, cell proliferation.
Conclusion: NF1 is characterized by a highly clinical variability. The identification of miRNA biomarkers is essential for an early NF1 diagnosis and to distinguish between different disease phenotypes.
Disclosure: The research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

EPO-430

Selective Screening of the Most Common Limb-Girdle Muscular Dystrophies in Russia Using Massive Parallel Sequencing

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Background and aims: Limb-girdle muscular dystrophies (LGMD) is a genetically and clinically heterogeneous group of diseases characterized by progressive muscle weakness mainly in the arms and legs. The most common forms among LGMD are those caused by mutations in CAPN3, FKRP and DYSF genes. However, the incidence of this pathology varies greatly in different populations. We would like to present the results of selective screening of muscular dystrophies in Russian patients.

Methods: The study included 435 patients (230 males and 215 females with median age of 39 years) with progressive muscle wasting especially with weakness in hip and shoulder muscles. Target regions of ANO, CAPN3, DYSF, FKRP, SGCA, SGCB, SGCD, SGCG, TCAP and GAA genes were investigated by massive parallel sequencing (NGS) in all patients.

Results: In 15 (2,3%) patients pathogenic and probably pathogenic nucleotide variants leading to the phenotype of the disease were revealed in the homozygous and compound heterozygous states. The largest number of patients – 5 (33%) – had mutations in the CAPN3 gene, by two patients each had pathogenic variants in the ANO5, DYSF, FKRP and GAA genes and by one patient – in SGCA and SGCB genes. We have not revealed pathogenic variants in the TCAP, SGCD and SGCG genes in our study, they lead to the presentation of muscular dystrophy with autosomal recessive inheritance. That can be explained by the lower prevalence of these diseases.

Conclusion: Our study has confirmed that the NGS could be successfully used for selective screening of muscular dystrophies and be cost effective.

Disclosure: All authors confirmed the absence of a reportable conflict of interests.

EPO-431

GNE myopathy: reclassification of distal hereditary motor neuropathy by clinical exome sequencing

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Background and aims: GNE myopathy is a rare autosomal recessive disorder caused by mutations in GNE gene which alter sialic acid biosynthesis. Clinically distal lower limb (LL) weakness with variable involvement of upper limbs and late proximal weakness, typically sparing quadriceps is encountered. Distal LL atrophy and weakness, absent reflexes and neurogenic features challenge the differential diagnosis.

Methods: We report on two unrelated patients carrying homozygous mutations in GNE.

Results: A 45-year-old woman with uneventful family history developed bilateral foot drop with progressive walking difficulties in her thirties, difficulty at climbing stairs and hand clumsiness. Clinical examination revealed mild weakness of finger flexors, severe weakness of ankle and toe dorsal flexors with steppage gait, and absent knee reflexes. Prominent fatty replacement of hamstrings and whole calf with distal myopathic changes was revealed at muscle MRI and needle electromyography (EMG), respectively. By SureSelect Focused Exome sequencing a biallelic pathogenic mutation was identified in GNE (p. Ile146Val). A 32-year-old male presented with progressive walking difficulties and muscle cramps in the LLs since the age of thirty. Family history was unremarkable. On neurological examination, severe weakness of anterior and posterior leg compartments was appreciated. Both myopathic and neuropathic features were revealed at EMG. Muscle MRI showed fatty replacement in the distal LLs. Focused exome sequencing disclosed homozygous pathogenic mutation in GNE (p.Ile477Thr).

Conclusion: GNE myopathy mimics distal hereditary motor neuropathy. As in our report, clinical exome sequencing may help in achieving a timely diagnosis, which is fundamental since novel targeted treatments aimed at substrate replacement are underway.

Disclosure: Nothing to disclose.

EPO-432

Phenotypic heterogeneity and pseudodominant inheritance of RFC1 gene expansion in a Portuguese family with CANVAS

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Background and aims: Cerebellar ataxia, neuropathy, vestibular areflexia syndrome (CANVAS) is characterized by late onset ataxia due to cerebellar, vestibular, and sensory neuropathic dysfunction. Recently, the gene RFC1 expansion was reported in patients with sporadic and familiar CANVAS with an autosomal recessive inheritance. We aimed to report five Portuguese patients from a family with CANVAS.

Methods: Case series.

Results: Our patients belonged to two consecutive generations of the same family. There was no known history of consanguinity. Four patients presented with progressive gait imbalance at the age of 50 years old. The other patient at the age of 61 years old remained asymptomatic. Three patients reported chronic cough. A variable phenotype severity was observed, ranging from asymptomatic or mild symptoms to severe ataxia with non-ambulatory gait. On neurological examination signs of cerebellar, vestibular and sensory neuropathic dysfunction were seen with different degrees of severity. Video-oculography and video head impulse test identified bilateral vestibular dysfunction, electromyography confirmed the presence of sensory neuronopathy, and brain magnetic resonance imaging showed cerebellar atrophy in all patients. Genetic testing disclosed a biallelic expansion of the AAGGG pentanucleotide of the RFC1 gene in all patients.

Conclusion: This family reflects an example of a pseudo-dominant autosomal inheritance associated to RFC1 expansion. This may be justified by the high prevalence of heterozygous carriers (between 0.7 and 4%) of the AAGGG expansion of RFC1 gene in the populations of European origin. Additionally, we highlight the phenotypic variability seen in patients with CANVAS even within the same family.

Disclosure: Nothing to disclose.

EPO-433

Novel compound heterozygous variants of SPG11 gene associated with juvenile amyotrophic lateral sclerosis

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Background and aims: SPG11 gene is localized on chromosome 15q21 and encodes spatacsin. Mutations of this gene are typically associated with autosomal recessive spastic paraplegia-11. We aimed to describe two novel compound heterozygous pathogenic SPG11 gene mutations associated with the juvenile form of amyotrophic lateral sclerosis (ALS).

Methods: Case report.

Results: Our case refers to a 30-year-old woman with progressive distal weakness of lower limbs since the age of 25 years. Family history was unremarkable. Neurological examination revealed upper and lower motor neuron signs in lower limbs, without sensory or cognitive impairment. Nerve conduction studies were normal. Needle electromyography showed loss of motor units in the bulbar, cervical and lumbosacral territories. A diagnosis of probable-laboratory supported ALS was made. Brain magnetic resonance imaging depicted significant width reduction of the corpus callosum and periventricular white matter signal changes defining the "ears of the lynx" sign. Genetic testing disclosed two novel compound heterozygous pathogenic SPG11 gene variants (c.6194C>A and c.7158del), which lead to a truncated protein or reduced transcript levels, and therefore to a loss of function of the protein. On follow-up, there was a progressive weakness of the four limbs.

Conclusion: This case portrays an ALS phenotype that shares characteristics with autosomal recessive spastic paraplegia, indicating that these two conditions probably are in the same clinical and neuropathological spectrum.

Disclosure: Nothing to disclose.

EPO-434

Full gene-splicing assay of coding and non-coding variants in the SCN1A gene

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Background and aims: Pathogenic variants in the SCN1A gene are the most frequent genetic cause of childhood-onset epilepsy. More then 2,000 variants are reported in the literature in patients with SCN1A-associeted epilepsy, both coding and non-coding. However, the majority lack any functional confirmation.

Methods: Bioinformatic analysis of all non-canonical splice-site intronic variants and all coding variants described in SCN1A was performed using SpliceAI. All 26 protein-coding exons of the SCN1A gene were covered with mini and midigenes containing 1-5 exons cloned to pSpl3-Flu2 splicing vector. Splicing pattern of wild-type mini/midigenes were evaluated 48 hours post transfection to HEK293T cells using RT-PCR. Tested variants were introduced using site-directed mutagenesis.

Results: Initial testing of plasmids containing all 26 exons revealed wild type splicing pattern for only 9 exons. For correction of splicing patter in wild type mini/midigenes several approaches were used – modulation of the genomic surrounding, decreasing plasmid promotor strength, mutagenesis of plasmid introns for U12 introns and mutagenesis of cryptic splicing sites. Functional analysis of 62 non-canonical splice-site variants revealed different splicing alteration with exon skipping being the most frequent. 11 out of 62 (17.7%) intronic variants had no impact on splicing, although being reported as pathogenic/likely pathogenic in the literature. Functional analysis of preselected based 10 missense and 1 nonsense variant revealed that 8 are in fact splice-affecting.

Conclusion: Full gene-splicing assay for the SCN1A gene was performed for the first time with the potential of evaluating the majority of reported or newly described splicing variants in SCN1A gene.

Disclosure: Nothing to disclose.

EPO-435

Genetic modifiers in hereditary and acquired TTR amyloidosis: a genome-wide association study

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Background and aims: Hereditary transthyretin (ATTRv) amyloidosis is a rare systemic and life-threatening condition caused by mutations in the transthyretin (TTR) gene. To date, considerable variability has been observed in age of onset (AOO), penetrance, progression rate and response to treatment, both across families and countries. This variability in ATTRv amyloidosis cannot be entirely explained by the specific mutation in TTR gene, as well as factors favoring wild-type TTR deposition in acquired age-related amyloidosis (wtATTR), are still unknown. Therefore, a role for genetic modifiers has been hypothesized for these two conditions.

Methods: The aim of this multicenter study is to identify genetic modifiers in ATTRv and wtATTR amyloidosis, employing an unbiased genome-wide approach.

Results: In patients with ATTRv amyloidosis we will perform a genome-wide association study (GWAS) to identify loci harboring genetic variations that alter 1) age of neurological onset; 2) clinical phenotype and progression; 3) response to anti-amyloidogenic treatments. Patients affected by wtATTR amyloidosis will also be tested in a complementary case-control GWAS. The TTR locus as well as significant loci from the GWAS will be further explored by long-read sequencing.

Conclusion: The proposed research will identify novel genetic risk factors, informing disease prognosis and guiding monitoring and treatment. Also, it will provide seminal information about the mechanisms involved in amyloid deposition, potentially leading to the identification of novel drug targets. The study is actively enrolling, and we would be pleased for additional Centres to join (if interested: andrea.cortese@unipv.it; l.obici@smatteo.pv.it).

Disclosure: Nothing to disclose.

EPO-436

The first German case of SPG21/Mast syndrome due to a novel homozygous stop mutation in ACP33 (SPG21)

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Background and aims: Spastic paraplegia 21 (SPG21)/ Mast syndrome was first described in 1967 in 11 similarly affected individuals in an Amish population. It took over 30 years to finally identify the causal gene ACP33 (HGNC nomenclature: SPG21). Since then, only a small number of cases with ACP33 mutations have been described in Asia and Europe. Besides spastic paraplegia, typical clinical signs so far known include early-onset dementia, parkinsonism and polyneuropathy.

Methods: Case: We present a female patient with gait disturbance and cognitive decline since her early 30s. She reached all milestones of development timely without major symptoms during childhood. Neuropsychological testing at the age of 30 years showed clear deficits but stayed stable over the following almost ten years (IQ 45). The progressive clinical symptoms of the patient included speech and cognitive impairment and severe ataxia leaving the patient unable to walk without help. Polyneuropathy was absent in our patient. MRI of the brain revealed a thin corpus callosum and general brain atrophy.
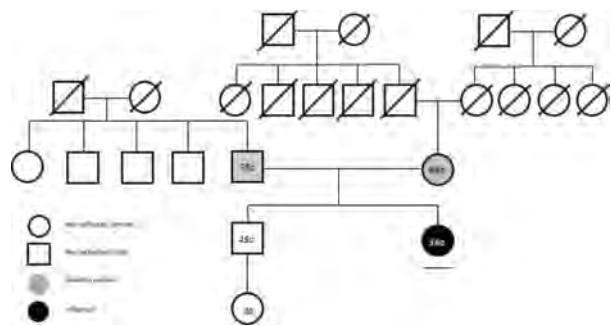
Figure 1: Pedigree of the family. No further cases of SPG21 are known, the parents are not knowingly consanguineous. The brother did not receive genetic testing. The numbers depict the age of the individuals.

Figure 2: Brain-MRI of the patient showing a thinning of the corpus callosum, cerebellar atrophy and, to a lesser extent, cerebral atrophy. Images with kind approval of Dr. Neumaier and colleagues, Regensburg.

Results: Genetic testing revealed a homozygous pathogenic ACP33 stop mutation confirming the diagnosis of SPG21/Mast syndrome. The parents, both heterozygous carriers, are not knowingly consanguineous.

Conclusion: Among the few described patients with this syndrome, this is the first German case of SPG21/Mast syndrome. We describe the long-term clinical course in this case with a new mutation, extending the knowledge of the clinical and genetic spectrum of this rare disease. Detailed clinical characterization and genetic evaluation are the first steps towards pathophysiological insights and potential future treatments of affected individuals.

Disclosure: Nothing to disclose.

Neurological manifestation of systemic diseases & Pain

EPO-437

Complex Regional Pain Syndrome and Risk Factors in Adult Population: A Systematic Review

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Background and aims: Complex Regional Pain Syndrome (CRPS) is a chronic debilitating pain condition whose physiopathology is still not fully understood and its treatment remains controversial. Therefore, understanding which risk factors may contribute to the development of this syndrome is a high-priority information for public health, physicians and the decision-making process.

Methods: A systematic review of case control and cohort studies was performed following the PRISMA guidelines. An electronic search among seven databases, MEDLINE, Cochrane, Scielo, Google Academy, Web of Science, Scopus and Embase, was conducted. Risk of bias was assessed following the Newcastle-Ottawa scale.

Results: From initially 708 identified studies, only 9 fulfilled the eligibility criteria. Among them, characteristics regarding the upper limb after fracture seemed to be a contributing factor for CRPS, this included high pain levels over 5 out of 10 on a numeric rating scale and characteristics of the fractures itself, high impact fractures or open methods reduction. Other risk factors such as being female, suffering other pain comorbidities, psychological, genetic and metabolic factors were also described.

Conclusion: Despite overall low risk of bias found in the included studies and the aforementioned risk factors, these results when combined were inconsistent for a meta-analysis, therefore, more research is advisable.

Disclosure: Nothing to disclose.

EPO-438

Bariatric beriberi, a preventable complication. Case report

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Background and aims: Wernicke encephalopathy (WE) is an acute neurological condition resulting from malnutrition. It's characterized by a clinical triad of ophthalmoparesis, ataxia, and confusion.

Methods: A 19-year-old woman presented during the past week, binocular diplopia, nystagmus, bradipsiquia and gait instability. She had a history of type 3 obesity (BMI>40) and pseudotumor cerebrii. She underwent bariatric surgery (duodenal switch) two months earlier with no subsequent vitamin supplementation. After a month of surgery she started repetitive vomiting. High-dose intravenous thiamine was started from admission.

Results: Basal thiamine levels were in the low limit. A cerebral MRI showed an increase in FLAIR and DWI signal, without a decrease in the ADC values, bilaterally in the posteromedial thalamus, mammillary bodies, tectal plate and periaqueductal gray matter. Progressive clinical improvement was observed after 24 hours of treatment, being discharged practically asymptomatic after 3 days with oral thiamine. A neuropsychological study was performed two months later, showing a slight impairment of working memory and mild bradypsychia.
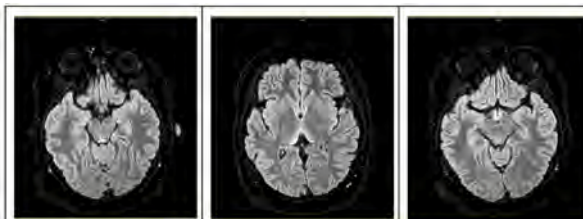
Figure 1. Cerebral MRI T2-FLAIR. Increase FLAIR and DWI signal, without a decrease in the ADC values, bilaterally in the posteromedial thalamus, mammillary bodies, tectal plate and periaqueductal gray matter.

Conclusion: Duodenal switch is considered a malabsorptive bariatric procedure, often having side effects. Multivitamin supplements are recommended after surgery as well as nutritionist counseling; its deficiency being nowadays considered a rare complication. In this patient, the coexistence of two phenomena explains the appearance of WE: the malabsorption due to a decrease in the gastrointestinal surface and the restriction due to dumping syndrome. This case turns out to be a representative case with the classic clinical triad, analytical findings and typical neuroimaging. Neurologists should be aware of this complication after surgical procedures.

Disclosure: We have no relationships/activities/interests related to the manuscript.

EPO-439

Long-term follow up of patients with neurvous system manifestations and sequelae after COVID-19 (NeuroCOVID)

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Background and aims: Neurological events are common after COVID-19. Our aims were to study the natural course and to characterize the long-term functional impairment of patients with neurological symptoms after COVID-19 infection.

Methods: In this national multicenter observational study, we describe the clinical spectrum of NeuroCOVID-patients. Neurological and psychiatric assessment, brain imaging, biochemical and cerebrospinal fluid (CSF) studies and neurophysiological tests, as well as disease course and several scales for functional impairment were assessed prospectively.

Study methods

Results: To date, 58 patients were followed for 12 months. (53.8% hospitalized, mean age 50.9 years (range 21–82), 42.9% men). The spectrum of neurological events were wide, ranging from stroke, polyradiculitis, encephalitis, epilepsy, critical illness symptoms to milder symptoms such as headache, cranial nerve impairment and long-COVID syndrome. Six patients were diagnosed with conditions not related to post-COVID (Arnold Chiari 1, nerve entrapments, spinal disc herniation, Lyme disease). Among the remaining participants, 20% reported complete remission, 66 % incomplete remission, 14 no remission or improvement. MRI findings were detected in 16% of the subjects, indicating inflammation including contrast enhancement of cranial nerves, spinal nerves or T2 signal increase in the hippocampus. Most findings did not change at the 12-month follow-up. Of the included patients, 36% (n=21) underwent a lumbar puncture, and CSF-Sars-CoV-2 antibodies were found in 30 % of these patients (n=7).
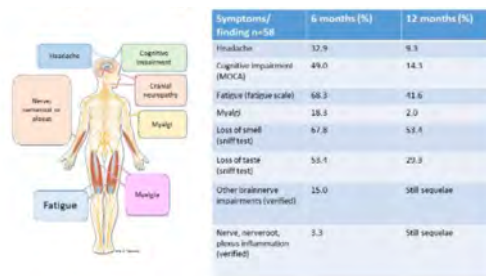
Details of symptoms and findings

Details of psychiatric evaluation

Conclusion: We found a large magnitude of neurological complications after COVID-19. This demonstrates the importance of an accurate neurological and psychiatric evaluation for neurological symptoms following COVID-19 infection. Future case-control studies are warranted to interpret the findings.

Disclosure: Nothing to disclose.

EPO-440

CNS manifestations of anti-GBM vasculitis: a diagnostic conundrum

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Background and aims: Goodpasture's syndrome(GBS) is a rare autoimmune disease. CNS involvement is rarely reported. We present a 60-year-old gentleman with a recent diagnosis of GBS who presented with a seizure and chorea.

Methods: A 60-year old smoker, hypertensive gentleman, was diagnosed with GBS-renovasculitis 3-months prior admission, following investigations for nephrotic syndrome. He had been given a 3-day course of MTP. He required indefinite RRT due to refractory hyperkalaemia and anuria. 2-months following diagnosis, the patient was admitted with a generalised tonic-clonic seizure. He was noticeably hypertensive [>180mmHg] with choreiform movements affecting his lower-extremities. He was loaded on levetiracetam 1g and maintained on 500mg daily.

Results: EEG and lumbar puncture were unremarkable. MRI revealed patchy areas of T2-signal change affecting bilateral cerebellar hemispheres, parieto-occipital lobes. Arterial beading within the right-M1, bilateral-M2, left-P1 was noted. A diagnosis of GBS-CNS-vasculitis vs Posterior reversible encephalopathy syndrome (PRES) was suspected. The patient received 4-cycles of PLEX and started on cyclophosphamide 50mg daily for possible GBS-CNS-vasculitis. Anti-GBM Titres • At diagnosis; 93.4U/mL • During admission; 37.5U/mL • 1-month post plasma-pheresis; 5.0u/mL He improved clinically and biochemically. An MRI was repeated after 5-days showed resolution of T2-changes. Beading on MRA was no longer appreciated. Cyclophosphamide was stopped.

Day 5; MR head showing resolution of T2 Flair signal change
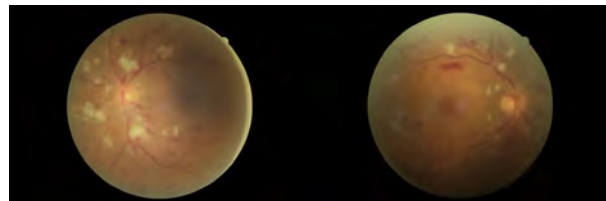
Fundoscopic examination showing bilateral cotton wool spots with retinal haemorrhages; due to an underlying undetermined retinal vasculopathy.

Conclusion: This case highlights the diagnostic dilemma of patients presenting with acute neurological symptoms on a background of a rare reno-vascular disease. The rapidly reversible MRA breading and MRI white-matter changes secondary to vasogenic oedema, together with the clinical findings are very typical of PRES.

Disclosure: Nothing to dicslose.

Day 1; MR head showing T2 Flair signal change affecting bilateral cerebellar hemispheres

EPO-441

Continuous partial status as a presentation of meningeal extranodal mucosa-associated lymphoid tissue (MALT) lymphoma.

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M. Mosquera Tapia [2], A. Torres Tienza [2], P. Gil Armada [1],
A. Castrillo Sanz [1], A. Mendoza Rodríguez [1],
F. Rodríguez Sanz [1], P. Guerrero Becerra [1],
M. Ferrero Ros [1], G. Suárez Fernández [1],
S. Cepeda Chafla [3], S. García García [3], I. Arrese Regañón [3],
J. Queizán Hernández [2], T. Zamora Martínez [4],
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Río Hortega of Valladolid, Pathological Anatomy,
Valladolid, Spanien

Background and aims: We present an extremely atypical case of extranodal mucosa-associated lymphoid tissue (MALT) meningeal non-Hodgkin's lymphoma type B that debuts as continuous partial status epilepticus.

Methods: A 63 year-old man presented to Emergency Department with a sudden onset of symptoms consisting of language alteration, initially diagnosed as an acute stroke, but during its evolution shows fluctuations, leading to a suspicion of epileptic aetiology. A cranial CT scan also detected a hypodense lesion in the left crossroads and he was admitted for further investigation.

Results: During admission, an MRI brain scan was completed, showing three ill-defined lesions of 4, 7 and 14mm, with enhancement after contrast injection, associated with vasogenic oedema and without diffusion restriction. In addition, slightly nodular meningeal enhancement was seen at the left parietooccipital level, adjacent to the focal lesions. EEG showed continuous left temporo-parieto-occipital activity, so the patient definitely required admission to the ICU with good clinical evolution, despite the fact that serial EEGs always showed epileptic activity. CSF was negative for cytology, but a significant reduction in intracranial lesions was observed after administration of corticoids. Finally, a biopsy was performed and an anatomopathological diagnosis of MALT lymphoma of the meningeal was made.
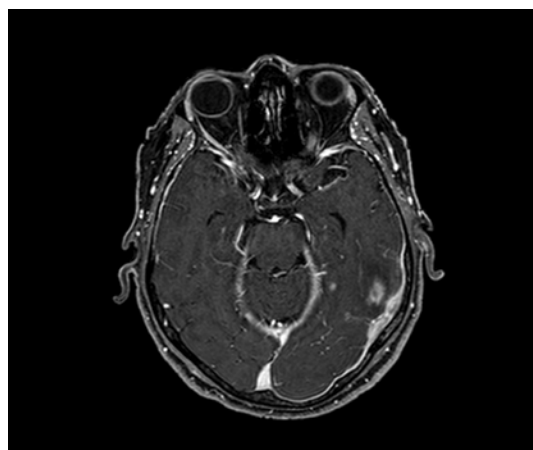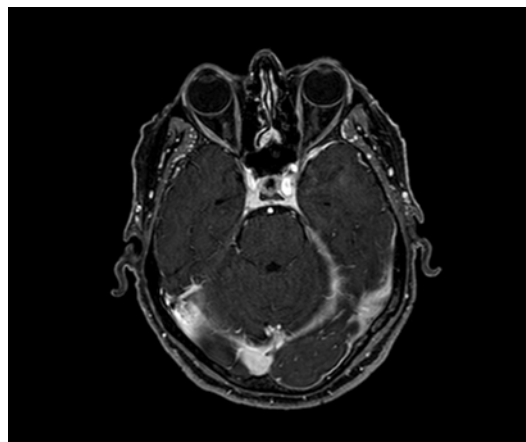
Conclusion: We would like to highlight this case for its extreme exceptionality of intracranial MALT lymphoma with associated pachymeningitis, presenting as a continuous focal status.Despite the therapeutic efforts, due to the intracranial lesion, the epilepsy has been super-refractory, with continuous epileptic activity in all of control EEGs over three years of evolution (2019–2021).

Disclosure: The author declare that there is no conflict of interests.

EPO-442

Sensory Phenotyping in Trigeminal Neuralgia with and without concomitant continuous pain

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Background and aims: Trigeminal Neuralgia is characterized by recurrent paroxysms of unilateral facial pain. Beside this characteristic paroxysmal pain, up to 50% of patients experiences a concomitant continuous pain.The aim of the present study is to investigate the sensory phenotype that characterize the presence of concomitant continuous pain in trigeminal neuralgia.

Methods: We enrolled 21 patients with clinically defined TN, 10 (47.6%) with concomitant continuous pain and 11 (52.4%) with purely paroxysmal pain. All of them underwent a Quantitative Sensory Testing following the standardized protocol of the German Research Network on Neuropathic Pain, on both sides of the face. In all patients, we compared sensory phenotyping between affected and not affected side. Finally, we compared sensory phenotyping in the affected side between patients with and without concomitant continuous pain.

Results: In the preliminary analysis of 21 patients, a trend towards loss of function was found in thermal sensibility bilaterally, but more pronounced in the affected side (CDT -1.88 ± 1.65 vs -1.21 ± 1.29; WDT -1.29 ± 1.52 vs -1.12 ± 1.30, Fig.1). These trends were more pronounced in the group with concomitant continuous pain (CDT -2.18 ± 2.06 vs -1.59 ± 1.21; WDT -1.51 ± 1.87 vs -1.09 ± 1.16, Fig.2). These differences were not statistically significant possibly due to a low population numerosity.
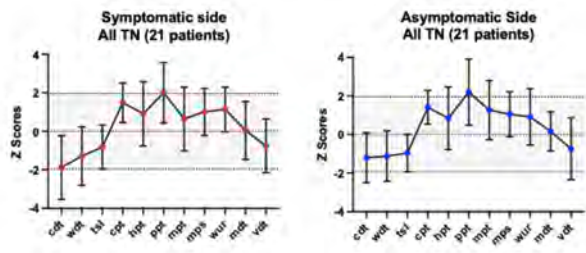
Mean face sensory profiles in 21 patients with Trigeminal Neuralgia, symptomatic and asymptomatic side
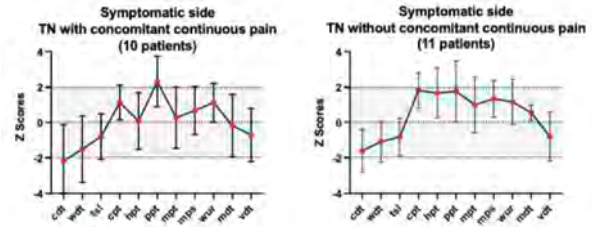
Mean face sensory profiles in symptomatic side of patients with Trigeminal Neuralgia with purely paroxysmal pain (n=11) and with concomitant continuous pain (n=10)

Conclusion: The observation that objective sensory abnormalities caused by axonal loss occurred more frequently in TN patients with concomitant continuous pain than in those with purely paroxysmal pain potentially gives support to the hypothesis that small fibre axonal loss may underly the pathophysiological mechanism of concomitant continuous pain.

Disclosure: This research was founded by the European Academy of Neurology through Research Fellowship Grant 2021.

EPO-443

Validation of the Czech language version of DN4 and PainDETECT questionnaire for assessment of neuropathic pain

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Background and aims: Questionnaires based on the presence of „neuropathic pain descriptors" represent the most important screening tool in the diagnosis of neuropathic pain. The aim of this study was to validate the Czech language version of Douleur Neuropathique en 4 Questions (DN4cz) and PainDETECT (PDQcz).

Methods: First, the language validation was performed. Second, a group of patients suffering from peripheral neuropathic pain (in diabetic neuropathy or polyneuropathies of other etiology) (n=65), and a group of individuals treated for nociceptive pain (in severe gonartrosis or coxartrosis or chronic low back pain) (n=74) were enrolled in the study.

Results: The patients with neuropathic pain reached significantly higher scores in both questionnaires comparing to nociceptive pain patients (Image 1). ROC analysis confirmed an excellent diagnostic validity (Image 2 and 3). The cut-off values proposed by the authors of the original language version were confirmed for the DN4 questionnaire. However, the optimal cut-off for the PDQcz was found significantly lower than had been recommended by original language version (in our study cut-off was set at 8). The value of Cronbach's alpha in both questionnaires ranged from 0.752–0.990.
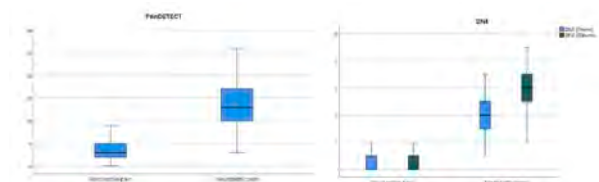
Image 1
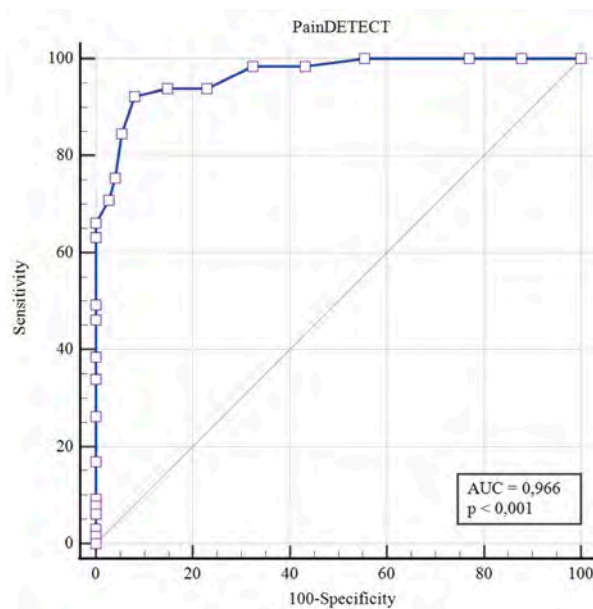
Image 2
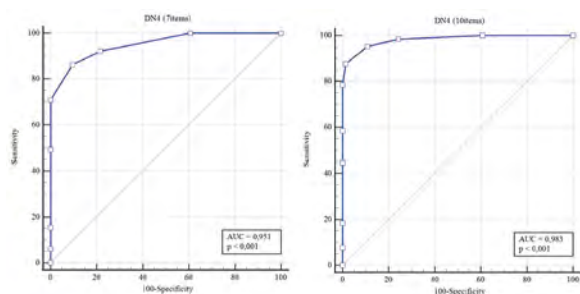
Image 3

Conclusion: The Czech language versions of both DN4 and PDQ proved excellent diagnostic validity in the discrimination of neuropathic and nociceptive pain. Both of them thus can be recommended for the assessment of neuropathic pain. For the DN4 questionnaire, the cut-off values are optimal. To reach optimal diagnostic validity, the cut-off of the PDQ should be set lower than had been previously recommended.

EPO-444

Rheumatoid Meningitis in a patient with Overlap Syndrome: the usefulness of ACPA determination in CSF

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Background and aims: Rheumatoid Meningitis (RM) is a rare complication of Rheumatoid Arthritis (RA) that can manifest as stroke-like episodes.

Methods: We present the case of a 63-year-old woman with past history of Overlap Syndrome (OS) and clinical manifestations suggestive of Amyopathic Dermatomyositis, Rheumatoid Arthritis and Systemic Lupus Erythematosus. She presented to the emergency department with sudden onset right sided clumsiness and numbness and a 2-week history of left hemicraneal headache.

Results: Laboratory workup revealed positive serum Antinuclear Antibodies (ANA), anti-Ro antibodies, Anti-Citrullinated Peptide Antibodies (ACPA) and elevated Rheumatoid Factor (RF). At CSF, lymphocytic pleocytosis, positive ACPA and anti-Ro antibodies with passive diffusion pattern and negative microbiological studies were demonstrated. Brain MRI showed predominant left fronto-parieto-occipital leptomeningeal and pachimeningeal enhancement. RM diagnosis was made and metilprenisolone IV mg/kg once a day was started.

Figure 1. (A) FLAIR postcontrast sequences showing pachimeningeal and leptomeningeal enhancement of fronto-parieto-occipital left lobes, right frontal lobe and falx cerebri (B) Resolution of meningeal enhancement two months after treatment initiation

Conclusion: Stroke-like episodes in the setting of a patient with lymphocytic pleocytosis and meningeal enhancement should raise suspicion of RM. Serum RF and ACPA levels should always be measured and we consider that ACPA in CSF too. Even in the absence of intrathecal synthesis, the ACPA presence in CSF could have a pathogenic role in RM. Due its ubiquitous presence in multiple autoimmune processes, Anti-Ro positivity in CSF is postulated as an autoinflammatory marker with no clear etiopathogenic relationship in our patient. To our knowledge, this is the first reported case of RM in the context of an OS. ACPA levels in CSF could be a relevant diagnostic clue in the setting of CNS disturbance and overlapping autoimmune conditions that include RA.

Disclosure: Nothing to disclose.

EPO-445

Trace elements in acquired hepatocerebral degeneration patients undergoing liver transplantation

M. Malaquias [1], H. Nascimento [1], C. Mendes Pinto [2], J. Silva [2], J. Alves [2], C. Ramos [2], S. Ferreira [3], J. Gandara [3], V. Lopes [3], S. Cavaco [4], H. Pessegueiro Miranda [3], A. Almeida [5], M. Magalhães [1]

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Background and aims: Liver transplantation (LT) improves the clinical outcome of acquired hepatocerebral degeneration (AHD) patients, albeit, the correlation with a decrease in blood manganese is not consistently reported. The role of other trace elements in AHD patients undergoing LT is less clear. We aimed to evaluate changes in blood levels of trace elements before and after LT in AHD patients.

Methods: Retrospective analysis of AHD patients undergoing LT. Trace elements blood levels were determined using inductively coupled plasma mass spectrometry.

Results: 6 patients (2 female), with mean age of 55±8.7 years, mean Model for End-Stage Liver Disease (MELD) score of 12±6, and heterogenous liver disease etiology (3 alcoholic, 3 others) were evaluated. After LT, a significant increase in zinc (4.71±6.77 vs 11.41±1.46 mg/L, p=0.028), selenium (127.2±47.3 vs 168.2±40.4 µg/L, p=0.028), and strontium (14.5±13.17 vs 18.6±12.3 µg/L, p=0.028) was observed. Manganese levels reduced, but without reaching statistical significance (p=0.116).

Conclusion: The decrease in zinc and selenium in chronic liver disease and improvement after LT is in agreement with previous reports and might lead to an improvement in the overall anti-oxidant/anti-inflammatory status. The relationship between strontium and liver disease is less well known. The increase following LT could be related to changes in bone metabolism, body's main strontium reservatory. In fact, early bone loss was described after LT and attributed to immunosuppressive agents. In conclusion, the imbalance of elements other than manganese is present in AHD patients and is influenced by LT, nonetheless, potential impact on neurological symptoms needs further studies.

Disclosure: Nothing to disclose.

EPO-446

An unusual presentation of autoimmune thyroiditis – severe hypothyroidism complicated with myopathy and neuropathy

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Background and aims: Chronic autoimmune thyroiditis (also known as Hashimoto's disease) is the most common cause of hypothyroidism. Most frequent neurological features of hypothyroidism are myopathy and polyneuropathy. Myopathy manifests clinically with proximal weakness, cramps, and myalgias often associated with mild to moderate elevations in creatine kinase. There is rarely involvement of the bulbar muscles.

Methods: We report a case of a 57-year-old male with severe hypothyroidism secondary to chronic autoimmune thyroiditis who presented with a 3-year history of progressive gait disorder, with fatigue, and upper and lower limb weakness and 4-month history of dysphonia.

Results: Neurological exam demonstrated proximal muscle weakness of grade 4/5 in his lower limbs with absent ankle and knee reflexes and vibratory anaesthesia, with wide-based high stepping gait with bilateral foot drop, severe dysphonia and dysarthria. Laboratory results revealed elevated thyroid stimulating hormone (TSH) level>75 microunit/ml and elevated creatine kinase (CK) level=1,606 UI/L. Brain MRI showed small vessels disease, with small white matter lesions and cervical spine MRI was normal, with no evidence of demyelinating or ischaemic features. The nerve conduction studies (NCS) demonstrated the existence of a distal sensitive axonal polyneuropathy and the electromyography (EMG) was normal. Treatment with levothyroxine was initiated at an initial dose of 100 microg daily. There were partial and gradual improvement in his neurological presentation once the TSH level normalized.

Conclusion: Longstanding chronic autoimmune hypo-thyroidism can have severe neuromuscular consequences. The most frequent consequence can be proximal myopathy, while bulbar muscle involvement is unusual reported.

Disclosure: Nothing to disclose.

EPO-447

Trace elements in acquired hepatocerebral degeneration – beyond manganese

H. Nascimento [1], M. Malaquias [1], C. Mendes Pinto [2], J. Silva [2], D. Rochate [3], C. Fraga [3], J. Alves [2], C. Ramos [2], J. Gandara [4], S. Ferreira [4], V. Lopes [4], S. Cavaco [5], H. Pessegueiro Miranda [4], A. Almeida [6], M. Magalhães [1]

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Background and aims: Trace elements have different deficiency/toxicity profiles depending on the organ affected. Manganese accumulation in the brain is a key feature in chronic liver disease patients with acquired hepatocerebral degeneration (AHD), although the mechanism is likely to be multifactorial. We aimed to evaluate blood levels of trace elements in AHD patients.

Methods: AHD patients were selected according to the following diagnostic criteria: (1) clinical neurological manifestations, (2) hyperintensities of GP in T1WI brain MRI and (3) chronic liver disease. Trace elements blood levels were determined using inductively coupled plasma mass spectrometry and results were compared to a control group (blood donors).

Results: 51 AHD patients (27.5% females), with mean age of 60±11.7 years, and Model For End-Stage Liver Disease (MELD) score of 12±6 were included. In most patients (38), cirrhosis was alcohol-related. Baseline values of trace elements were significantly different from the control group [higher Mn, Li, B, Ni, As, Sr, Mo, Cd, Sb, Tl, and Pb; and lower Se and Rb ($p<0.001$ for all)]. Child-Pugh score had a negative correlation with Se levels ($r=-0.340$, $p=0.015$). Cu/Se ratio (inflammation marker) was significantly higher in AHD patients ($p<0.001$).

Conclusion: We found several trace elements imbalances in our large cohort of AHD patients. The higher levels of Pb and lower levels of Se, in particular, could be related with the predominant alcoholic etiology of liver disease. Our study supports the hypothesis that multiple substances, either in excess or deficiency, could contribute to perpetuating oxidative stress and neuroinflammation in AHD brains.

Disclosure: Nothing to disclose.

EPO-448

Objective measurement of pain related to cardiac surgery: a study using algometry.

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Background and aims: Algometry is a safe and objective technique to quantify pain, up to now used in headache research, but to a lesser extent to assess pain related to surgery. We aimed to analyze the demographic characteristics of pain related to cardiac surgery, assessed using static algometry.

Methods: Adult patients consecutively undergoing cardiac surgery were prospectively recruited. Pressure pain thresholds (PPT) were measured in both sides of sternum manubrium, body (five measures) and xiphoid process, preoperatively and on days 1, 3 and 7 postoperatively. Linear mixed-effects models were employed to assess the longitudinal changes and results were corrected for multiple comparisons following a false discovery rate procedure.

Results: We included 70 patients (41.4% female) with a median age of 67.5 years (range 26-85). Regarding the baseline values, PPT were significantly lower in women and patients older than 65 years. After the surgery, there was a significant reduction of PPT in all assessed regions, which was partially compensated after seven days. Moreover, postoperatively, differences associated with age disappeared and those associated with sex were almost negligible. These differences related to age and sex increased after seven days of surgery, but this difference was lower in comparison with the baseline situation (Table 1, Figure 1). Postoperative pain perception was significantly higher (lower PPT) in both sexes.

Characteristics	Coefficient [95% CI]	p-value	Adjusted p-value (FDR)
Baseline			
A) Men ≤ 65 (ref.)	6.81 [6.41, 7.21]	< 0.001	< 0.001
B) Men > 65	-0.94 [-1.51, -0.37]	0.002	0.004
C) Women ≤ 65	-2.77 [-3.57, -1.97]	< 0.001	< 0.001
D) Women > 65	1.33 [0.35, 2.31]	0.011	0.015
Day 1 vs. Baseline			
A) Men ≤ 65 (ref.)	-4.17 [-4.64, -3.70]	< 0.001	< 0.001
B) Men > 65	0.96 [0.29, 1.64]	0.007	0.011
C) Women ≤ 65	2.43 [1.48, 3.37]	< 0.001	< 0.001
D) Women > 65	-1.13 [-2.28, 0.02]	0.063	0.067
Day 3 vs. Baseline			
A) Men ≤ 65 (ref.)	-3.37 [-3.84, -2.90]	< 0.001	< 0.001
B) Men > 65	0.70 [0.03, 1.38]	0.048	0.055
C) Women ≤ 65	2.15 [1.21, 3.09]	< 0.001	< 0.001
D) Women > 65	-1.04 [-2.19, 0.11]	0.088	0.089
Day 7 vs. Baseline			
A) Men ≤ 65 (ref.)	-2.56 [-3.11, -2.01]	< 0.001	< 0.001
B) Men > 65	0.87 [0.11, 1.64]	0.030	0.040
C) Women ≤ 65	2.16 [1.10, 3.22]	< 0.001	< 0.001
D) Women > 65	-1.35 [-2.63, -0.07]	0.045	0.055

Ref. = reference value; FDR = False discovery rate; 95% CI = 95% confidence interval. Except the reference value, the algometry values are obtained adding the value of the pertinent coefficient to the reference. For men > 65 or women ≤ 65, the algometry value is obtained adding the coefficient from A) and the coefficient from B) or C), respectively. For women > 65, the algometry value is obtained adding the coefficients from A), B), C) and D) simultaneously. For longitudinal values, the same operations are performed, and the result is added to the result from the equivalent baseline operation.

Table 1: PPT values in the left manubrium throughout time depending on sex and age.
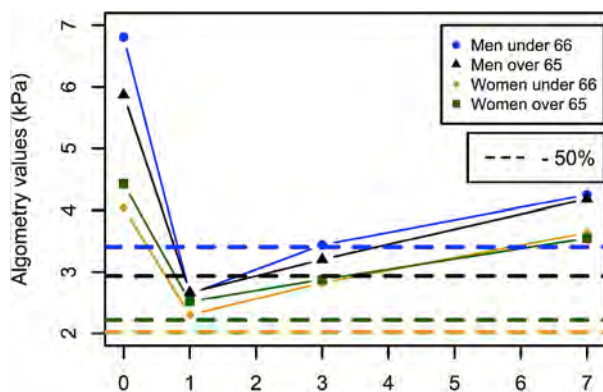
Figure 1: Average PPT values in left manubrium throughout time depending on sex and age.

Conclusion: Pain related to cardiac surgery can be measured with algometry, mainly during first postoperative days. Differences in pain sensitivity related to age and sex decrease after surgery.

Disclosure: No conflict of interest.

EPO-449

Tuberculosis of the Central Nervous System (CNS-TB) in Europe: Report of a Case and Systematic Review of the Literature

P. Stamatelos [1], K. Kaziani [1], M. Kanari [1], P. Andrikogiannopoulos [2], A. Argyropoulou [2], V. Vantali [3], D. Exarchos [3], V. Sevastianos [1]
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Background and aims: TB is a scourge for public health, especially among developing countries. CNS-TB is a rare and devastating manifestation of extrapulmonary TB.

Methods: We present a case of CNS-TB from our hospital, along with a systematic review of the literature concerning CNS-TB cases from European centers. We applied our search to MEDLINE and we identified 33 articles. After screening abstracts and references, 19 articles were included.

Results: A 33-year-old previously healthy Pakistani male presented to the E.R. with neuropathic pain in the upper back extending in the anterior chest wall (T4-T5 dermatomes). Spine MRI revealed an extensive abscess anterior to T2–T4 vertebrae. After a diagnostic CT-guided puncture of the abscess, the classic four-drug regimen was initiated. The pus culture yielded Mycobacterium tuberculosis, susceptible to the primary anti-tuberculous drugs. Due to poor clinical response, a second CT-guided puncture of the abscess was performed followed by placement of an 8F drainage catheter for 5 days with excellent clinical-radiological response. After literature review, we found 7 Case-Series and 12 Case-Reports of CNS-TB, 47 patients in total from 8 European countries (Mean age: 44 years, 35 Males-74%, 25 Immuno-compromised-53%). The most common findings are brain tuberculomas (66%), meningitis (47%) and spinal abscesses (17%). Anti-TB medication combined in selected cases with invasive procedures is the treatment of choice.
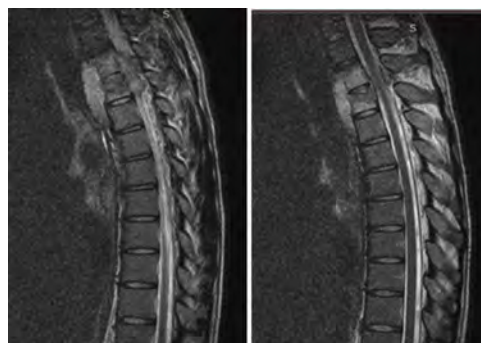
MRI T2 images of the Thoracic Spine depicting an extensive prevertebral abscess (T2-T4 vertebrae) with concomitant spondylodiscitis (high signal in T2 -W sequence) and incipient spinal cord compression.

One month post-drainage, an MRI depicted improvement concerning dimensions, abscess extent and the absence of spinal cord compression and a normal vertebrae signal in the T2-W image.
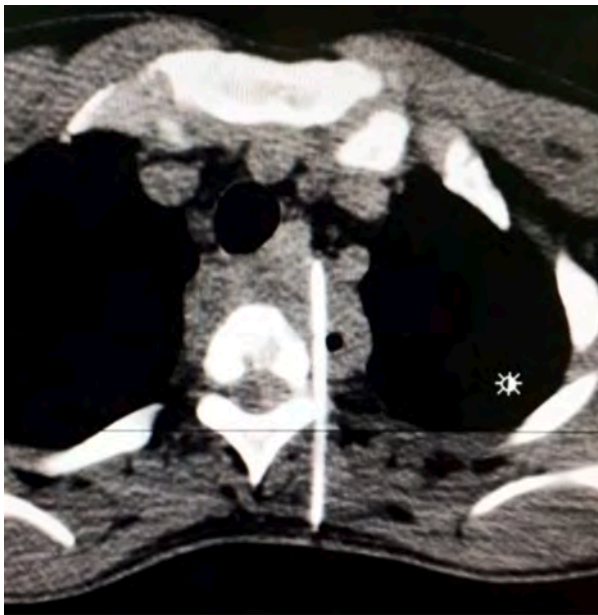
CT-guided placement of a drainage catheter in the abscess

Conclusion: CNS-TB is a treatable but potentially fatal disease with increasing incidence in Europe due to socioeconomic factors. Physicians must be alert for CNS-TB, especially among young immunocompromised patients. Early diagnosis and targeted intervention (including minimally invasive procedures) improve prognosis.

Disclosure: Nothing to disclose.

EPO-450

Blinking Rate Comparison Between Patients with Chronic Pain and Parkinson's Disease

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Background and aims: Blinking can be spontaneous, voluntary, or reflex. Spontaneous blink rate (SBR) is strictly related to dopamine levels in the central nervous system and is considered a reliable noninvasive biomarker of central dopaminergic activity. Reduced spontaneous blinking rate is a common finding in Parkinson's disease and other parkinsonian syndromes suggesting involvement of fronto-striatal system and a reduced Dopamine tone. Recent evidence indicates a possible relationship between the central dopaminergic system and pain modulation in both animal and human studies. A subpopulation of dopaminergic neurons within the ventrolateral periaqueductal grey (PAG), which is included in the pain modulatory network, projects to brain regions known to be involved in pain modulation. D1 and D2 receptors are expressed in the PAG and seem to have an antinociception activity. The aim of this study is to investigate changes of SBR in patients with Chronic Pain (CP) compared to normal subjects and PD.

Methods: A number of 284 patients affected by Chronic Pain, 46 healthy participants and 46 extrapyramidal patients underwent evaluation using eye-tracking evaluation. All experiments were conducted in a dedicated room with constant ambiental conditions. Prior to the formal testing, to ensure the subjects understating of each task, a briefing for the participant was made.

Results: The results of our study demonstrate a significant increase of spontaneous blink rate in patients with chronic pain with respect to normal subjects and Parkinson's Disease patients.

Conclusion: Blink rate evaluation using eye-tracking tasks on Chronic Pain and Parkinson's diseases patients suggest a possible role of Dopamine in nociception.

Disclosure: All authors declare no conflict of interest.

EPO-451

EBC Value of Treatment (VOT) Study – A Comparison of Optimal Management vs Current Management of Chronic Pain

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Background and aims: Chronic Pain leads to a significant economic burden as well as a considerable physical and psychological burden associated with depression, disturbed sleep, anxiety, limited functioning, reduced mobility. Efficient pain management is therefore essential to maximise patient´s quality of life. The EBC VOT study seeks to assess the cost-effectiveness of Interdisciplinary Multimodal Chronic Pain Management (IMCPM) across the EU, meaning care pathway programmes for adults of working age in three Chronic Pain conditions: Non-specific low back pain, fibromyalgia, diabetic neuropathic pain.

Methods: A Cost effectiveness (CE) Model is designed with a multi-disciplinary expert team comparing the clinical and economic outcomes associated with current practice to those of an optimised care model defined as IMCPM. The study includes a care pathway analysis for the three chronic pain conditions followed by an economic evaluation. Data will come from literature review or other sources such as guidelines or flowcharts based on expert consensus. A core CE model is developed for Germany, which will subsequently be adapted for other countries.

Results: Detailed patient pathways (current and optimal) have been built including the outcome parameters of physical functioning, pain intensity and health-related quality of life. CE analysis will follow to assess the impact of variables in the treatment pathway and to identify the main cost driver in the treatment of chronic pain.

Conclusion: The results of this study will demonstrate the impact of an IMCPM on patient outcomes and whether this is cost effective.

Disclosure: The study receives financial support from Pfizer and Grünenthal.

Neuro-oncology 2

EPO-452

(White) mattern of concerns in leukoencephalopaties: does the CSF analysis help?

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Background and aims: On July 2021, a 48-year-old woman, with familiarity for neoplasms came to our attention with one month history of gait imbalance, dizziness and asthenia.

Methods: We present our diagnostic workup.

Results: Before the admission to our Neurological Department, she underwent a brain MRI, showing temporal-parietal and sub-tentorial hyperintense-FLAIR lesions with Gadolinium enhancement (Gd+) and compressive effect. On spectroscopy high Choline/Creatinine ratio and lactate, low N-acetylaspartate were detected. Moreover, a cerebral biopsy with histological exam showed reactive gliosis, perivascular lymphocyte-T infiltrate, Ki67 not detectable. Steroid therapy helped clinic improvement. During our diagnostic work up, CSF exam showed mild lymphocytic pleocytosis; no OCBs detected. CSF cytometry identified 90% T-cells lymphocytes without any neoplastic cells. The MRI follow-up showed worsening of bilateral frontal white matter lesions, sparing U-fibers, and capsular lesions incompletely Gd+. Therefore tests for Alexander Disease, Methacromatic Adrenoleukodistrophy and CADASIL/CARASIL were performed. After intravenous Methylprednisolone, a first MRI follow-up showed no longer Gd+. One month later, three new T2/FLAIR hyperintense lesions homogeneously enhancing were detected. A new cerebral biopsy lead to the histological diagnosis of Primary CNS Lymphoma (non-Hodgkin, diffuse large B-cell).
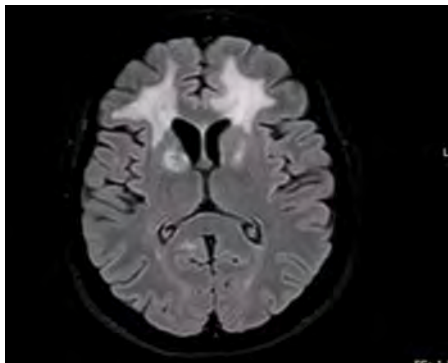
MRI on admission showed « worsening of bilateral frontal white matter lesions, sparing U-fibers, and capsular lesions incompletely Gd+»
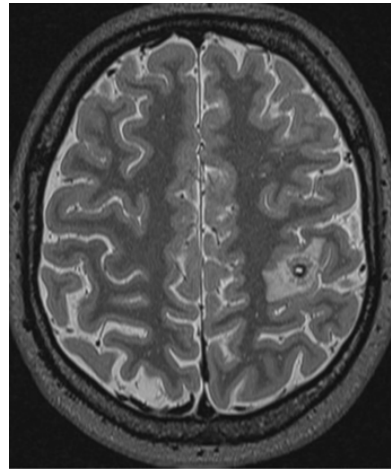
One month follow up MRI
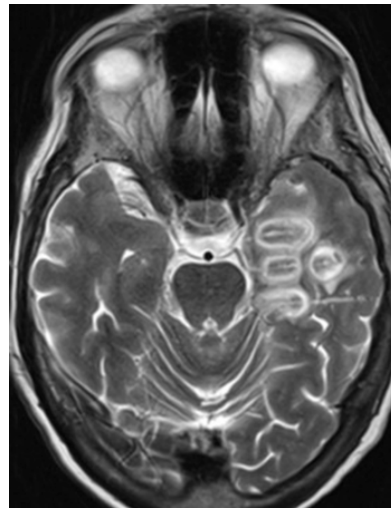
One month follow up MRI

Conclusion: Diagnosing adult leukodystrophies, as in the presented case, remains complex. MRI can be a powerful paraclinical tool, but, at first, radiological features were not typical for Primary CNS Lymphoma. Moreover, although sensitivity of CSF cytology varies (2–32%), in our patient did not lead to a conclusive result, as well as the first cerebral biopsy. Therefore, an interdisciplinary approach is needed to face these challenging cases with an early diagnosis.

Disclosure: I have no disclosures.

EPO-453

Case report: Response of corticotroph adenoma to Temozolomide in a patient with Nelson syndrome

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Background and aims: Nelson syndrome is a rare complication after total bilateral adrenalectomy (TBA), which is a treatment option in controlling hypercortisolism in Cushing's disease refractory to transnasosphenoidal surgery (TNS). Classical findings are growth of an ACTH-producing pituitary adenoma, high ACTH-secretion and hyperpigmentation. These tumors are rare, limited data regarding treatment exist. We describe a patient suffering from Nelson syndrome with good response to Temozolomide.

Methods: Case.

Results: Our patient developed Cushing's disease due to an ACTH-secreting pituitary microadenoma. After TNS, he experienced several relapses, making two further TNS and gamma-knife treatment necessary. Then he turned again symptomatic with overt hypercortisolism, but without MR-tomographical detection of a tumor-relapse. TBA was performed. 10 months later, he developed Nelson syndrome. The following relapses lead to gamma-knife treatment, four TNS, pasireotid, cabergoline and 177Lu-DOTATOC. Nevertheless, the tumor progressed. Palliative chemotherapy with temozolomide was induced, despite an unmethylated promotor of the methyl-guanine-methyltransferase-gene (MGMTp-methylation status 3%) as a negative prognostic and predictive biomarker for treatment response in glioblastoma. However, the tumor regressed almost completely. Therapy was terminated after 6 months/cycles, with stable disease 11 months later. 16 months after the last temozolomide, the tumor asymptomatically progressed. Re-Exposure to Temozolomide for further 3 months/cycles was unsuccessful.

Conclusion: Optimal treatment strategy for Nelson syndrome tumors still needs to be defined. Temozolomide is considered as a last treatment option in favor of local treatments. Our case challenges this as temozolomide induced long-term remission without major side effects. Furthermore, temozolomide should also be evaluated despite an unmethylated MGMTp-status. However, temozolomide re-exposure was unsuccessful.

Disclosure: No.

EPO-454

Paraneoplastic Anti-Ma2-antibody associated encephalitis: a case report

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Background and aims: A 36-years-old man was admitted to the neurological department with complaints on severe drowsiness, sudden falling asleep, fatigue, unsteadiness when standing and walking, inability to speak and write intelligibly, increased body temperature and appetite. The first symptoms occurred 2 month before admission. To note, before the onset of the disease, patient felt a pain and dissension in the testes.

Methods: There weren`t any significant findings in neurological status, unless mild cognitive (MMSE - 20 points) and behavioral impairments. He had been administered a list of analysis: hematology (WBC 10.9 10^9). Liquor analysis (slightly positive Pandi reaction, 27 cells), blood sugar - 6.8 mmol/l. Treponema pallidum, HIV, Herpes I and II type, HHV-6, EBV, Enterovirus, Cytomegalovirus, Borrelia burgdorferi, tick-borne encephalitis virus, SARS-CoV-2 markers were negative. EEG, ECG, heart ultrasound, CT of the chest - without significant abnormalities. CT of the abdominal cavity showed enlargement of the splenum (162*53*119 mm).

Results: MRI of the brain with MR-spectroscopy and MR-perfusion with contrast enhacement: focal changes in the thalamic region bilaterally - paraneoplastic Anti-Ma2-antibody associated encephalitis. Paraneoplastic markers had been received. He underwent a surgery - resection of the right testicle. Testicle biopsy: a site of fibrosis, which may correspond to either complete therapeutic pathomorphosis of germinogenic tumor, or complete regression of germinogenic tumor («burned-out» tumor).

Test:	Result:	Reference range:	Method:
Hu D abs (ANNA Type1, CSF)	negative	negative	BLOT
Ri antigen abs (ANNA type2)	negative		BLOT
AANNA-3 abs (CSF)	negative	negative	IFT
Yo abs (Purkinje cells)	negative		BLOT
PCA-2 abs (CSF)	negative	negative	IFT
Tr abs (CSF)	negative	negative	IFT
CV 2 abs (CRMP5), CSF	negative		BLOT
CRMP 5 abs (CSF)	9.17 ab ratio	< 10.0	RIP
Ma2 (Ta) (CSF)	strongly positive		BLOT
Amphiphisin 1 abs (CSF)	negative	negative	IFT

Paraneoplastic biomarkers

Marker:	Result:
General cytoceratins (DAKO, clone AE1/AE3)	positive reaction in the cells of testicles
Glipican 3 (Cell Marque, clone 1G12)	negative reaction
CDX-2 (DAKO, clone DAK-CDX2)	negative reaction
GATA3 (Cell Marque, clone L50-823)	negative reaction
OCT3/4 (Diagnostic Biosystems, clone NRG1.1)	negative reaction
Placental alkaline phosphatase (PLAP) (DAKO, clone 8A9)	negative reaction
SALL4 (Cell Marque, clone 6E3)	negative reaction
CD30 (DAKO, clone Ber-H2)	positive reaction in plasma cells

Immunohistochemistry
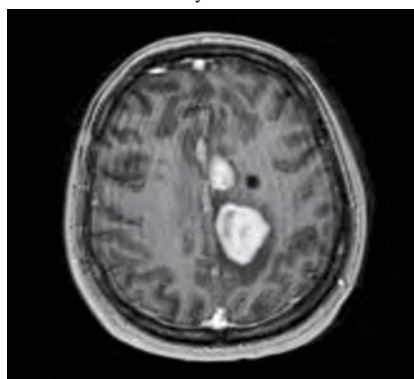
MRI of the brain

Conclusion: Patient had been receiving methylprednisolone therapy 1000 mg for 5 days and on the fifth day the patient showed significant changes in his mood and condition: sleepy feeling had been eliminated as well as dizziness during walking.
Disclosure: We have nothing to disclose.

EPO-455

Chemotherapy-induced peripheral neuropathy (CIPN) during paclitaxel

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Background and aims: Chemotherapy-induced peripheral neuropathy (CIPN) is a common dose-dependent side effect. The mechanisms responsible for this pain are unknown. Using a mouse model of paclitaxel-induced (PTX) painful peripheral neuropathy, we studied the dynamics of mechanical allodynia.
Methods: The experiments were carried out on C57BL/6j mice. PTX and the transport drug were administered intraperitoneally at a dosage of 2 mg/kg. Injections were made every other day four times, that is, the cumulative dose was 8 mg/kg per mouse. The formation of peripheral polyneuropathy in mice was assessed using monofilament (0.2 g; 1.5 g; 3 g) on days 7 and 24.
Results: As seen in Figure 1, PTX (vehicle/paclitaxel) treated animals developed a significant reduction in mechanical threshold by day 7 compared to 0.2g monofilament mice treated with vehicle (vehicle/vehicle). This decrease in threshold was also observed on day 24. At

1.5g and 3g, there was a trend that PTX (vehicle/paclitaxel) animals had lower thresholds than vehicle animals, but this trend was not significant (p=0.06).
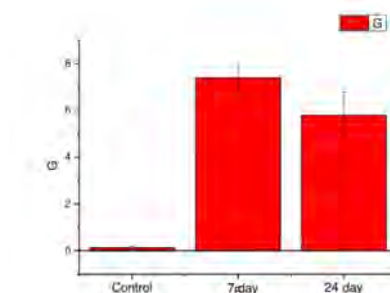
ис-1

paw-withdrawal-_n_-to-monofilament-0.2g

Conclusion: Our results have shown that PTX can reduce pain threshold, that may be one of the mechanisms for the development of neuropathic pain in the treatment of anticancer agents. Mechanical allodynia develops in the early stages of PTX use and can be observed for screening peripheral chemoinduced neuropathy in the early stages. Pain syndrome is associated with Aδ and C-fibers, their sensitization determines the features of pain syndrome in CIPN, therefore Aδ and C fibers are an attractive therapeutic target in CIPN.
Disclosure: The authors declare no conflict of interest.

EPO-456

Flair pseudoprogression after PCV chemotherapy alone in patients with anaplastic oligodendrogliomas

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Background and aims: In glioma patients, pseudoprogression (PP) has been well described after radiotherapy (with or without chemotherapy) but not after chemotherapy alone. Herein, we describe the occurrence of PP after chemotherapy alone in patients with anaplastic oligodendrogliomas.

Methods: We retrospectively reviewed the medical and radiological files of 6 patients with 1p/19q codeleted, IDH-mutant anaplastic oligodendrogliomas treated with PCV chemotherapy alone who presented MRI modifications raising the question of a tumor progression and in whom the final diagnosis was a PP.

Results: Median age at diagnosis was 40 years (range: 28–56 years). After surgery (complete n=3 or subtotal n=3 resection), patients were treated with PCV chemotherapy alone (6 cycles n=4, 5 cycles n=2). After a median time of 11 months (range: 3–49 months) after chemotherapy onset, the patients developed asymptomatic white matter MRI modifications around the surgical cavity raising the question of a tumor progression. These modifications appeared as hyperintense on Flair sequence, hypointense on T1 sequence. They lacked mass effect (6/6), contrast enhancement (6/6), restriction on diffusion weighted-imaging (6/6), rCBV increase on perfusion MRI (5/6) and hypermetabolism on F-Dopa PET (3/6). One patient underwent a surgical resection demonstrating no tumor recurrence. The five other patients were considered as having post-therapeutic modifications based on imaging characteristics and were followed. At last news, after a median follow-up of 3 years (range: 1–5 years), all patients were still progression-free.

Conclusion: Anaplastic oligodendroglioma patients treated with PCV chemotherapy alone occasionally develop PP. PP characteristics after chemotherapy alone seem different from those of PP after radiotherapy.

Disclosure: Nothing to disclose.

EPO-457

CLIPPERS and lymphoma: a unified syndrome

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Background and aims: Chronic Lymphocytic Inflammation with Pontine Perivascular Enhancement Responsive to Steroids (CLIPPERS) is a defined inflammatory central nervous system disorder characterized by established lesions, predominantly on the cerebellum and pons, with punctate gadolinium enhancement on the MRI and responsiveness to glucocorticosteroid-based immunosuppression. Its pathogenesis is unknown.

Methods: A 54-year-old man, with history of obesity and alcoholism, was admitted to our emergency ward due to fever, disorientation, and behavior disorder for 3 days. The neurological examination manifested left eye ptosis and unceasing left gaze torsional nystagmus. He tested positive for SARS-CoV2. A lumbar puncture revealed 41 leucocytes/mm^3, with negative antibody determinations. MRI depicted hyperintense lesions on cerebellum, brain stem, left temporal lobe and right parieto-occipital cortex, with punctate gadolinium enhancement. There was a radiological and clinical response to glucocorticosteroid treatment. He was diagnosed of possible CLIPPERS.

Results: Several months following the discharge, after the patient voluntarily abandoned the treatment, the symptoms reappeared. A new MRI showed extensive lesions suitable with primary lymphoma. A biopsy confirmed the diagnosis. In situ hybridization detected Epstein-Barr virus (EBV).

Conclusion: Reports describing the development of lymphoma on patients previously diagnosed with CLIPPERS, and the fact that both conditions share anatomopathological findings such as infiltrating CD4+ lymphocytes, support the theory of a syndrome with various prestages encompassing both entities. Furthermore, a nexus between B-cell lymphoma and EBV has already been established, but recent studies dwell on the possibility of this same infection being one of the main triggers of CLIPPERS and its progression into lymphoma.

Disclosure: No conflicts of interest to declare.

EPO-458

Next generation sequencing in adult patients with glioblastoma in Switzerland: a multi-centre decision analysis

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Background and aims: Next generation sequencing (NGS) provides timely information about the genetic landscape of tumours and might detect targetable mutations. To date, differences exist in the application and NGS assays used in glioblastoma as it remains unclear to what extent these variants may affect clinical decision making.

Methods: Eight interdisciplinary, primary care centres for Neuro-Oncology in Switzerland participated in this survey. The NGS assays used as well as criteria for the application of NGS in glioblastoma were investigated. Decision trees were analysed for consensus and discrepancies using the objective consensus methodology.

Results: Seven out of eight centres (87.5%) perform NGS in adult glioblastoma patients using a custom made or a commercially available assay (Oncomine Comprehensive Assay® or the TrueSight Oncology 500 assay®). The criteria most relevant to decision making were age, suitability of standard treatment and fitness. NGS is more often used in fitter patients under the age of 60 years who are not suitable for standard therapy, while NGS is rarely performed in patients in poor general health status.

Conclusion: NGS is frequently used for the management of glioblastomas in adults in Neuro-Oncology centres in Switzerland despite lacking evidence of this procedure and infrequently changing the course of treatment to date.

Disclosure: Supported by an unrestricted grant by Bayer AG, Switzerland.

EPO-459

Solitary Fibrous Tumour/Hemangiopericytoma of the Left C7 Nerve: Case Report

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Background and aims: Solitary fibrous tumours (SFTs) are rare mesenchymal fibroblastic tumours, with an annual estimated incidence of 3.5 per 1 million individuals. There have been isolated reports of SFTs involving spinal nerves. Having the NAB2-STAT6 fusion protein as a molecular hallmark, SFT/hemangiopericytoma is currently considered as a single pathologic entity.

Methods: We report the case of a 34-year old Caucasian female who presented with paresthesias and weakness in the left upper limb, with insidious onset and progression for 3 months. Neurological examination revealed motor deficit of the left brachial triceps 4/5 MRC, diminished left tricipital jerk, mild hypopallesthesia and reduced pinprick sensation of the left hand, in the C7 dermatome. Magnetic resonance imaging (MRI) of the cervical spine showed an extradural tumour lesion compatible with a left C7 schwannoma. Surgical excision of the cervical lesion was performed, with subsequent histopathological examination.
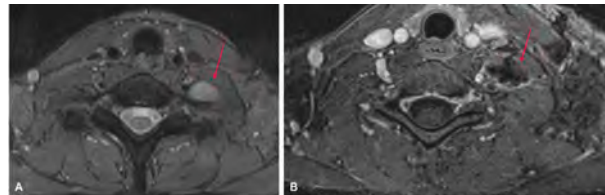
Cervical spine MRI. Axial T2-weighted image showing an extradural hyperintense lesion involving the left C7 nerve (A) and axial contrast-enhanced T1-weighted image showing the complete surgical excision of the left C7 nerve lesion (B).
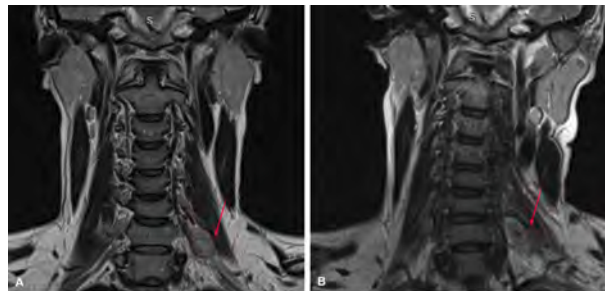
Cervical spine MRI. Coronal T2-weighted images showing the left extradural C7 nerve lesion (A) and its complete surgical excision (B).

Results: Histopathological evaluation was consistent with a SFT/hemangiopericytoma grade III WHO, and immunohistochemical analysis showed STAT6 nuclear expression, Bcl-2, CD34 and vimentin positivity. The

patient underwent local adjuvant radiotherapy. The systemic workup for potential recurrences with PET-CT performed 3 months postoperatively was normal.
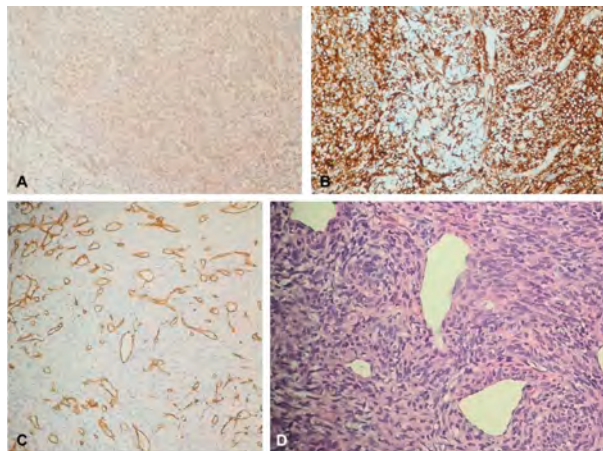
Immunohistochemical stains 200 times enhanced showing nuclear STAT6 positivity (A), Bcl-2 positivity (B) and vessel CD34 positivity (C). Histopathological specimen hematoxylin and eosin stained, 200 times enhanced, with high mitotic activity (D).

Conclusion: The radiologic differential diagnosis of SFTs is difficult since imaging findings are similar to those of other soft tissue tumours. SFTs of the spinal nerve are exceedingly rare. Genetic advancement has enabled a better understanding of the pathologic spectrum of SFTs, with ensuing impact on their management.

Disclosure: The authors have nothing to disclose.

EPO-460

Isolation of circulating tumor cells in a multifocal glioblastoma case and correlation with tumor mutational status.

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Background and aims: Circulating Tumor Cells (CTCs) are considered to be one of the important causes of tumor recurrence and distant metastasis. For many years, glioblastoma (GB) was thought to be restricted to the brain. Nevertheless, a growing body of evidence indicates that, like many other cancers, hematogenic dissemination is a reality. The absence of a procedural uniformity in literature prompted us to develop an innovative and sensitive method to obtain CTCs in GB. Our aim is to define the genetic background of single CTCs compared with the primary GB tumor and its recurrence to assess whether or not their presence in the peripheral circulation correlates with GB migration and dissemination.

Methods: CTCs were enriched from whole blood of one patient with multifocal GB with Parsortix Cell Separation System and analysed on DEPArray system. After that, CTCs Copy Number Aberrations (CNAs) and sequencing analysis was performed to compare CTCs genetic background with the same patient's primary and recurrence tissues, analysed by NextSeq 500 (whole exome sequencing).

Results: We obtained 211 mutations in common between primary and recurrence tumor. Among these, three somatic mutations (c.430 G>A in PRKCB gene, c.815 C>T in TBX1 gene and c.1,554 T>G in COG5 gene) were selected to investigate their presence in recurrence CTCs. Almost all of the sorted CTCs (9/13) had at least one of the mutations tested.

Conclusion: In confirmation of the hypothesis, the CTCs detected in the patient's blood were actually cancer cells deriving from GB tumor.

Disclosure: I have nothing to disclose.

EPO-461

Neurosarcoidosis or Erdheim Chester Disease? A case report

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Background and aims: ECD is a rare histiocytic neoplasm with heterogeneous features, involving diagnostic challenges because of its clinical and radiologic features similar to other granulomatous disorders.

Methods: On February 2021 came to our attention a 60-years old woman with a 3 years history of progressive bilateral vision loss associated with mild dyspnea and bone pain.

Results: Before the admission to our Neurological Unit, the patient underwent a total body Computed Tomography (CT) that highlighted ground-glass opacities and bronchovascular bundles including centrilobular nodules and one bone rarefaction area of the left femoral metaphysis. Moreover, Magnetic Resonance Imaging (MRI) scans showed lesions in the right femoral diaphysis and in the left tibial epiphisis; in the brain, one contrast enhancing occipital nodular lesion was evident in T1 weighted sequences. Neurosarcoidosis was suspected and when she hospitalized, we performed a follow-up brain MRI, cerebrum spinal fluid (CSF) analysis and the evaluation of Angiotensin-converting enzyme on serum and CSF. The steroid treatment showed no clinical nor MRI changes. We evaluated the 24h calciuria and phosphaturia and performed cardiac MRI scans that showed one lesion in the right atrium suggesting a neoplastic disease. Then, a FDG-PET/TC detected high glucose metabolism areas in cerebral, cardiac and skeletal tissues, suggestive for Erdheim Chester Disease (ECD).

Conclusion: Multidisciplinary collaboration is mandatory for appropriate management to avoid misdiagnosis. In our case, biopsy was not performed, making impossible histological diagnosis.

Disclosure: All authors had no disclosures.

EPO-462

Prolonged Response to Vismodegib in an Adult with Multi-Recurrent SHH-activated Medulloblastoma

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Background and aims: Medulloblastoma (MB) is the most common primary malignant tumor of the central nervous system (CNS) in children. Conversely, MB has a low incidence in adults (0.6–1 cases/million). According to the 2021 WHO Classifications of tumors of the CNS, MB are classified in 6 different groups, based on the molecular profile. There is mounting interest in the use of targeted therapy, and particularly in SHH inhibitors, to treat medulloblastomas.

Methods: Here, we present a case of a 25-year-old woman that showed a prolonged response to vismodegib in a multi-recurrent SHH-activated MB (SHH-MB).
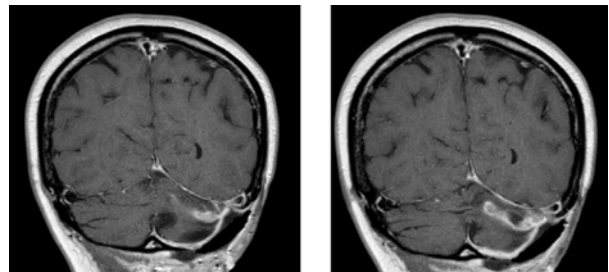
Coronal T1-weighted contrast-enhanced brain MRI before Vismodegib
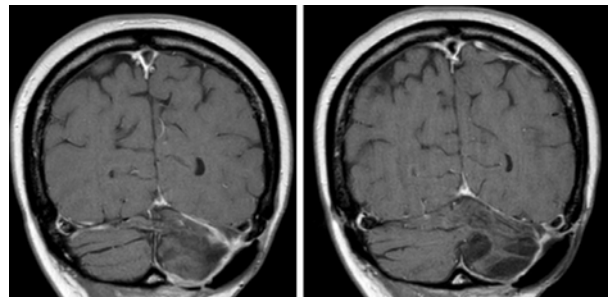
Coronal T1-weighted contrast-enhanced brain MRI after 12 months of Vismodegib

Results: The optimal treatment for local relapse remains controversial, and no randomized controlled trials are available. The SHH pathway inhibitors might provide a useful therapeutic option to extend survival in this group. To our knowledge, this is the longest progression free survival (PFS) in an adult with recurrent MB SHH-activated treated with vismodegib described in literature.

Conclusion: Vismodegib should be considered as a therapeutic option at the recurrence with a significant impact on overall survival and PFS.

Disclosure: I have no conflict of interest to disclose.

EPO-463

Stroke-like migraine attacks after radiation therapy (SMART syndrome): a delayed and reversible complication

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Background and aims: Survival of CNS malignancies has increased in recent years due to a more intensified treatment, but complications of therapy are frequently observed. Late side effects of cranial radiation therapy such as leukoencephalopathy and radiation necrosis are seen quite often. SMART syndrome is a rare complication occurring years after brain irradiation.

Methods: A 57-years-old man with history of right frontal oligodendroglioma treated with surgery, chemotherapy and cranial radiotherapy in 2006, under valproic treatment for symptomatic epilepsy. Presented severe pulsatile headache and recurrent episodes of transitory left hemiparesis and dysarthria.

Results: EEG, blood test, and cerebral CT were normal. Brain MRI showed prominent gyral enhancement with cortical thickening without diffusion restriction confined to the right frontal lobe. Four days after admission he started to improved spontaneously despite no specific treatment. A short course of corticosteroids was added with complete recovery after a week. SMART syndrome was suspected given the history of previous radiotherapy, suggestive symptoms and compatible MRI.
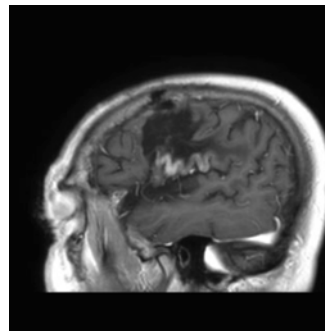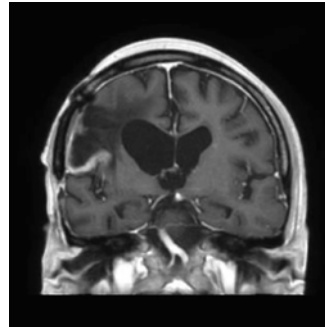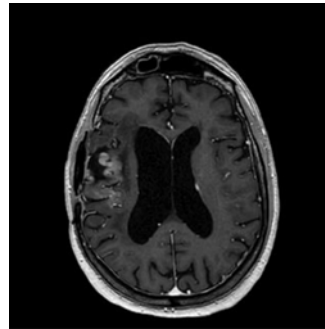
Conclusion: SMART involves complex headache with focal neurologic findings following years (usually 1–5) after cranial irradiation, but there are descriptions up to 30 years later. Pathophysiology is thought to be due to neuronal hyperexcitability and endothelial damage. Diagnosis is clinical-radiological. It should be considered in patients with previous cranial radiotherapy who present with recent onset headaches, seizures and neurological deficits. Causes like tumour recurrence, leptomeningeal disease or ischemic disease should be ruled out. It is important to make a rapid diagnosis to avoid aggressive interventions, taking into account that it is self-limited in the majority of patients.

Disclosure: Nothing to disclose.

EPO-464

Abstract withdrawn.

EPO-465

Neurologic manifestations of systemic lymphoma: Experience of a single neurological center from Tunisia

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Background and aims: A wide clinical spectrum of neurological manifestations is already known.in systemic lymphoma (SL). It's important to quickly recognize a SL associated to neurological manifestations. The aim of our study was to review the spectrum of neurologic complications associated with SL.

Methods: The clinical data of all patients hospitalized in our department who were diagnosed with SL and presented neurologic complications were retrospectively reviewed.

Results: Of the 24 patients enrolled in the study, 16 patients (66,7 %) had non-Hodgkin lymphoma followed by Hodgkin lymphoma observed in 8 patients (33,3%). The median age at onset was 49 years. Neurological signs were the first symtoms of SL in 3 cases (16,6%). The most frequent neurological signs were headache (78%) followed by gait disturbance (50%), sensory-motor deficit (46%) and dizziness (25%). Detailed clinical examination, biological and radiological work-up allowed us to associate neurological signs to leptomeningeal metatstases (10 patients, 41,6%), peripheral neuropathies as an iatrogenic clinical condition or related to LD symptoms in 7 patients (29,16%), intracranial metastases (4 patients, 17%), paraneoplastic syndromes (19 patients,8%) and finally lymphomatosis cerebri (4%). After the hospitalization, all the patients continued their follow-up in the department of oncology.

Conclusion: Neurologic manifestations of LS are various including both central and peripheral nervous system and can precede or follow the diagnosis of SL. Metastatic effect of SL is the main involved mechanism in our cohort. It is important to recognize neurologic complications of SL to avoid delays in instituting appropriate treatment and to preserve the quality of life of these patients.

Disclosure: All authors report none of conflict interest.

Neurorehabilitation

EPO-466

Correlations between aerobic fitness and MRI measures in multiple sclerosis: focus on insula

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Background and aims: In this study, we investigated the contribution of insula structural integrity to aerobic fitness level in multiple sclerosis (MS) patients.

Methods: Six-minute walk test (6MWT), timed 25-foot walk test (T25FW) and Cardiopulmonary Exercise Testing were obtained from 61 MS patients (20 relapsing-remitting, 41 progressive) and 20 healthy controls (HC). 3D T1-weighted and T2-weighted MRI were acquired for MS patients and 60 additional HC. Voxel Based Morphometry (VBM) analysis was applied to identify regional grey matter (GM) atrophy in MS patients, with a focus on insula and its portions (left-right, anterior-posterior). Correlations between clinical variables and MRI data were explored. Comparisons were performed between MS and HC, as well as between patients with (MS-WL) and without (MS-WOL) insula lesions.

Results: Compared to HC, MS patients showed a significantly lower 6MWT distance, maximal oxygen consumption (VO2max) and insular volumes (p<0.001); while T25FW and heart rate reserve (HRR) were significantly higher (p<0.001). MS patients compared to HC showed a distributed pattern of GM atrophy, involving also bilateral insula (Figure 1). In MS patients, volume of areas strictly connected to the insula was positively correlated to 6MWT and VO2max (p<0.001). Compared to MS-WOL, MS-WL showed a trend towards a lower VO2max (p=0.066) and 6MWT (p=0.05). Higher HRR showed a trend towards higher lesion loads in the insula (p=0.065).
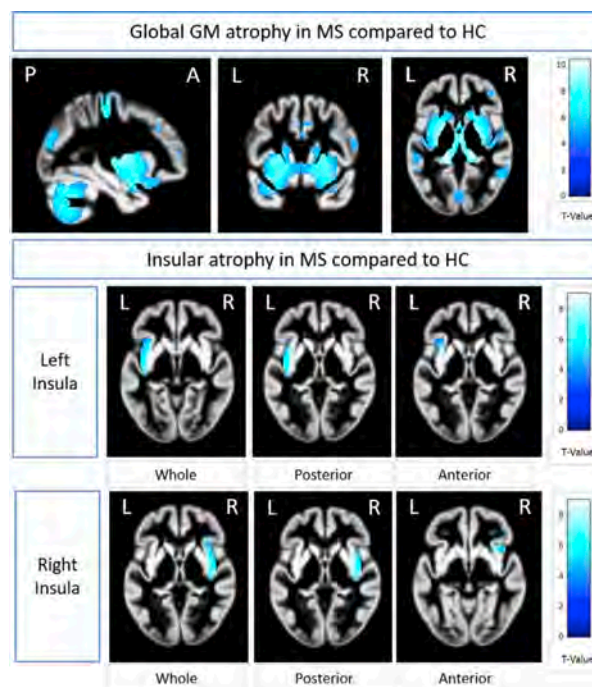
Fig 1: VBM analysis (FWE-corrected p-value<0.05) for MS and HC comparison. GM atrophy areas in MS patients are reported in blue. In the first row, global GM atrophy results are shown.

Conclusion: By exploring regional atrophy and correlations between MRI measures with aerobic fitness level, we confirmed the essential role of insula in establishing cardiopulmonary fitness level in MS.

Disclosure: Nothing to disclose.

EPO-467

Improving the quality of life of patients with Chemotherapy-Induced Peripheral Neuropathy by TENS and acupunture

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Background and aims: Chemotherapy-induced peripheral neuropathy (CIPN) increases the degree of disability and greatly reduces the quality of life of cancer patients.

Methods: 35 patients with a confirmed diagnosis of CIPN were studied. 10 patients underwent exclusively a course of drug therapy. In addition to drug therapy, 13 patients underwent a course of transcutaneous electroneuro-stimulation (TENS) and 12 patients underwent a course of acupuncture. To determine the dynamics of the quality of life of patients during treatment, we used SF-36 before and after treatment.

Results: The use of TENS and acupuncture significantly improves the quality of life of patients with CIPN by an average of 12.8% soon after treatment and by 8% at the end of a 2-month of follow-up period. The improvement in the physical component of SF-36 was 11.7% after treatment and at the end of follow-up period 7.8%, and the improvement in the mental component of SF-36 was by 13.9% after treatment and by 8.2% at the end of follow-up period. TENS turned out to be more effective than acupuncture in improving the physical component of SF-36 by an average of 78% and did not differ significantly from acupuncture in the study of the mental component of SF-36.
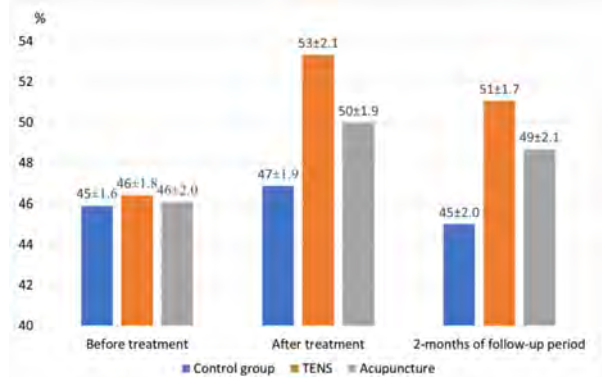
Dynamics of the physical health component according to the SF-36 questionnaire in patients with CIPN before and after treatment
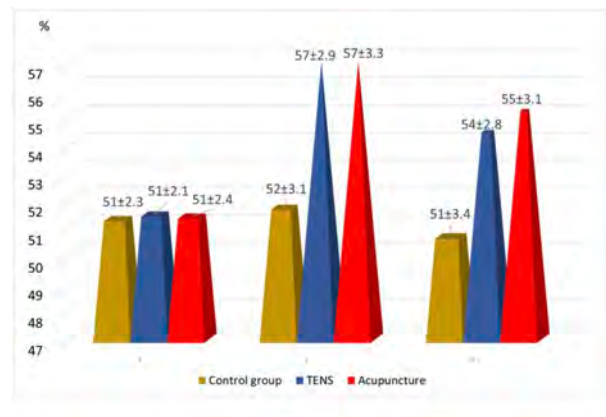
Dynamics of the mental health component according to the SF-36 questionnaire in patients with CIPN before and after treatment.

Conclusion: TENS and acupuncture significantly improve quality of life of patients with CIPN. TENS more effective than acupuncture in increasing the level of physical functioning, role physical functioning and general health. No difference between TENS and acupuncture in enhancing quality of live in vitality, social functioning, role emotional and mental Health.

Disclosure: Nothing to disclose.

EPO-468

The use of endonasal TENS in the treatment of patients with post-covid anosmia

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Background and aims: Our objective is to study the effectiveness of intranasal combined use of high frequency and low frequency transcutaneous electroneurostimulation (TENS) in the treatment of patients with post-covid anosmia

Methods: Materials and methods: 30 patients with a confirmed diagnosis of COVID-19 were under our supervision. All patients suffered from post-covid anosmia. 15 patients underwent only drug therapy (control group) and 15 patients, in addition to drug therapy, underwent a course of intranasal TENS. All patients underwent testing of olfactory nerve function with the Sniffin 'Sticks test before and after treatment. Stable method of olfactory nerve stimulation was used. Saline-soaked intranasal cathode was fixed in both sides. Anode was fixed over the nasal bridge. stimulation was carried out with the use of high-frequency TENS (100Hz – 100 μs) for 5 minutes and then with the use of low-frequency TENS (1 Hz – 200 μs) for another 5 minutes.

Results: It was found that the use of intranasal olfactory TENS significantly enhances the effectiveness of drug therapy in improving the parameters of the olfactory nerve in the threshold test by 143.5% ($p < 0.01$), the discrimination test by 129.5% ($p < 0.01$), the identification test by 184.5% ($p < 0.01$) and by the total number of points by 148.7% ($p < 0.01$).

Results of the Sniffin 'Sticks Discrimination test before and after treatment in the control and TENS groups
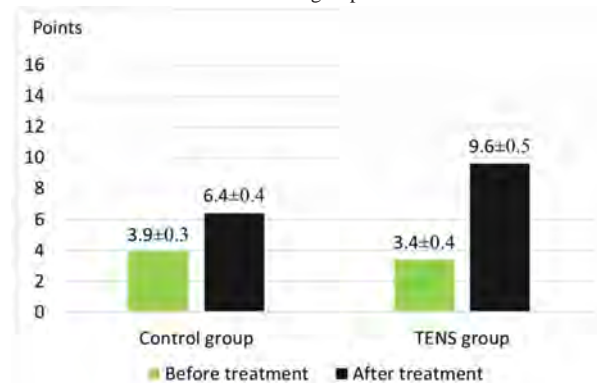
The results of the Sniffin 'Sticks Threshold test before and after treatment in the control and TENS groups

Conclusion: High efficiency of intranasal combined use of high-frequency and low- frequency TENS in the treatment of patients with post-covid anosmia.

Disclosure: Nothing to disclose.

Results of Sniffin' Sticks Identification Test before and after treatment in the control and TENS groups

EPO-469

Event-related Desynchronisation during Action Observation is an Early Predictor of Recovery after Stroke. An EEG Study

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Background and aims: A timely rehabilitation for arm recovery is essential after stroke and the identification of meaningful biomarkers that can predict recovery and guide rehabilitation processes is warranted. Quantitative Electroencephalography (qEEG) is an emerging tool to assess brain dynamics, moreover the Event-Related Desynchronisation (ERD) in the alpha rhythm is one of the most promising EEG measures. The aim of this study was to test the predictive role of ERD during action observation (AO) at 4 weeks after stroke on arm motor recovery.

Methods: 29 stroke patients (17 males, 67 years old) underwent a qEEG at 4 weeks after stroke, whereas arm motor recovery was assessed by the Fugl-Meyer Assessment (FMA) after 12 weeks.

Results: The most interesting results were found in subcortical stroke (n=16), where different patterns of ERD during AO were highlighted. A greater alpha desynchronization in the affected parietal ($R2=0.47$; $p=0.03$) and central electrodes ($R2=0.53$; $p=0.017$) was a predictor of good recovery in patients with moderate arm paresis. Conversely, a greater alpha desynchronization in the unaffected frontal electrodes predicted a poor outcome ($R2=0.93$; $p=0.03$) on patients with severe arm paresis.

Conclusion: A poor prognosis was documented when the unaffected hemisphere has to vicariate the functions of the affected one early after stroke, especially in the frontal area, while the prognosis was better when the affected hemisphere is able to reorganize its activities from the acute stages. Our work confirms the role of ERD during AO as an early predictor of motor recovery in stroke patients.

Disclosure: Not Applicable: there is no funder award/grant.

EPO-470

Development of a patient journey map for people living with cervical dystoni

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Background and aims: Patient journey maps are increasingly used as a tool that enables healthcare providers to refine their service provision to best meet patient needs. We developed a cervical dystonia patient journey map (CDPJM) that describes the holistic patient experience from pre-diagnosis through to long-term treatment.

Methods: The CDPJM was developed in 2 stages; a survey of 15 patients with CD informed the design of the CDPJM, which was then refined and validated by an expert-patient focus group.

Results: Qualitative analysis supported 5 stages of the patient journey: symptom onset, diagnosis and therapeutic relationship with healthcare professionals, initiation of CD care, start of treatment, and living with treated CD. Following symptom onset, patients described multiple visits to their family doctor who prescribed pain killers and muscle relaxants, and referred their patient to up to 10 specialists for diagnosis. Over half (53.3%) had received ≥1 misdiagnosis. Patients reported relief upon correct diagnosis but a lack of understanding of the prognosis and treatment options; 46.7% said their neurologist did not spend enough time addressing their concerns. While botulinum toxin (BoNT) was consistently discussed as first-line treatment, few neurologists mentioned physiotherapy, counselling or other complementary approaches. Patients reported a 'rollercoaster' of relief with BoNT treatment with symptoms (and subsequent impact on daily life) returning towards the end of an injection cycle.

Conclusion: We present the first patient journey map for CD that can be used to guide local service mapping and to compare current provision with what patients say they want and need.

Disclosure: This work is generated within the European Reference Network for Rare Neurological Diseases - Project ID No 739510. Support for this project was also provided by Ipsen.

EPO-471

Stroke-induced immunodepression: role in the neurorehabilitation setting

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Background and aims: Stroke-induced immunodepression is a well-known phenomenon characterized by the suppression of cellular and humoral immune responses in peripheral blood, with a neutrophil/lymphocyte ratio (NLR) >5. The aim of this study is to assess the role of stroke-induced immunodepression as a prognostic factor of rehabilitative outcome.

Methods: We enrolled 98 patients (54 males, age 70.6 ± 14.3) with ischemic (88.7%) or hemorrhagic (11.3%) stroke. Immunodepression was defined as a NLR >5 at admission in the Rehabilitative Unit (NLR+, n=14, 14.3%). Clinical and disability scores were recorded at baseline and at hospital discharge (average duration: 48.9 ± 18.6 days).

Results: When compared to patients without immunodepression (NLR-), NLR+ group showed worse baseline scores at the Functional Independence Measure (56.5 ± 27.5 vs. 74.8 ± 25.1, p=0.015), Barthel Index (23.2 ± 22.3 vs. 43.4 ± 25.4, p=0.006), Tinetti scale (5.7 ± 8.4 vs. 12.7 ± 9.8, p=0.014), and NIHSS (11.0 ± 5.9 vs. 7.0 ± 4.5, p=0.006), while gait indicators (Hauser index and speed of gait) did not differ between groups. All these parameters improved at hospital discharge, and the degree of improvement was comparable between NLR+ and NLR- groups. Despite this amelioration, NLR+ were still more disabled when compared to NLR- group at hospital discharge. Infectious complications were more prevalent in NLR+ group (84.6% vs 25.9% in NLR- group, p=0.001), as expected.

Conclusion: Stroke-induced immunodepression is a negative prognostic factor in the neurorehabilitation setting. Indeed, patients with a NLR above 5 showed poorer functional and motor independence, higher rate of infectious complication and a more severe clinical picture at hospital admission and discharge. Nonetheless, a significant clinical improvement was achieved in both groups.

Disclosure: The Authors have no conflicts of interest to declare as regards this study.

EPO-472

Sporadic cerebral amyloid angiopathy and functional outcomes at discharge from intensive in-patient rehabilitation

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Background and aims: Sporadic cerebral amyloid angiopathy (CAA) is an age-related cerebral small vessel disease causing a long-term disability. However, whether CAA may affect rehabilitation outcomes has not yet been addressed. In this observational prospective study, CAA and No-CAA functional outcomes after a rehabilitation stay have been compared.

Methods: All adults severe Haemorrhagic Brain Injuries (sHBI) admitted to the IRCCS-Don Gnocchi Foundation from March 2020 to June 2021 were enrolled. CAA was diagnosed according to the modified-Boston Criteria. Demographic and clinical data including time post-onset (TPO), length of Stay (LoS), Early Rehabilitation Barthel Index (ERBI), Coma Recovery Scale-Revised, Functional Independence measure (FIM), Level of Cognitive Functioning scale and Glasgow Outcome Scale-Expanded (GOS-E) were recorded.

Results: Among 102 sHBI patients (age: 66 [IQR=16], 53% female), thirteen (13%) were classified as possible or probable CAA. TPO and functional assessment scales were comparable at admission, but CAA were significantly older (76 [IQR=12] years, p=0.001). After a similar LoS (87 [75] vs 84 [66]; p=0.52), CAA presented a higher care burden (ERBI:-225 [176] vs -160 [113]; p=0.025), a poorer functional recovery (FIM: 18 [3] vs 24.5 [19]; p=0.02) and a lower level of global independence (GOS>4) (15.4% vs 46.9%; p=0.03). In multivariate analysis, higher care burden (ERBI: OR=0.039, p=0.039) and poorer functional recovery (FIM: OR=1.5, p<0.001) at discharge were independently associated to CAA independently of age, gender, LoS and TPO.

Conclusion: CAA seems to be independently associated to poorer rehabilitation outcomes, suggesting the importance of a better knowledge of this disease to customize the rehabilitation pathway.

Disclosure: The authors declare that they have no relevant or material financial interests that relate to the research described in this paper.

EPO-473

Abstract withdrawn.

EPO-474

Dual-task improves cognition and resting-state functional connectivity in patients with Parkinson's disease

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Background and aims: To demonstrate whether dual-task with Action Observation Training (AOT) and Motor Imagery (MI) ameliorates cognitive performance and resting-state (RS) brain functional connectivity (FC) in Parkinson's disease (PD) patients with postural instability and gait disorders (PIGD).

Methods: 20 PD-PIGD patients were randomized into: i) DUAL-TASK+AOT-MI group, who performed 6-week training of AOT-MI with observed-imagined gait and balance exercises; ii) DUAL-TASK-group, who performed the same exercises with landscape-videos observation. At baseline and after 6 weeks, all patients underwent neurological and motor evaluations, computerized cognitive assessment (using Cambridge Neuropsychological Test Automated Battery) and RS functional MRI scans. Cognitive and RS-FC changes (and their relationships) over time within and between-groups were assessed.

Results: After training, all PD-PIGD improved their accuracy and reaction times in executive-attentive (dual-task) skills. Within-group analyses showed that: DUAL-TASK+AOT-MI had increased RS-FC within the Anterior Salience Network (aSAL), right Executive Control Network and Precuneus, and reduced RS-FC within the anterior Default Mode Network (aDMN); while the DUAL-TASK showed increased RS-FC within the Visuospatial Network. Group x Time interactions showed that, compared to DUAL-TASK, DUAL-TASK+AOT-MI had increased RS-FC within the aSAL, which correlated to reduced response latency, and reduced RS-FC within the aDMN, which correlated to better accuracy in this group.

Conclusion: In PD-PIGD patients, both trainings promote cognitive improvement and brain functional reorganization. The DUAL-TASK+AOT-MI training is further useful for obtaining specific functional reorganization of extramotor brain networks involved in motor control and executive-attentive abilities with specific effects on dual-task mobility and balance, which are the most challenging for these patients.

Disclosure: Nothing to disclose.

EPO-475

Effect of proprioceptive training in patients with balance disorders

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Background and aims: Disorders of the balance function (BF) have to long-term recovery and worsen the daily activity of patients. The social significance of BF disorders is due to their impact on the life's quality, significantly limiting daily activity, negatively affecting the emotional sphere and forming person's functional dependence. To evaluate the effect of proprioceptive training in patients with BF disorders.

Methods: 42 patients with multiple sclerosis (MS) (34 ± 5.6 years) with BF disorders by the stabilometry biofeedback (BFB) (Stabilan, Russia). To assess the effect of proprioceptive training on recovery of BF, combined kinesiotherapy sessions using a vibration platform (Fitvibe Medical, Gymnauniphy N.V., Belgium), with frequency of 20–22 Hz, lasting no more than 15 minutes, and training on the stabiloplaform with visual BFB used. Before and after the course of kinesiotherapy, the effectiveness evaluated using stabilometry with BFB and on the Berg's scale "Berg Balance Scale – BBS".

Results: The effectiveness of the combined using of proprioceptive training (exercises on vibration platform with classes on the stable platform with BFB) in MS patients reliably established. The quality of the BF an increase in (BF) from 71[38.2; 94.5]% to 81.1[67.3; 95]% after proprioceptive training, ($p<0.0022$) according to stabilometry data; significant improvement on the Berg's scale from 38.2[] point to 42.3 [] point ($p=0.002$).

Conclusion: The using of combined proprioceptive training with classes on the BFB platform is effective in restoring BF in MS patients, which based on the influence of vibrations on the proprioceptors of joints and muscles and the formation of new motor stereotypes of BF control.

Disclosure: There is no conflict.

EPO-476

Effect of Non-invasive Brain Stimulation on Somatosensory Evoked potentials in Chronic Ischemic Stroke

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Background and aims: Upper extremity motor impairments remain challenging in post-stroke rehabilitation. While investigating efficacy of newer innovative techniques like non-invasive brain stimulation, neurophysiological surrogate markers are of importance. The objective of this study was to investigate the effects of transcranial electrical and magnetic non-invasive stimulation protocols on somatosensory evoked potential in chronic ischemic stroke cases.

Methods: After screening, 33 patients were randomly assigned to one of the four treatment groups of the transcranial direct current stimulation and repetitive transcranial magnetic stimulation. Somatosensory evoked potential parameters were recorded before and after ten days of the treatment session. All the statistical analyses were carried out using SPSS version 19.

Results: 29 (87.90 %) were males. The mean age was 48.79 (SD; 11.67), and 54.5% were in the age group ≥50. There is a statistically significant improvement in the N20-P22 mean amplitude after treatment sessions in all groups except sham tDCS and sham rTMS group. On paired t-tests, the difference in SEP amplitudes post and prestimulation for the real tDCS and real rTMS coupled group was 1.045±0.732 (p value=0.005). For sham tDCS, real rTMS group, 1.05± 0.96 (P=0.04); for real tDCS, Sham rTMS 0.543± 0.332 (P=0.01) and for double sham stimulation, 0.204± 0.648 (P= 0.4) respectively.

Conclusion: True transcranial direct current or/and transcranial magnetic stimulation significantly enhanced the amplitude of cortical somatosensory potentials and may suggest their beneficial facilitatory effects in neurorehabilitation for upper extremity motor impairment. Clinical Trial Registry of India; CTRI/2019/11/022009

Disclosure: Nothing to disclose.

EPO-477

3D Printing Technology for Amyotrophic Lateral Sclerosis Patients

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Background and aims: The conventional model of orthosis development for ALS does not fully respond to the problems of individual patients. The key issues of the rehabilitation treatment concerns the recovery of the musculoskeletal functions necessary for improving quality of life and enabling activities of daily living. 3D printing offers the unprecedented ability to create orthosis matched to the patient's anatomy. Here, we investigated the ability of 3D printing to develop personalized 3D printed wrist brace and neck orthosis, minimally invasive, lightweight, and breathable to be used for the rehabilitation of patients with ALS.

Methods: Orthosis were 3D printer using FDM technology. Subject satisfaction with each 3D printed orthosis was rated using the modified Quebec User Evaluation of Satisfaction with Assistive Technology (QUEST 2.0).
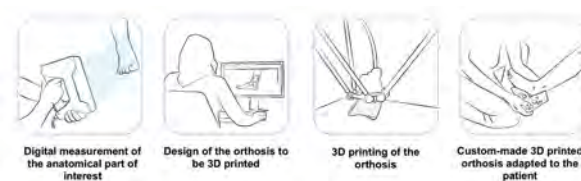
Representative sketch of the 3D Printing workflow for ALS patients

Results: We developed 3D printed personalized wrist brace and neck orthosis minimally invasive, lightweight, shape-memory, and breathable. On a cohort of 20 ALS patients (37–80 years) the usability, and effectiveness of such orthosis were tested. In daily life usage patients reported the following key benefits: size of the orthosis, polymer used, breathability, shape, ease of adjustment, stability, safety, efficacy, and comfort. No evidence of overwork weakness or muscle damage has been reported.
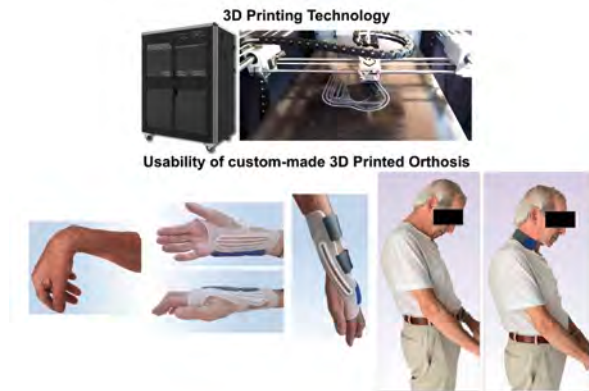
Usability of custom made 3D printed wrist brace and neck orthosis on ALS patients

Conclusion: 3D printing has potential in rehabilitative treatment of ALS. Overall challenge includes learning the technology. Overall benefits include versatility and cost savings. We foresee that 3D orthotic for ALS will become simpler and efficient, thus over time the use of this technology to provide treatment solutions will be mainstream in clinics and hospitals.

Disclosure: Nothing to disclose.

EPO-478

Interaction between children and the humanoid in rehabilitation - risk or progress?

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Background and aims: Nowadays, fastly developing technologies and AI are increasingly involved in our daily lives and provide a new environment for pediatric neurorehabilitation. Robot Pepper has been branded as an "all-around" social robot with multiple functions with high levels of anthropomorphization and functionality (Søraa et al., 2020). Aim of our study was to evaluate children's interaction with Pepper during the neurorehabilitation of social deficit in evaluating possible risks or benefits.

Methods: Child-like robot Pepper (h 120 cm, w 28kg; created by Softbanks 2014) was developed by authors for social skills training in children with social deficits (SD). A therapist guided training process with robot was performed in Tartu University. Pepper was programmed with behavioral and communicative applications to train social skills using Neurotolge technology. During the meeting Pepper introduced itself to the child. Training protocol consisted of 8 different topics. Interaction was studied after 1st session in two ways: therapists' observations and a survey fitted to four sociocultural concepts (15 questions). 32 children aged 5–10 yr. with different neurological diagnoses and SD participated.

Interaction between Pepper and a 5-year-old boy

Results: Observation data showed that children were quickly engaged (up to 3 min) with the robot. They used verbal and non-verbal communication skills: full sentences, holding eye-contact, expressing positive emotions, and liking physical contacts. Survey revealed children's perception as likability 98%, perceived safety 83%, perceived intelligence 81% and anthropomorphism 64%.

Communication with physical contact between Pepper and a 10-year-old girl

Conclusion: Children's messages about robot interactions were positive, they found Pepper to be friendly, cheerful, smart, safe, and showing some human characteristics by adding benefits to rehabilitation process.

Disclosure: No conflict of interests. This work was supported by the Estonian Research Council grant (PRG 789).

EPO-479

Recovering sight with zolpidem: a placebo-controlled multimodal case report

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Background and aims: Zolpidem is a common hypnotic which was described to elicit transient increase of awareness in a fraction of brain-injured patients. We report the case of a stroke patient with almost total blindness recovering sight after zolpidem administration.

Methods: A 63-year-old male with history of bilateral occipital ischaemic stroke presented chronic visual field deficits. He was referred after fortuitous observation of vision improvements with zolpidem intake. He underwent multimodal assessments after the single-blind administration of 10mg zolpidem and placebo (before each exam). Visual function, neuropsychological scores, brain metabolism and connectivity were compared blindly between the two conditions and healthy subjects.

Results: Compared to placebo, the patient showed a spectacular improvement five minutes after zolpidem intake in visual acuity (1/20 to 9.5/10), right visual field detection, visual evoked-potentials amplitude ($+6.0\mu V$) and latency (-8.3ms), allowing him to walk unaided. He scored better in 9/12 neuropsychological tests. Fluorodeoxyglucose positron emission tomography demonstrated metabolic ameliorations in left visual regions. High-density electroencephalography showed preserved connectivity in both conditions. Compared to controls, functional magnetic resonance imaging after placebo revealed preserved connectivity in auditory and default mode networks but decreased connectivity in the visual network, which subsequently improved in the zolpidem condition, essentially in the left occipital pole. The patient reported an effect duration of 3–5 hours.
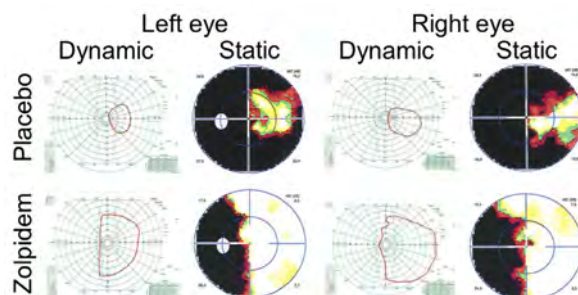
Standard automated perimetry. In the placebo condition, the patient displays a small area of preserved residual vision in the right hemifield. In the zolpidem condition, the patient recovers the totality of right hemifield vision and central vision.
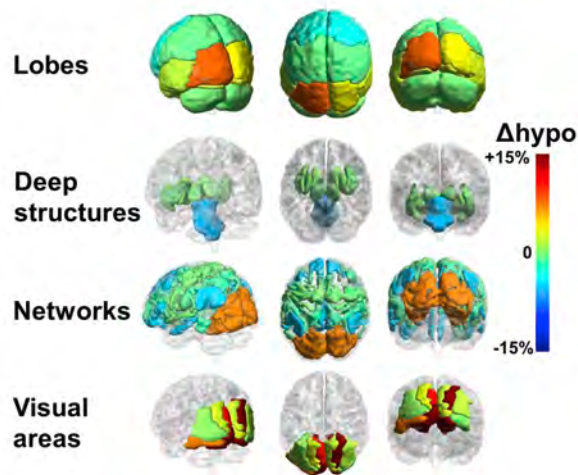
Regional differences in brain hypometabolism between zolpidem and placebo conditions. Regions of interest are color-coded for variations in percentage of hypometabolic voxels, defined as voxels with significantly lower metabolism than controls (n=33).
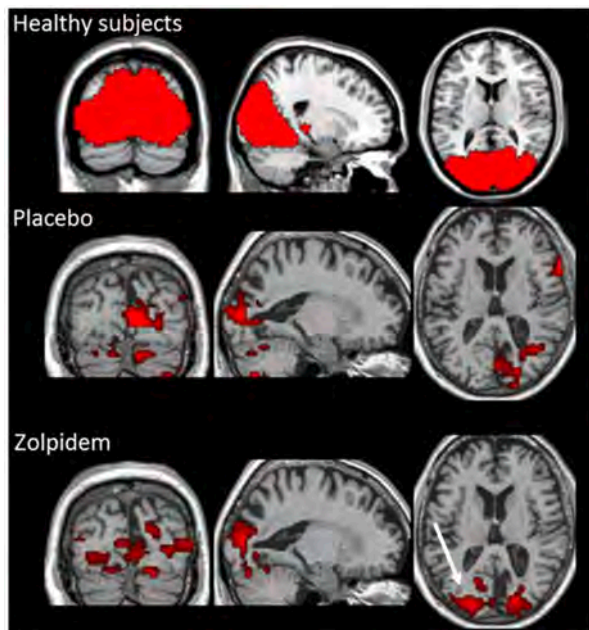
Visual network seed-to-voxel-based connectivity. Functional magnetic resonance imaging showing connectivity of brain regions with visual network areas in 24 controls and the patient in the placebo and zolpidem conditions (significant voxels in red).

Conclusion: We describe the first account of transient right-hemifield vision recovery with zolpidem after bilateral occipital stroke, with consistent brain activity/connectivity increases in left visual regions. The mechanisms may resemble previously described paradoxical effects of zolpidem in the general population and brain-injured patients.

Disclosure: Nothing to disclose.

EPO-480

Trunk Control Test as a potential predictor of modified Barthel Index after stroke rehabilitation.

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Background and aims: Trunk control plays a crucial role in stroke rehabilitation; the Trunk Control Test (TCT), measured at admission to intensive post-stroke rehabilitation has been reported as a predictor of several discharge functional outcomes. However, although modified Barthel Index (mBI) is one of the most widely recommended tools for assessing stroke rehabilitation functional outcomes, the predictive value of TCT on modified Barthel Index (mBI) has not yet been investigated.

Objectives: to verify whether TCT, collected upon admission to intensive inpatient post-stroke rehabilitation, and combined with other variables, potentially affecting rehabilitation outcomes, is independently associated with functional outcome at discharge, measured by mBI.

Methods: Retrospective analysis of data consecutively collected on stroke patients admitted to two intensive inpatient rehabilitation. The primary outcome was mBI at discharge.

Results: 278 post-stroke patients were included. All variables collected to admission and significantly associated with mBI at discharge in the univariate analysis (i.e., TCT, mBI, pre-stroke modified Rankin Scale, mRS, aetiology, gender, age, ambulation, cognitive status, communication ability, Cumulative Illness Rating Scale, bladder catheter, and bedsores) were entered in the multivariate analysis. Three variables independently influencing functional recovery were identified: TCT, mBI, and premorbid disability (mRS) (p<0.001); the model explained 59% of the outcome variance (adjusted R2).

Conclusion: TCT, mBI, and pre-stroke mRS, collected at admission to post-acute intensive inpatient stroke rehabilitation, independently predict mBI at discharge. While TCT is confirmed as a potential predictor of stroke rehabilitation outcome, other variables collected at admission could possibly improve the prediction of stroke rehabilitation global functional outcome.

Disclosure: No potential competing interest was reported by the authors.

ePosters

Monday, June 27 2022
Ageing and dementia 3

EPO-481

The clinical, imaging, and pathology characteristics of 'late cases' of sporadic CJD in the UK

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Background and aims: Sporadic Creutzfeldt-Jakob disease (sCJD) characteristically presents with rapidly progressive dementia and motor features. Early diagnosis is important for prognostication, care planning, and mitigation of public health risks. Here we aim to characterise 'late' cases referred after autopsy to the National CJD Research and Surveillance Unit (NCJDRSU) in whom CJD was not considered in-life, hypothesising these may have presented with atypical features.

Methods: We interrogated the NCJDRSU database for information on clinical, neuroimaging, and neuro-pathological characteristics of cases referred to the NCJDRSU from 2016–2021 after autopsy diagnosis. Local clinical notes were reviewed and relatives contacted for illness timelines.

Results: We interrogated the NCJDRSU database for information on clinical, neuroimaging, and neuropathological characteristics of cases referred to the NCJDRSU from 2016–2021 after autopsy diagnosis. Local clinical notes were reviewed and relatives contacted for illness timelines.

Conclusion: Our data highlights the need to consider CJD in older individuals with undiagnosed or atypical extrapyramidal and/or neuropsychiatric syndromes. Evolution of in-life diagnosis occurred in all cases and illness duration was significantly longer than the average CJD disease duration. MRI retained its high diagnostic utility in this group. The in-life diagnosis of VPSPr is challenging and current diagnostic modalities are not as useful in-life as for CJD.

Disclosure: UK National CJD Research and Surveillance Unit, Centre for Clinical Brain Sciences, University of Edinburgh Funding statement: The UK NCJDRSU is funded by the Department of Health and Social Care Policy Research Programme and the Government of Scotland ("The National CJD Research and Surveillance Unit (NCJDRSU)", PR-ST-0614-00008_18). The views expressed in this publication are those of the author(s) and not necessarily those of the Department of Health and Social Care or the Government of Scotland."

EPO-482
Abstract withdrawn

EPO-483

Arterial stiffness and its influence on cerebral morphology and cognitive function

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Background and aims: Recently, arterial stiffness has been associated with cerebral small vessel disease, brain atrophy and vascular dementia. Arterial stiffness is assessed via pulse wave velocity measurement and is strongly dependent on arterial blood pressure. While, circadian blood pressure fluctuations are important determinants of end organ damage, the role of 24-hour pulse wave velocity variability (PWV) is yet unclear. We here investigated the association between PWV and its circadian changes on brain morphology and cognitive function in community-dwelling individuals.

Methods: The study cohort comprised elderly, community-based participants of the Austrian Stroke Prevention Family Study which was started in 2006. Subjects with any history of cerebrovascular disease or dementia were excluded. The present study considered those 84 study participants who underwent ambulatory 24-hour PWV measurement. White matter hyperintensity volume, brain volume and peak width skeletonized mean diffusivity were evaluated by 3 Tesla MRI. A subgroup of patients was evaluated for cognitive function using an extensive neuropsychological test battery.

Results: Pulse wave velocity was significantly related to reduced total brain volume (p=0.013) in multivariable analysis. This association was independent of 24-hour blood pressure. Only night-time PWV values were associated to reduced total brain volume (p=0.005). Neither MRI markers of cerebral small vessel disease nor cognitive functioning were related to PWV.

Conclusion: This study shows a relationship of arterial stiffness and reduced total brain volume. The association is independent of blood pressure, and elevations in pulse wave velocity during night-time are of greater importance than day-time measures.

Disclosure: The authors declare that there is no conflict of interest.

EPO-484

Dampened frontal gamma activity in Alzheimer's disease patients as revealed by combined TMS-EEG

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Background and aims: In AD animal models, synaptic dysfunction has been recently linked to a disorder of high-frequency neuronal activity. In patients with AD, the relation between oscillatory activity and cognitive dysfunction is still elusive, due to the technical limitations of standard electroencephalographic recordings.

Methods: Here, we used a novel approach combining transcranial magnetic stimulation and electroencephalography to probe local transcranial evoked potentials and oscillatory activity in specific hubs of the fronto- parietal network, which is directly involved in AD pathology. To achieve this, we performed different recordings targeting the left dorsolateral prefrontal cortex, the left posterior parietal cortex and the precuneus in a large sample of mild-to-moderate AD patients (n=60) that were compared with a group of age-matched healthy controls (n=21).

Results: We found that patients with AD show a dramatic reduction of cortical oscillatory activity in the gamma range in the dorsolateral prefrontal cortex. Furthermore, we identify the most expressed frequency in oscillatory activity in the left dorsolateral prefrontal cortex for each AD patient in order to explore the possible relation between individual oscillatory activity and clinical progression. We found that patients with a more prominent decrease in the frontal natural gamma activity were the ones who showed a stronger cognitive decline at subsequent follow-up evaluation at 24 weeks.

Conclusion: The current results point to the combined approach of TMS and EEG as a novel promising technique to measure frontal gamma activity in patients with AD. This index could represent a useful biomarker to predict disease progression and to evaluate response to novel pharmacological therapies.

Disclosure: Nothing to disclose.

EPO-485

Alien limb syndrome in sporadic Creutzfeldt-Jacob disease: A 16 year case series from a national CJD surveillance centre

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Background and aims: Alien limb syndrome is a rare neurological phenomenon, characterised with loss of volitional control and sense of ownership of the limb. Previous reports are limited to outline clinical characteristics and prevalence in sporadic CJD (sCJD). We report the first large national case series of alien limb syndrome in sCJD and describe clinical, imaging, CSF biomarker and genetic characteristics.

Methods: We surveyed NCJDRSU database for probable and definite sCJD cases diagnosed between February 2005-April 2021 presenting with alien limb syndrome. Clinical presentation, CSF and MRI findings and prion protein gene codon 129 polymorphisms were evaluated. Radiological findings were compared with clinical findings of the presenting alien limb syndrome.

Results: A total of 103 cases were identified. 34 cases were definite (autopsy confirmed). Median age of onset was 68years; 47% were male. Mean survival was 4.8 months. 99 individuals had MR brain imaging. Of these, 86 had typical radiological findings of sCJD; 98% (n=81) had contralateral cortical ribbon sign in the parietal cortex and/or putaminal signal change. The prevalence of alien limb syndrome was 6% in our cohort and it was the presenting symptom in 37% of these cases. Posterior type of the syndrome was the most frequent type (95%). RT-QuIC sensitivity was 85%, codon 129 subtypes were MM 82%, MV and VV 9%.

Conclusion: sCJD should be considered in individuals presenting with an alien limb syndrome. Accurate diagnosis of sCJD is important for avoidance of unnecessary investigations, prognostication, care planning, and institution of appropriate public health measures.

Disclosure: Authors have no conflict of interest to disclose.

EPO-486

Neuroadaptive reconfiguration of dopaminergic networks in Prodromal dementia with Lewy bodies

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Background and aims: Dopaminergic deficits are a core feature of dementia with Lewy bodies (DLB). Aim of the study is to examine local and long-distance dopaminergic changes in prodromal DLB patients in comparison with overt DLB dementia and Parkinson's disease (PD) patients.
Methods: 132 subjects entered the study namely 20 prodromal DLB (pDLB), 29 with DLB dementia and 73 healthy controls (CG). Each subject underwent a standardized neurological examination and 123I-FP-CIT SPECT imaging. The occipital-adjusted specific binding in cortical and subcortical regions was calculated in spatially normalized images. Molecular connectivity within the ventral and dorsal dopaminergic networks was measured by partial-correlation analysis.
Results: pDLB and DLB patients showed comparable putamen and caudate dopamine deficits compared with CG. Molecular connectivity analyses revealed a common loss of connections in pDLB and DLB patients involving the thalamic-basal ganglia and cingulate/frontal cortex circuits. The pDLB group showed also widespread metabolic connectivity reconfigurations, more severe in the dorsal than the ventral DA network. Of note, the putamen-thalamic and cortical connections appeared hyper-connected in pDLB and lost in the DLB group.
Conclusion: This study supports a specific loss of extranigrostriatal dopaminergic connectivity in DLB, since the prodromal phases. The shift from an increased to a decreased bilateral putamen-thalamus-cortex connectivity might be a hallmark of transition from prodromal to clinical DLB.
Disclosure: Nothing to disclose.

EPO-487

Clinical outcome of patients with hip fracture and dementia. Data on 7876 patients from Swedish registry SveDem

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Background and aims: Hip fractures and dementia are two age-related disorders, with severe negative impacts on the quality of life. Both are expected to increase in numbers as the population ages. Dementia patients are known to fare worse than the cognitively intact following a hip fracture.
Methods: This was a registry-based cohort study using the Swedish National Hip Fracture Registry (RIKSHÖFT) in conjunction with the Swedish registry for cognitive/dementia disorders (SveDem). Totally 122,614 individuals suffering a first hip fracture between 2010 and 2018 were included. Of those, 7,876 were diagnosed with dementia and registered in SveDem. The primary outcome measures were loss of function at 4 months, and all-cause mortality during the study period.
Results: Patients with dementia were older, had a higher level of co-morbidity, suffered worse fractures, and had higher rates of in-hospital mortality during initial care. At follow-up, they had a greater loss of function, and mortality throughout the study period was higher.
Conclusion: Individuals with dementia performed worse after a hip fracture. Future studies must find the causes so that effective post-surgical care can be developed for this group.
Disclosure: Nothing to disclose.

EPO-488

Clinical characteristics of Mild Cognitive Impairment cohort with grade of alcohol consumption

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Background and aims: Alcohol is a modifiable risk factor for dementia. However, alcohol's role in the development of cognitive impairment and dementia disorders remains unclear as it is poorly studied and probably underdiagnosed, especially in a clinical context outside epidemiological studies.

Methods: We performed a cross-sectional observational study, including 251 subjects with (mild cognitive impairment [MCI] stage, from Memory Clinic, Karolinska University Hospital in 2015. We compared subgroups with different levels of alcohol consumption, concerning social parameters, cognitive, radiological, laboratory profiles as well as comorbidities and burden of drugs. Follow-up was also started especially in regards to conversion to dementia.

Results: Mini-mental State Examination score was not associated with alcohol consumption. Light to moderate drinkers were significantly higher educated. There were significantly more subjects using antianxiety medications among heavy drinkers in comparison with light to moderate drinkers. Finally, never/rare drinkers had significantly lower levels of erythrocyte mean corpuscular volume in their blood tests.

Conclusion: Alcohol consumption was not correlated with a more pronounced cognitive deficit or a distinct clinical severity at an early stage of cognitive impairment apart from higher usage of antianxiety medications. The advice for MCI group about drinking was important in follow-up.

Disclosure: Nothing to disclose.

EPO-489

Plasma progranulin in patients with frontotemporal dementia

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Background and aims: Mutations in GRN gene are one of the most frequent genetic causes of frontotemporal dementia (FTD). They decrease the plasma level of progranulin glycoprotein (PGRN), and the latter has been proposed for diagnostic purposes. However, the level of PGRN can be influenced by gender, age and various SNP in risk genes, like rs5848 SNP in GRN gene.

Methods: We analyzed blood serum from patients with FTD (n=19, five with mutations in GRN gene, Tab. 1) and the control group (n=12). PGRN serum level was determined by Cloud Clone Corporation reagent kit (USA, China) according to the manufacturer's method. rs5848 SNP was verified by Senger sequencing.

	Onset, y	Disease duration, y	Familial cases, %
All FTD patients (N=19)	56 [53;63] (34-67)	3 [2;4] (1-7)	58
bvFTD (N=8)	57 [48;65] (44-67)	2 [2;4.5] (2-5)	50
nfvPPA (N= 10)	55.5 [53;61] (34-63)	3.5 [1.7;4.5] (1-7)	60
svPPA (N=1)	65	3	100

bvFTD – behavioral variant of FTD, svPPA – semantic variant of primary progressive aphasia, nfvPPA – non fluent variant of primary progressive aphasia.

Table 1. Characteristics of the studied groups.

Results: The level of PGRN in patients with mutations in exons of the GRN gene was reduced compared to the FTD group without mutations: 14[8;19] vs 31[16;45] ng/ml (p<0.05). Interestingly, a patient with an intron GRN variant had a high PGRN level (Tab. 2). The PGRN level in the FTD group without GRN exon mutations was elevated compared to the control group (p<0.05). We found no association with clinical, demographic factors or rs5848 variants.

Patient #	*GRN* mutation	Position	Plasma PGRN level	FTD form
1	Gly35fs (rs6371073)	exon 2	19 ng/ml	bvFTD
2	Gly35fs (rs6371073)	exon 2	6,9 ng/ml	bvFTD
3	Gly384fs*	exon 9	10,5 ng/ml	nfvPPA
4	Gly384fs*	exon 9	18 ng/ml	nfvPPA
5	IVS9+1G>A (rs63750707)	Splice Donor Variant	44 ng/ml	nfvPPA

* Not described *GRN* variant

Table 2. Plasma PGRN level in patients with GRN-associated FTD.

Conclusion: Decreased plasma PGRN level could be considered as a biomarker of exon mutations in the GRN gene in FTD patients. Elevation of PGRN level in the case of the intron GRN variant and in FTD patients without GRN mutations may be regarded as compensatory and indicate neuroprotective function of this glycoprotein.

Disclosure: Nothing to disclose.

EPO-490

Non-invasive Brain Stimulation by TPS (transcranial pulse stimulation) improves Deficits in Alzheimer's Disease

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Background and aims: An effective treatment of symptoms in Alzheimer's disease (AD) has not yet been found. Transcranial pulse stimulation (TPS) individually tracked by MRT-scans (figs. 1 and 2) offers new perspectives to ameliorate deficits in AD. Pilot studies show beneficial effects on learning and memory by TPS.

Methods: A 72 year-old out-patient with Alzheimer's disease with serious deficits of executive functions received 6 treatment sessions in 2 weeks (6,000 pulses TPS 0.2 mJ/mm^2 per single pulse, frequency 4 Hz per session). The application of the pulses with Neurolith by Storz Medical was inividually navigated by current MRT-images of the patients (fig. 3). TPS-pulses were administered bilaterally into the frontal, parietal and temporal cortex. Cognitive capabilities of the patient were tested using the Stroop-Test (colour-word-interference-test) and CERAD. The Stroop-Test is a standardized test for executive functions. The patients was tested using a pre – post design (t0 pre stimulation : t1 after 6 sessions, two weeks later and t3 after an interval of 3 months.

Results: TPS-stimulation over a period of two weeks (6 sessions) showed ameliorating effects on performance in the Stroop-Test. The mean-score was diminished significantly (pre vs. post ; $p<0.05$ – paired T-test). The patient showed an extraordinary improvement by cutting completer times by halve and even exhibited a further improvement 6 weeks later. No significant side-effects occured during all the stimulation-sessions.

Fig. 2

Fig. 3

Conclusion: This pilot-trial shows that cognitive impairments of executive functions in Alzheimer's disease may be ameliorated using TPS as a noninvasive brain stimulation method. No severe side-effects were observed.

Disclosure: There was no external funding.

Fig. 1

EPO-491

Common and distinct brain regions involved in visual short-term memory in Alzheimer's Disease

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Background and aims: Visual Short-Term memory (VSTM) deficits can be useful to detect Alzheimer's Disease (AD) in its earliest phases. However, the brain structural underpinning of selective abilities within VSTM remains poorly described.

Methods: 35 AD and 35 healthy elderly controls (EHC) were recruited from the Oxford Centre for Cognitive Disorders. They performed the "What was where?" task on a tablet, (Figure 1) and underwent 3T MRI imaging. We applied the Mixture Model of Working memory to extract the following metrics: Target detection rates, Imprecision (width of the distribution around the target), Guessing (probability of random guessing), Misbinding (erroneously localizing an item to the remembered location of another item), and Absolute Error (distance from the response location to the original item). VBM (Voxel-Based Morphometry) was applied to investigate correlations between brain atrophy regions and behavioural impairment.
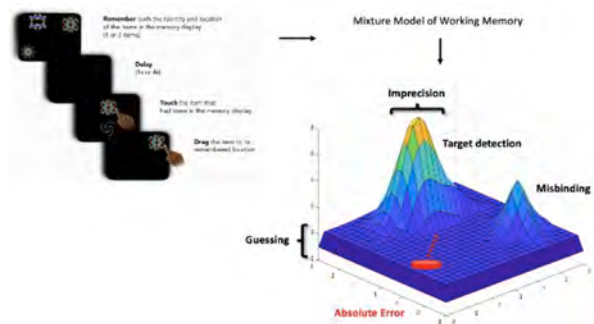
Figure 1:| "What was where?" Short-Term Memory task and Mixture Model of Working Memory

Results: Atrophy of the precuneus correlated with increased random Guessing, Imprecision, and Absolute Error in AD patients (Figure 2). Lower grey matter (GM) volumes in right middle and inferior temporal gyrus associated with increased Imprecision in AD patients. In EHC, greater atrophy in the left supramarginal gyrus correlated with poorer memory precision. Lower GM volume in the right hippocampus associated with higher Guessing rates in AD and EHC.
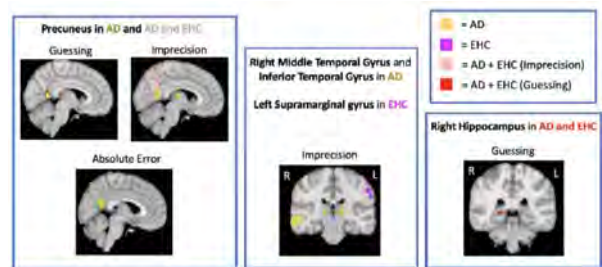
Figure 2: Common and distinct brain regions involved in visual short-term memory in Alzheimer's Disease

Conclusion: The precuneus is crucial for different VSTM abilities. In addition, greater memory Imprecision correlates with atrophy in right middle and inferior temporal gyrus in AD and left supramarginal gyrus in controls, while increasing Guessing associates with lower GM volumes in the right hippocampus in AD and controls.

Disclosure: Nothing to disclose.

EPO-492

Criticality in Electroencephalograms of patients with Mild Cognitive Impairment after Prospective Memory training

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Background and aims: Criticality, a dynamical state characterized by scale-free oscillations, optimizes the capacity of spatially segregated brain areas to couple and transfer information. The aim of the present study was to investigate the clinical improvement of patients with amnesic Mild Cognitive Impairment (MCI) by measuring criticality indices on electroencephalographic (EEG) recordings, correlating criticality and homeostatic brain plasticity.

Methods: We compared "before" and "after" stationary resting state EEG records of right-handed MCI patients (n=17), that participated in a 6-month single-blinded randomized clinical trial of Prospective Memory training. The method of critical fluctuations and Haar wavelet analysis were employed for signal analysis.

Figure 1: Processing of a time series for the estimation of laminar lengths
(A) Time series of EEG records. Stationary parts of at least 1*10^5 points were selected. The red lines mark the laminar region that derives from the histogram. (B) Histogram of a time series, where the distribution of the turning points is shown. The discontinuity is a possible indication of a fixed point. (C) The region near the fixed point is the laminar region used for the analysis.

Processing of a time series for the estimation of laminar lengths (method of critical fluctuations)

Results: Despite the discrepancy between observed and expected (according to the methodology) values, a statistically significant improvement was found in electrodes T6 [t (10)=-2.3, p=0.044] and F4 [t (10)= -2.82, p=0.018]. Improvement of criticality indices was observed in most electrodes.
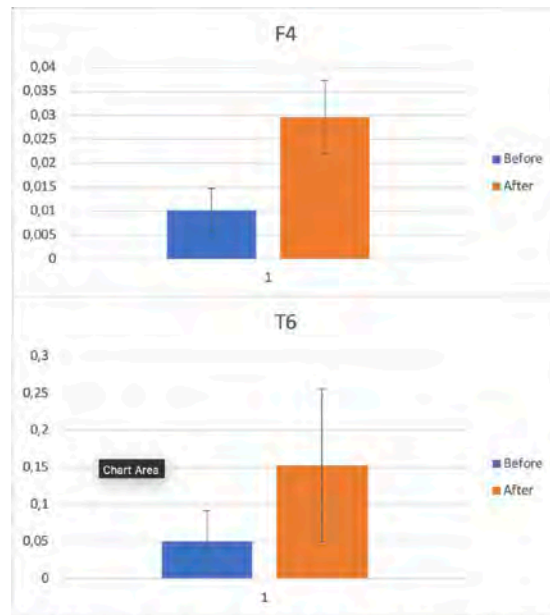
Figure 2: The mean values of the critical parameter (lambda) for the electrodes F4 and T6 that presented statistically significant improvement.

The mean values of the critical parameter (lambda) for the electrodes F4 and T6 that presented statistically significant improvement.

The critical parameter lambda in stationary electrodes

Electrode	Before prospective memory training		After prospective memory training		
	λ	SE	λ	SE	p*
PG1	0,0159	0,00617	0,012	0,00556	0,682
PG2	0,0787	0,0574	0,125	0,111	1,000
Fp1	0,00884	0,00773	0,003394	0,00301	0,720
Fp2	0,0037	0,00439	0,0057	0,00697	0,512
F3	0,00551	0,00450	0,00300	0,00191	0,069
Fz	0,0294	0,00885	0,067	0,0506	0,922
F4	0,0102	0,00449	0,0296	0,00761	**0,018**
F7	0,0188	0,00543	0,021	0,00728	0,814
F8	0,019	0,00581	0,0136	0,00288	0,622
P3	0,0899	0,0421	0,0748	0,0414	0,806
P4	0,0548	0,0273	0,0519	0,0154	0,886
T3	0,0187	0,00762	0,0154	0,00795	0,483
Cz	0,0211	0,00644	0,0164	0,00435	0,570
T4	0,0233	0,00772	0,0246	0,0111	0,935
T5	0,022	0,0268	0,0416	0,0762	0,910
T6	0,0827	0,0415	0,287	0,153	**0,044**
O1	0,0366	0,0423	0,0363	0,0798	0,413
O2	0,147	0,072	0,154	0,0663	0,906
A1	0,0465	0,0181	0,0378	0,0125	0,488
A2	0,05	0,0132	0,114	0,0936	0,216

Table 1: Comparison between "before" and "after" prospective memory training in stationary electrodes.

*5% level of statistical significance

Comparisons between "before" and "after" prospective memory training in stationary electrodes

Conclusion: Our results demonstrate statistically significant changes in neuronal activity of Brodmann areas 37, 39, 19, 8 and 6 [right parieto-occipital region, temporo-parieto-occipital (TPO) junction and frontal lobe]. Our findings are consistent with the improvement of the patients' executive functions, as assessed by appropriate neuropsychological tools. Thus, the method is verified and in concordance with previous studies in clinical data of MCI in terms of results in the temporoparietal and frontal regions, highlighting the methodology as a possible biomarker and emphasizing the need for further research.

Disclosure: This study received no funding. EEG data were provided by "Alzheimer Hellas".

Cerebrovascular diseases 4

EPO-493

The potential Drug-Drug Interactions (pDDIs) which include antimicrobials in patients with acute ischemic stroke

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Background and aims: Prevalence of post-stroke infection is up to 65% of patients. Potential drug–drug interactions (pDDIs) are among the leading preventable causes of adverse drug events. Antimicrobials are among the common drug groups in studies about pDDI.

Methods: A 3-years retrospective study was conducted at the Clinic of Neurology, University Clinical Center Kragujevac, Serbia. A total of 696 patients with acute ischemic stroke (AIS) have been hospitalized in the neurological intensive care unit (NICU). The Micromedex softwer was used to determine pDDIs which include antimicrobials.

Results: From 552 (79.3%) AIS patients with antimicrobials a total of 323 (46.4%) patients were exposed to 109 different pDDIs. The most common pDDIs were Ciprofloxacin-Diclofenac (16.09% of patients), Diclofenac-Levofloxacin (10.20%) and Aspirin-Levofloxacin (9.05%). The most common contraindicated pDDIs was Ceftriaxone-Ringer Solution (6.90%). Fatal outcome was more frequent (p<0.01) in the group of AIS patients (43.7%/28.6%) who were exposed to pDDIs which insclude antimicrobials. Binary logistic regression showed that gender (p<0.01, B=0.623, 95% CI 0.439–0.884) and the number of prescribed drugs (p<0.01, B=1,255, 95% CI 1.203–1.310) were significant factors associated with his pDDIs in AIS patients.

Conclusion: A total of 46.4% of patients with AIS stroke were exposed to pDDIs which include antimicrobials and fatal outcome was more prevalent in group of AIS patients with this pDDIs. Gender and number of prescribed drugs were significant factors associated with pDDIs which include antimicrobials in AIS patients.

Disclosure: Nothing to disclose.

EPO-494

Abstract withdrawn

EPO-495

Abstract withdrawn

EPO-496

The effectiveness of anticoagulant therapy in COVID-19 associated ischemic stroke

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Background and aims: Study was aimed to study the effect of various anticoagulant agents used in COVID-19 associated ischemic stroke on hemorheological parameters.

Methods: 62 patients with COVID-19-associated acute ischemic stroke were selected for the study. These patients (n=62) were divided into three groups. In the group A, n=33 (53.12%) patients received heparin for 2 weeks at 24,000–36,000 ED per day, n=17 (27.4%) patients in the group B received enoxiparin 1mg/kg/day for 2 weeks, and group C n=12 (19.4%) patients received rivaroxaban 15–20 mg per day for 2 weeks.

Results: As a result of anticoagulant therapy in groups,the hemorheological parameters (D-demir, fibrinogen, prothrombin time, APTT) were regressed in the groups A, B and C of patients in the following order: D-dimer from 581.4±1.6 ng/ml to 334.8±2.1 ng/ml; from 628.6±1.4 ng/ml to 336.7±2.3 ng/ml; from 541.1±1.9 ng/ml to 496.6±1.4 ng/ml, fibrin degradation products from 7.71±1.1 μg/ml to 3.6±1.3 μg/ml; from 7.42±0.9 μg/ml to 3.8±1.19 μg/ml, from 7.52±1.2 μg/ml to 3.71±1.3 μg/ml, prothrombin time from 15,2±1.1sec to 9.4±0.8 sec; from 14.9±1.1 sec to 9.6±0.8 sec; from 15,6±1.1 sec to 9.2±0.8 sec, APTT from 31.51±1.29 sec to 24.16±0.8 sec; from 28.2±1.71 sec to 26.9±1.65 sec; from 29,76±1.13 sec to 25.21±1.26 sec;(respectively, p<0.001).

Conclusion: All anticoagulants have a significant positive effect on fibrinogen and prothrombin time, heparin and enoxyparin are effective against D-dimer, heparin and riboraxaban are effective against APTT. However, riboraxaban has almost no positive effect on D-dimer while enoxiparin has almost no positive effect on APTT.

Disclosure: Nothing to disclose.

EPO-497

Transient global amnesia – being a woman is a liability? – a retrospective analysis.

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Background and aims: Transient global amnesia (TGA) is a rare clinical syndrome characterized by sudden-onset, temporary episode of memory loss (with anterograde and retrograde amnesia) that typically lasts for up to 24 hours Our study aimed to investigate the vascular approach in both genders and multiple age groups, in a retrospective observational study on cases admitted on ward with TGA during three years.

Methods: The group included 64 patients, hospitalized with the diagnosis of TGA, who underwent vascular investigations, such as: ultrasonography Doppler of cerebral arteries, cerebral magnetic resonance imaging (MRI) and electroencephalography. Moreover, we considered treatment at discharge, whether the therapeutic decision was for vascular secondary prevention or not after such an event.

Results: Female was by far the most persistent gender, and mostly in age group 61–65. The most frequent preexistent pathology was high blood pressure, by far most of them being female, 76,7% compared with 65%. On cerebral MRI, most of the patients had not had any acute vascular lesions. On ultrasonography Doppler of carotid arteries examination, sort of surprise, commonly were the men who had carotid plaques of atheroma, 75% as opposed to 58,1%. Electroencephalography was mostly normal, for male and female alike, 65%. For more than 90% of the patients, at discharge, secondary vascular prevention treatment was recommended.

Conclusion: As a deduction, women who are 60 years old and over, with high blood pressure in history, are prone to experience the TGA and vascular prevention treatment recommendation was the rule.

Disclosure: Nothing to disclose.

EPO-498

High CRP and fibrinogen concentrations are related to prolonged hospital stay in CVT.

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Background and aims: Prolonged hospital stay in patients with CVT (cerebral venous thrombosis) increases morbimortality and poor outcome related to complications intrinsic to the length of the hospital stay, condition that is seldom studied. In systemic thrombosis many biomarkers such as CRP (C-reactive protein), fibrinogen and D-dimer are associated to clinical outcomes, in CVT this relationship is recently being explored. The aim of this study is to determine if any blood biomarker at admission is related to prolonged hospital stay.

Methods: We conducted a retrospective, single centre study in a tertiary hospital in Mexico City. Electronic medical files of consecutive patients with CVT admitted to ER (emergency room) were reviewed from January 2018 to June 2020. Complete blood tests, acute phase reactants and clinical variables were obtained. Patients were allocated in 2 groups: prolonged hospital stay (PHS) (>7 days) and short hospital stay (SHS) (<7 days).

Results: 20 patients were enrolled, 14 (70%) women, the median age was 33.5 (26–50). SSS (superior sagittal sinus) was the more frequently involved sinus (65%). Median hospital stay was 8 days (6–9) (Table 1). The group comparison showed that CRP $\geq$3 mg/dL (OR 15.7; IC95%, 1.7–141.4) and Fibrinogen $\geq$300 mg/dL (OR 3.2; IC95% 1.5–6.6) were associated to PHS (Table 2, Fig. 1, Fig. 2). Other clinical and laboratory variables were not statistically significant (Table 2).

Variable	SHS n=9	PHS n=11	p value
Sex, women, n (%)	8 (89)	6 (54)	0.15
Age, years, md (IQR)	33 (24.5-48.5)	34 (26-56)	0.53
Smoking, n (%)	3 (33)	5 (46)	0.67
Special risk factors*, n (%)	5 (56)	4 (36)	0.65

*Oral contraceptive (OC) use, malignancy, pregnancy, puerperium.

Table 1: Baseline characteristics.

Variable	SHS n=9	PHS n=11	p value
NIHSS >5, n (%)	2 (22)	5 (45)	0.37
Chronic etiology*, n (%)	2 (22)	6 (55)	0.19
Arrival delay, days (%)	5 (56)	8 (73)	0.64
Disability at discharge (mRS ≥2), n (%)	2 (22)	5 (45)	2.374
Epilepsy, n (%)	6 (67)	6 (55)	0.67
DD >1 μg/mL, n (%)	4 (44)	8 (73)	0.36
CRP ≥3mg/dl, n (%)	2 (67)	9 (82)	0.022**
Fibrinogen >300 mg/dl, n (%)	5 (56)	11 (100)	0.026**

* Thrombophilia (n=4), malignancy (n=2), autoimmune disorders (n=2).
** Fisher's exact test

Table 2: Variable comparison between SHS and PHS groups.
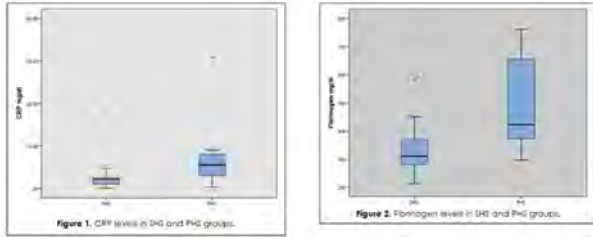
Figure 1 and 2: CRP and fibrinogen levels in SHS and PHS groups.

Conclusion: High CRP and fibrinogen levels are related to PHS in patients with CVT. Future studies are to be developed to further support this finding.
Disclosure: Nothing to disclose.

EPO-499

Impact of asymptomatic intracranial hemorrhage following mechanical thrombectomy on early and long-term stroke outcome.

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Background and aims: Asymptomatic intracranial hemorrhage (aICH) is a common phenomenon in patients with acute ischemic stroke (AIS) treated with mechanical thrombectomy (MT), however, their impact on the functional outcome remains unclear.
Methods: The aim of the study was to analyze the influence of aICH on early (1 and 3 months) and long-term (12 months) functional outcome. 153 patients (56% females, mean age 69,6±11) with AIS due to large vessel occlusion in the anterior circulation treated with MT (80% with TICI 2b-3) were enrolled and followed-up for 12 months.
Results: 62 patients (40,5%) had aICH at 24h follow-up CT. Median age (72 vs.71), prestroke mRS(0 vs.0), baseline NIHSS (16 vs.16) and door-to-needle (DTN) (42,5 vs.39 min) were similar between aICH and noICH patients, respectively. However, those with aICH had (p<0,05) longer onset-to-groin (OTG) (279 vs.234 min), onset-to-TICI (OTTICI) (334 vs. 283,5 min), higher 24h NIHSS (14,5 vs.10), mRS at discharge (5 vs. 4), after 1 (5 vs. 3), 3 (4,5 vs. 3) and 12 months (6 vs. 3,5). There was a significant difference between the aICH and noICH group in the overall distribution of mRS scores at 1 month and a trend at 3 and 12 months, favoring noICH group (Fig.1-3). However, in the logistic regression analysis, after adjustment for confounders (age, baseline NIHSS, DTN, OTTICI) aICH was an independent predictor for 1 month mortality (RR 2,46; 95% CI 0,9–6,76, p=0,07).
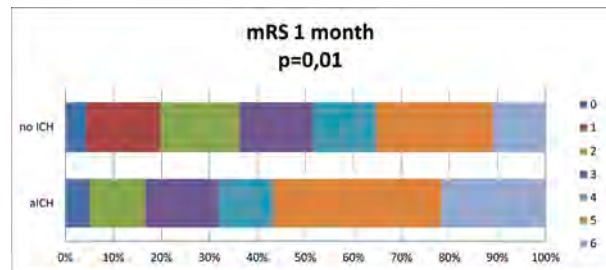
Fig. 1: mRS after 1 month
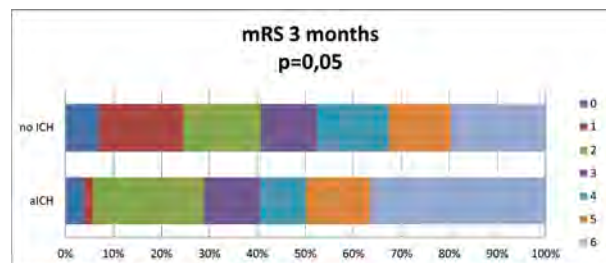
Fig. 2: mRS after 3 months
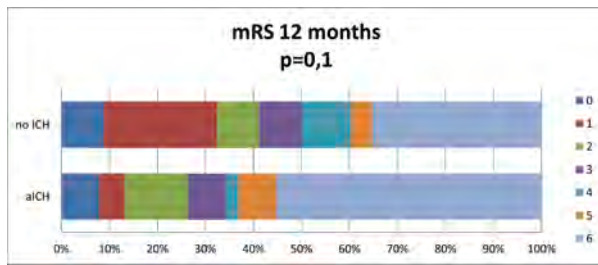
Fig. 3: mRS after 12 months

Conclusion: aICH was associated with worse outcomes in stroke patients treated with MT especially in the short term observation. Further validation of our findings in large cohort studies is warranted.

Disclosure: The authors declare no conflict of interest.

EPO-500

Ischemic Stroke and Infective Endocarditis: a single center analysis of patients risk factors

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Background and aims: Ischemic Stroke (IS) represents the most frequent complication of Infective Endocarditis (IE), occurring in about 40% of all cases. IE symptoms and inflammatory aspects are often non-specific. This study aims to describe clinical and laboratory features of patients with IS and IE, in order to identify potential red flags suggesting IE.

Methods: We enrolled the patients admitted between 2014 and 2022 to our Neurology Department with diagnosis of IS and definitive/possible IE according to modified Duke criteria.

Results: We included 21 patients (clinical, radiology and laboratory data are summarized in Table 1). Reperfusion therapies (RT) for IS was administered in 5 cases. 9 patients presented with a native-valve endocarditis, whereas 11 carried a prosthetic heart valve (PHV) pathology (4 mechanical, 7 biological). About risk factors for IE, 10 patients had previous valvular surgery, 2 patients had central venous catheter recently placed, 2 patients reported drug abuse, 3 patients had chemotherapy and 2 patients revealed a previous IE. Blood tests showed a normal range of white cells in 5 patients, whereas the C-reactive protein was normal in 2 patients. 11 patients underwent cardiosurgery, 8 were treated by medical therapy. 10 patients developed hemorrhagic infarction, 4 of whom received RT. Microbiological pathogens were isolated in 11 cases.

Abbreviations: CRP, C-reactive protein; F, female; ICA, internal carotid artery; ICH, intracerebral hemorrhage; IE, Infective Endocarditis; IVT, intravenous thrombolysis; M, male; MCA, middle cerebral artery; MT, mechanical thrombectomy; mRS, modified Rankin scale; NIHSS, National Institute of Health stroke scale; VB, vertebro-basilar; WBC, white blood cells

Table 1: Patients data

Conclusion: IE should be considered in patients with IS and a suggestive clinical history, in order to make an early diagnosis and allowing appropriate management. According to laboratory data the evaluation of risk factors may help to identify presence of IE.

Disclosure: Nothing to disclose.

EPO-501

Predictors of Disability in Stroke Survivors

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Background and aims: Post-stroke disability is influenced by several factors, e.g. older age, lower education, severity of symptoms or stroke recurrence. To assess the variation in disability as predicted by individual differences in health status, risk factors and healthy behaviors, environmental and social support in stroke patients who had the acute event at least 6 months before.

Methods: WHODAS-12 was used to assess disability. Objective measures of patient's state of health were BMI, hypertension, handgrip, cognitive functioning (MoCA), FIM, comorbidities, anxiety and depression (BDI-II), duration and severity of disease (NIHSS). Risk factors and healthy behaviors were smoking, alcohol consumption, fruit and vegetable consumption, physical activity. Environmental and social support were assessed as number of close people to count on and perceived social support (MOS-SSS).

Results: 122 participants (75 males, 97 with sequelae of ischaemic stroke) were included, mean age was 64.1. Mean NIHSS was 2.9 and average distance from acute event was 5.1 years. WHODAS-12 mean score was 30.9: STAI-T and BDI-II were independent predictors of WHODAS-12 ($R2=0.361$, $F(2.119)=35.2$; $p<0.001$).

Conclusion: In this study, anxiety and depression were independent predictors of disability in stroke survivors. Anxiety and depression can slow down the recovery process, worsen functional independence and cause reduced ability to cope with daily stressors and activities. Anxiety and depression symptoms should be part of routine screening and rehabilitation programmes, providing more complex, multidimensional and effective intervention, as these symptoms impact on one third of patients' experienced disability.

Disclosure: Nothing to disclose.

EPO-502

Impact of sociodemographic factors and comorbidities on ischemic stroke severity in the Tunisian island of Kerkennah

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Background and aims: Stroke represents the 2nd cause of death and acquired disability in adults in Tunisia. Sociodemographic factors and comorbidities are a hallmark of stroke that both increase the stroke severity. Our aim is to evaluate the impact of sociodemographic characteristics and comorbidities on stroke severity of patients admitted in a tunisian regional hospital in the island of Kerkennah (Sfax).

Methods: Data of 136 patients with acute ischemic stroke were collected prospectively for 10 years. Clinical and radiological findings were recorded. Severity of stroke was analyzed according to the National Institutes of Health Stroke Scale (NIHSS) score.

Results: Among 136 patients, 60% were over 70 years old with a sex ratio of 1,09. 97 patients had at least one comorbidity (71%) versus 29% without comorbidities. According to NIHSS score, 83 patients had a moderate to severe stroke (53% and 8% respectively). There was not a significant correlation between the initial clinical severity and the different sociodemographic characteristics and comorbidities.

Conclusion: Despite their advanced age, 29% of our islanders had no comorbidity factor and stroke was minor in 8% of cases. These findings associated to the absence of significant correlation between the initial clinical severity and the sociodemographic characteristics and comorbidities represent a particularity of our study which would probably be linked to the sociogenetic characteristics specific to our islanders. Extension of expected lifespan among our islanders should emphasise primary prevention strategies of cardiovascular disease among them.

Disclosure: Nothing to disclose.

EPO-503

Some pathophysiological mechanisms of development of cerebral hemorrhage.

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Background and aims: Stroke is one of the important problems of cerebrovascular disease and is the second leading cause of death and the first in terms of residual disability. The aim of the study was to study the state of microcirculation,the level of neurotransmitter amino acids, inflammatory (TNF-@) and anti-inflammatory (IL-10) cytokines, nitric oxide products, in cerebrospinal fluid during intracerebral hemorrhages.

Methods: Microcirculation in the glial arteries was studied by intravital biomicroscopy in experimental intracerebral hemorrhage with a breakthrough into the subarachnoid space in 90 experimental animals (white laboratory male rats,weighing 200–240 g). The group of patients with intracerebral hemorrhage consisted of 30 patients (in 10 patients in the right hemisphere,in 18 – in the left hemisphere and in 2 patients – cerebellar localization).

Results: Continuous biomicroscopy of pial microvessels in experimental animals revealed that an increase in blood flow during dilatation of arterioles increases the rate of blood flow, while actively functioning vascular shunts appear, which disappear as blood flow normalizes in the study area.

Conclusion: Intracerebral hemorrhages are characterized by an increase in the production of the pro-inflammatory cytokine TNF-@ from the first day of the disease,which indicates the development of an inflammatory response of the brain in response to hemorrhagic damage.The delay of pro-inflammatory activity is somewhat delayed and gradually increases by the third day of the disease, and the more, the higher the activity of pro-inflammatory cytokines.

Disclosure: Nothing to disclose.

EPO-504

Long-term mortality, motor recovery, cognitive profile and quality of life after cerebral venous sinus thrombosis

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Background and aims: Cerebral venous sinus thrombosis (CVST) is an important cause of stroke and often has a relatively favourable short-term outcome. We endeavoured to evaluate long-term mortality and motor, cognitive, behavioural and quality of life outcome in CVT and their determinants.

Methods: This ambispective cohort study from a comprehensive stroke care centre in India included 225 radiologically confirmed CSVT subjects. Neurological disability graded using modified Rankin score (mRS), daily activity as Barthel index, cognitive deficits as Montreal Cognitive Assessment score (MOCA), behavioural outcome as Hamilton depression rating scale (HDRS) and quality of life as Stroke Specific Quality of Life Scale (SSQoL). Univariate and multivariate analysis were performed for factors associated with outcomes. STATA 14.2, StataCorp, Texas used for analysis.

Results: 52% female, mean age 33.5 (SD 11.4). Median follow up 30 months (IQR:24–42). Only 4 died in acute phase, while 7 during follow up. Motor outcome 83.6 % scoring 0–2 on mRS. But 65.8% had cognitive impairment; Mean HDRS score 9 (range 1–30,SD 4.8) and mean SSQOL 209.7 (SD 24.9). On multivariate analysis, mass effect (p=0.042), hemiplegia (p=0.0001), and mRS at presentation (p=0.001) had significant association with poor motor outcome. Low SE status associated with cognitive impairment (p=0.012).and depression was associated with anaemia (p=0.031) and mass effect (0.04).

Conclusion: In one of the largest series long term follow up of CVST, though mortality and motor outcome were excellent, long-term neuropsychiatric impairment was common. Acute care and long-term management must have plans to prevent and manage these occult neuropsychiatric deficits.

Disclosure: Nothing to disclose.

EPO-505

Factors related to longterm anticoagulation in cvt patients from a tertiary hospital

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Background and aims: Anticoagulation on CVT is followed until 6 to 12 months according to guidelines. Longer periods of treatment are used in patients with high thrombotic risk. We describe the duration of treatment with OAC and what risk factors are related to longer treatment.

Methods: We conducted a retrospective single centre study in a tertiary hospital in México City. Electronic medical files of consecutive patients with CVT were reviewed from January 2018 to June 2020. Clinical, radiological and laboratory variables were obtained. Patients were allocated according to the time of use of OAC (less or more than a year).

Table 1. Comparison of baseline features in the groups treated with OAC within and over 12 months

Variable	< 12 months with OAC n=11	> 12 months with OAC n=9	p value
Sex Women, n (%)	9 (82)	5 (56)	0.33
Age, years, md (IQR)	36 (25-52)	29 (23-43.5)	0.49
Smoking, n (%)	2 (18)	6 (67)	0.065
Special risk factors, n (%)	7 (64)	2 (22)	0.092

OAC. Oral anticoagulation

Results: We collected data from 20 patients. 14 (70%) were female, with a mean age of 33.5 (26-50). 40% (n=8) were smokers, 20% (n=4) used hormonal contraceptives, 15% (n=3) were pregnant or in puerperium and 10% (n=2) referred vaccination for SARS-CoV-2. superior sagittal sinus was the most frequently affected (65%). The median time of AOC treatment was 13 months (6.7–16.7). In the bivariate analysis, the existence of a chronic cause (OR 14; IC95%, 1.25–156; p= 0.028), and prolonged hospitalization (OR 15.7; IC95% 1.7–141.4 p= 0.22) were associated with AOC treatment over a year. Initial NIHSS, mRS at discharge, D-dimer values or seizures al presentation showed no correlation.

Table 2. Factors related to chronic use of OAC

Variable	< 12 months with OAC n=11	> 12 months with OAC n=9	p value
NIHSS >5, n (%)	2 (22)	5 (45)	0.37
Chronic etiology, n (%)	1 (11)	7 (64)	0.028
Long stay >7d, n (%)	2 (22)	9 (82)	0.022
Disability at discharge (mRS ≥2), n (%)	4 (44)	7 (64)	0.65
Seizures, n (%)	5 (56)	7 (64)	1.0
D-dimer >1µg/ml, n (%)	4 (44)	8 (73)	0.36
Fibrinogen >350mg/d, n (%)	4 (44)	7 (64)	0.65

Chronic etiology, thrombophilia (n=4), malignancy (n=2), autoimmune disorders (n=2)

Conclusion: Use of OAC in a tertiary centre is related to chronic conditions with high thrombotic risk and with long hospital stay, according to the guideline's recommendations.

Disclosure: I declare that I don´t have any conflict of interest.

EPO-506

Insomnia, A Late Complication Of Non-Traumatic Aneurysmal Subarachnoidal Hemorrhage

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Background and aims: Sleep disturbances and decreased health-related quality of life are well-documented sequelae encountered after aneurysmal subarachnoidal hemorrhage (SAH). The aim of this study was to analyze the impact of the vascular event on the quality of sleep and decide which aspects of sleep habits are the most affected in survivors of SAH.

Methods: We conducted an observational, retrospective study that included survivors of non-traumatic aneurysmal SAH, admitted into our clinic between 2017 and 2021. Patients self-assessed their sleep quality using the Pittsburgh Sleep Quality Index (PSQI). 26 patients took part in this study – 11 men and 15 women. Data were analyzed for statistical correlation between the severity of insomnia and location of the aneurysm, Hunt&Hess grade, mRS grade, age, pre-existing comorbidities. We analyzed as well the declared onset of insomnia in relation to SAH (pre-existing/novel symptoms).

Results: The mean GlobalScore of PSQI was 7.27, indicating severely impaired sleep quality. There was no statistical correlation between the Hunt&Hess grade upon admission and the GlobalScore of PSQI (p-value=0.94). Sleep quality was similar between male and female patients, with a mean GlobalScore of 6.45 and 7.87 respectively. The most impaired aspects were sleep latency (mean score of 1.54 out of 3) and sleep disturbances (mean score of 1.46 out of 3).

Conclusion: Insomnia is a frequent late complication of non-traumatic SAH, with sleep onset and sleep maintenance being the most impaired components overall. This may guide further clinical evaluation into identifying subjects with emotional disorders, given the well-known specific sleep pattern of depressive patients.

Disclosure: The authors have nothing further to disclose.

EPO-507

Acute Transient Contrast-Induced Neurologic Deficit in the Era of Endovascular Treatment

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Background and aims: Acute transient contrast-induced neurologic deficit (ATCIND) is a group of acute neurological syndromes correlated with arterial contrast administration during an endovascular procedure.

Methods: Description of two individual cases of patients who developed acute transient contrast-induced neurological deficit (ATCIND) in the setting of coronary and cerebral angiography. The main purpose is to discuss the diagnosis, management, and outcomes of ATCIND.

Results: A case is presented of ATCIND in a 68-years-old male patient who had an elective angioplasty with stenting for left internal carotid artery stenosis. This patient presented early neurological deterioration after cerebral angiography with global aphasia. The second case reported was a 57-years-old man presenting with acute coronary syndrome during cryoablation of atrial fibrillation. An urgent coronary angiography was performed, after angiography, the patient presented neurological deficit mimicking total anterior circulation stroke and generalized tonic-clonic seizures. In both cases, alternative causes of neurological dysfunction were discarded. A computed tomography scan revealed an absence of new infarct or hemorrhage showing hemispheric cerebral edema suggesting contrast-induced encephalopathy. Both patients received intravenous hydration and antiepileptic drugs, with complete neurological recovery.

Conclusion: ATCIND should remain as one of the options in differential diagnosis for patients who present acute neurological deficit or seizures in the setting of endovascular procedures. ATCIND is acute and can have a severe presentation with full recovery expectation.

Disclosure: Nothing to disclose.

Child neurology/developmental neurology & Coma and chronic disorders of consciousness

EPO-508

Clinical and Diagnostic Features of Agenesis of the Corpus Callosum in Children of Sumy Region

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Background and aims: Corpus callosum is the most powerful interhemispheric connection, containing more than 300 million axons and plays an important role in coordinating information and exchanging sensory stimuli between hemispheres. Agenesis of the corpus callosum is often associated with CNS malformations: Dandy-Walker anomaly, micro- and macrocephaly, malformations of the cardiovascular system, gastrointestinal tract and urogenital system, middle cleavage syndrome, and may be a manifestation of genetic syndromes.

Methods: Retrospective data on clinical and diagnostic features of agenesis of the corpus callosum in children of Sumy region were analyzed

Results: The frequency of cases of agenesis of the corpus callosum for 16 years was 6 per 219,235 newborns, which is 1:36,000 (0.003%). All cases were sporadic and combined with CNS pathology were detected in the early neonatal period during neurosonography by detection of widely spaced lateral ventricles, enlarged occipital horns of the lateral ventricles and forward displacement of the third ventricle. Dandy-Walker anomaly was diagnosed in 2 cases, cardiovascular and gastrointestinal malformations with microcephaly in 4 cases. Two children died: one had progressive ventriculomegaly, died at the age of 3.5 months; the other at the age of 1 year 4 months from severe pneumonia. Both children had cleft palate. Two children are currently alive, one has reached the age of 6 with mental retardation, the other 3 years with normal intelligence.

Conclusion: Agenesis of the corpus callosum is a rare complex pathology that often accompanies genetic developmental abnormalities and is combined with other malformations of the CNS.

Disclosure: Authors have nothing to disclose.

EPO-509

Cranial nerves involvement in SURF1 related syndrome: neuroimaging findings and an unusual Blink Reflex

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Background and aims: Involvement of the peripheral nervous system is frequent in the complex phenotype of mitochondrial diseases (MDs). Variants in the SURF1 gene are the most frequent causes of Leigh syndrome (LS) due to cytochrome c oxidase deficiency. The development of demyelinating neuropathy frequently falls within the clinical spectrum. However, the possible involvement of cranial nerves has never been characterized.

Methods: The patient was a 6-year-old boy affected by LS associated with demyelinating neuropathy caused by two heterozygous mutations in SURF1 (c.240+1G>T/c.870insT). Neurological examination showed severe psychomotor delay, dyskinetic movements, intentional tremor, diffuse hyposthenia, kyphoscoliosis and hollow foot.

Results: Neuroradiological investigations assessed from baseline to six months follow-up revealed, in addition to the typical brain anomalies of LS, enhancement of the cisternal tracts of the cranial nerves, more evident along the optic and trigeminal nerves bilaterally. Neurophysiology revealed, at first, the typical peripheral neuropathy. During the follow-up, a peculiar pattern at the Blink Reflex was observed with a marked and diffuse increase in the latency of the responses, compatible with dysfunction of the trigeminal afferent pathway and the facial nerve efferent pathway.
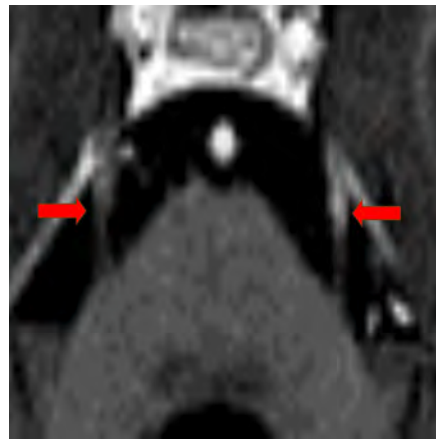
Figure 1. Trigeminal nerves enhancement on T1-weighted brain MRI.
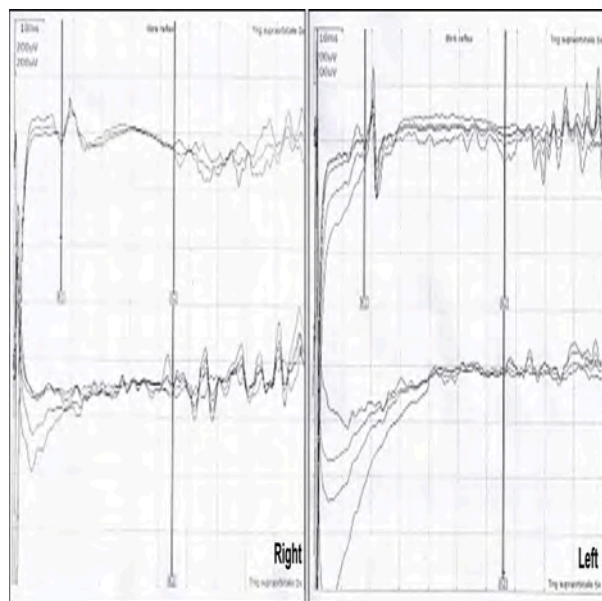
Figure 2. Blink Reflex showing marked and diffuse increase in response latency and increased cMAP latency for facial nerve stimulation.

Conclusion: Taken as a whole, the alterations observed were interpreted as the expression of an involvement of the cranial nerves in the pathological process, a process that is probably dynamic and not observable in the early stages of the disease. The case described therefore represents the first instrumental evidence of involvement of the trigemino-facial contingent of demyelinating type on a genetically predetermined basis related to mitochondrial pathology.
Disclosure: Nothing to disclose.

EPO-510
Abstract withdrawn

EPO-511
Akinetic mutism in a disorder of consciousness: a combined neuroimaging and neurophysiology case-report study

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Background and aims: Akinetic mutism (AM) is a rare neurological condition characterized by the absence of spontaneous behavior and speech, frequently associated with a bilateral disruption of frontal-subcortical circuits. Due to the lack of responsiveness, AM is often misdiagnosed especially when occurring in the context of a disorder of consciousness. Here, we report the unique case of a post-hemorrhagic patient with AM who was investigated through both neuroimaging and neurophysiological techniques.
Methods: Using a 3T Siemens Prisma, the patient underwent a structural MRI (3D-FLAIR) and a functional MRI (fMRI) with an active motor command following paradigm. The brain lesion was segmented on 3D-FLAIR, registered to the MNI space and the gray matter brain regions most affected by connectivity disruption were predicted with the Network Modification Tool (NeMo). Neurophysiological evaluations were performed through EEG and transcranial magnetic stimulation combined with EEG (TMS-EEG).
Results: In the case presented here, even if behavioral evidence for consciousness were particularly ambiguous, high-complexity in the parietal cortex at the TMS-EEG exam indicated the presence of consciousness, whereas a low-complexity pattern persisted in frontal premotor areas. Neuroimaging assessment showed a bilateral damage of the frontal medial cortical regions, in particular a significant disconnection of premotor areas was revealed by NeMo. Interestingly, the fMRI confirmed a preserved capacity of command following, otherwise undetected by behavioral evaluation.
Conclusion: This unique combination of neuroimaging and neurophysiological techniques was able to provide glimpses into the diagnosis and the underlying pathophysiology of a rare neurological syndrome such as AM.
Disclosure: This work was supported by ERA PerMed JTC2019 "PerBrain".

EPO-512

The impact of medical complications on 6-month outcome in prolonged disorders of consciousness

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Background and aims: Patients with prolonged disorders of consciousness (pDoC) show severe functional disability and high risk to develop medical complications (MCs). The present longitudinal study aimed at evaluating the impact of MCs on 6-month clinical-functional outcome, by means of Machine Learning (ML) approach.

Methods: 176 inpatients (123 males, mean age: 60.2 year<A[IQR = 21.7]), with prolonged (≥1 months post-onset) DoC (VS=91, MCS=85) were consecutively enrolled in 23 intensive neurorehabilitation units. Patients' demographic data, medical history, consciousness level (by Coma Recovery Scale-Revised, CRS-R), and functional status (by Glasgow Outcome Scale-Extended, GOS-E) at admission were gathered. MCs developed in the first 3 months of rehabilitation stay were recorded and grouped in 10 categories with respect to the organ system involved. All patients were followed-up at 6-months from injury by means of GOS-E. An Orthogonal Matching Pursuit (OMP) model was trained and k-fold cross-validated using data taken at admission, with GOS-E ≥4 at 6 months as target. Then, predictions were concatenated with MCs collected and with such dataset a cascade OMP was also validated.

Results: OMP trained at admission reached a cross-validation accuracy of 81.1%, while OMP trained at three months resulted in an accuracy of 88.3%. High number of MCs was associated with poor outcome (GOS-E<4), whereas younger age, higher CRS-R communication score and absence of invasive feeding modality predict good outcome (GOS-E ≥4).

Conclusion: Occurrence of MCs negatively impact prognosis in patients with DoC and calls for appropriate levels of care and high level of multidisciplinary medical expertise.

Disclosure: No conflict of interests to be declared.

EPO-513

From the diagnosis of arteriovenous malformation to cerebral proliferative angiopathy: a case report

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Background and aims: In cerebral proliferative angiopathy, there is an increase in brain vascularization with abnormal vessels in a healthy brain parenchyma.It can be confused with arteriovenous malformations (AVMs), although its natural history and pathophysiology are totally different.

Methods: We introduce the case of an 8-year-old child diagnosed with proliferative cerebral angiopathy after having received a diagnosis of AVM for years.

Results: 8-year-old girl who began at 4 with left hemiparesis self-limited episodes lasting 30 minutes. In cranial magnetic resonance imaging (MRI), an extensive right parasagittal vascular malformation is observed, and a diagnosis of focal seizures secondary to this malformation is assumed. They added carbamazepine to her treatment. Two years later, she had a focal aware seizure and a focal to bilateral tonic-clonic seizure, for which she was admitted. Cranial MRI showed intracranial hypertension and increased size of AVM. Lumbar puncture showed opening pressure of 48 cm H_2O and treatment with acetazolamide was started leading to clinical improvement. She was referred to our center two years later. The cerebral arteriography was interpreted as cerebral proliferative angiopathy with right hemispheric hypoperfusion. The patient is currently awaiting surgery (encephaloduroarteriosynangiosis) and pharmacological treatment (bevacizumab).
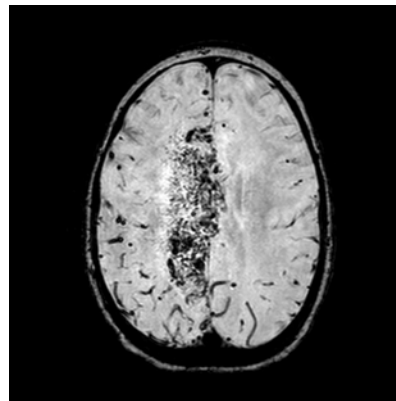
Cranial MRI, BOLD. Extensive right parasagittal vascular malformation due to cerebral proliferative angiopathy.
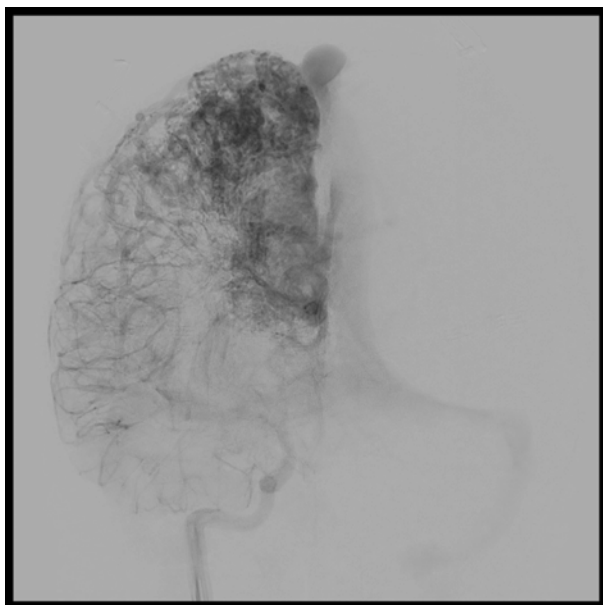
Angiography, coronal. Extensive right parasagittal vascular malformation due to cerebral proliferative angiopathy
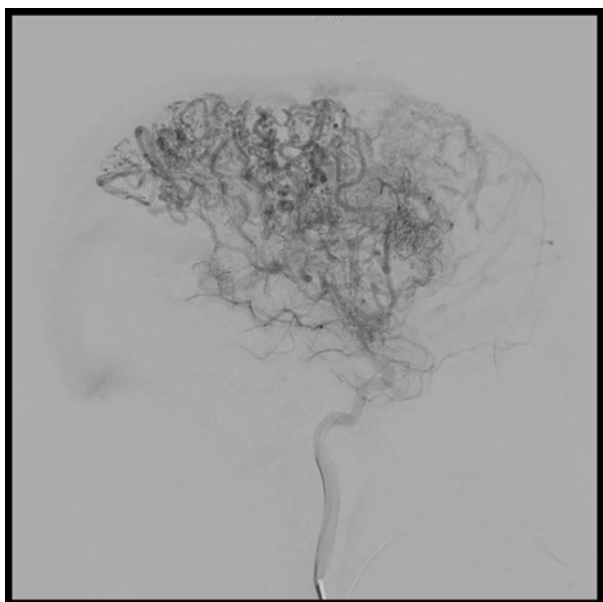
Angiography, sagital. Extensive right parasagittal vascular malformation due to cerebral proliferative angiopathy

Conclusion: It is important to include cerebral proliferative angiopathy in the differential diagnosis of cerebral vascular malformations. This disease, sometimes mistaken for an AVM, has a different natural history, prognosis, and treatment. Early diagnosis and targeted treatment can improve the quality of life of patients. This case shows us the importance of angiography in the precision diagnosis in cases of cerebral vascular malformations.

Disclosure: Nothing to disclose.

EPO-514

Quality of life in children with ischemic stroke

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Background and aims: Analysing the quality of life (QoL) in children after stroke is useful for appreciating the patient's needs in psychological, physical and social support. The study aimed to evaluate the child QoL after pediatric ischemic stroke and its predictors.

Methods: We evaluated 58 children in the post-stroke period (>6 months), 3–12 years old (MA 5.29 years), 36 were boys. QoL was assessed using the PedsQL pediatric questionnaire, post-stroke neurological deficiencies were evaluated utilising the Pediatric Stroke Outcome Measure (PSOM) and the modified Rankin Scale (SRm). Age, sex, socioeconomic status, neurological deficits were correlated with QoL score. Excel and SPSS statistical programs were used.

Results: The average PedsQL total score was 51.88 points (SD±21.26). A maximum average value was obtained on the emotional scale (62.28 points), the minimum average value - on the physical scale (45.13 points). Fifty-one percent of parents rated their children's QoL as low (<50 points), 40.63% as average and 8.47% as high. Multivariate analysis showed that gender and socioeconomic status did not influence QoL. Age at onset of stroke partially influenced QoL, the highest predictive value being in the 1-12 months age group (p=0.013). Neurological deficits negatively affected QoL (p<0.001), being a significant predictor.

Conclusion: QoL of most children after stroke is medium or low level, the physical health is the most affected scale. Age at onset of stroke and neurological deficits negatively influence QoL. The assessment of the QoL in children after stroke provides information on its long-term results and the rehabilitation therapy effectiveness.

Disclosure: Nothing to disclose.

EPO-515

Davidoff-Dyke syndrome: a multidisciplinary approach.

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Background and aims: There are multiple pathologies that pose a diagnostic and therapeutic challenge, requiring the intervention of various medical specialties and the subspecialties of neurology themselves. We present one of these examples, referring to a clinical case.

Methods: Woman, 24 years old, native from Ecuador, resident in Spain for two years, referred from Otorhinolaryngology (follow-up for congenital cofosis) for epilepsy control. Anamnesis was carried out on the mother, who did not live with her: childbirth and normal psychomotor development up to 3 years of age, where she began with generalized seizures and right limbs paresia. Treated with LEV 500mg / 12hrs since she was 14, with good control, except for disconnection episodes lasting seconds, 1 per month. Physical examination: right brachial paresis 4/5 with spasticity, choreoathetosic movements of the right extremities, predominantly upper, and local pain. EEG: no findings. MRI (images 1, 2 and 3): marked comparative atrophy of the left cerebral hemisphere, compatible with Davidoff-Dyke syndrome, of probable chronic ischemic etiology.
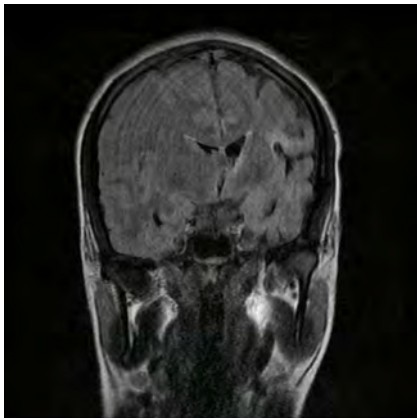
MRI coronal section, FLAIR sequence: Left hemisphere hemiatrophy.
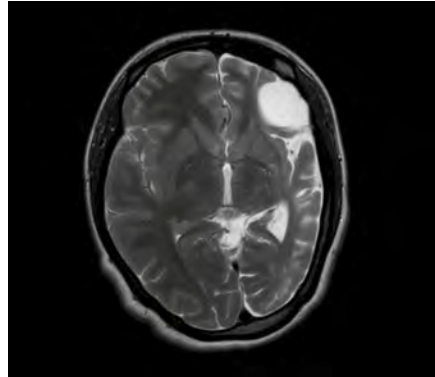
MRI axial cut, T2 sequence: left frontal porencephaly.
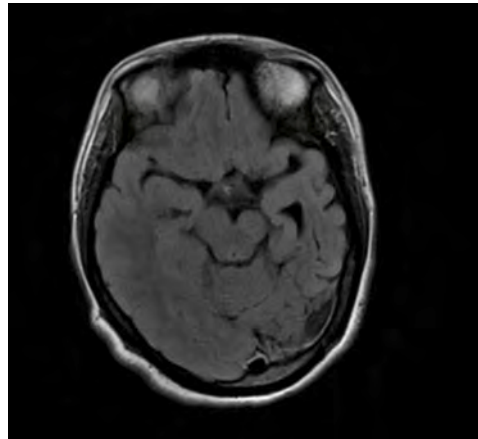
MRI axial section, FLAIR sequence: marked atrophy of the left hemisphere that conditions midline displacement.

Results: In epilepsy consultation, the LEV dose is increased to 750mg / 12hrs, reducing disconnection episodes to 1 per year. In general neurology consultation, trihexyphenidyl is initiated. In the neurosonology consultation, botulinum toxin was infiltrated for the right hemidistonia, with improved posture and pain in the right upper limb. In otorhinolaryngology, a cochlear implant is pending.

Conclusion: Davidoff-Dyke syndrome is not only an infrequent cause of structural epilepsy, but also presents other therapeutic challenges, such as paresis-dystonia secondary to the brain injury that causes the syndrome, being a multidisciplinary approach important.

Disclosure: Nothing to disclose.

EPO-516

Intracranial hypertension (IH) without headache, in a patient with CIPA, and RESLES. An extremely rare case.

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Background and aims: Congenital insensitivity to pain with anhidrosis (CIPA) is a genetic syndrome linked to mutations in the domain of the NTRK1 gene on chromosome 1q23.1, with autosomal recessive inheritance, which is included within hereditary sensory-autonomic neuropathies. It is characterized by total insensitivity to somatic and visceral pain, including the cranial meninges, leading to repetitive injuries, self-mutilation, recurrent infections, fractures, joint deformities, defects in thermoregulation, and anhidrosis. We present a case of IH and meningeal inflammation, masked by a CIPA

Methods: A 15-year-old woman with a genetic diagnosis of (CIPA) and a compatible clinical syndrome, including multiple trauma complications, fractures, deformities, and infections. She was admitted due to acute vertiginous symptoms with vomiting, ataxia and bilateral sixth nerve paresis, with papilledema in both eyes. The study of the CSF revealed an inflammatory profile with 6 cells/µL, and pathological IgG index: 0.95 and high opening pressure up to 35 mmHg. Acute infection was ruled out by viral/bacterial microbiological study and negative serology. Neuroimaging shows a lesion in the splenius of the corpus callosum, suggestive of reversible splenial lesion syndrome (RESLES) with diffusion restriction.
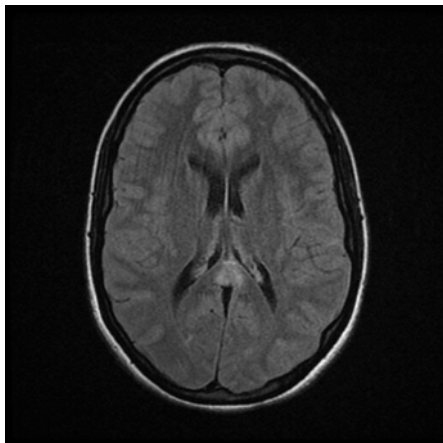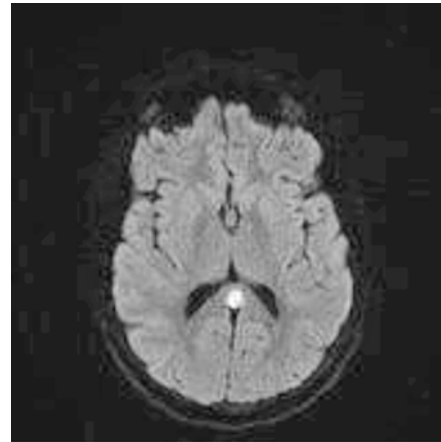
MRI diffusion sequence shows a lesion in the splenius of the corpus callosum, suggestive of reversible splenial lesion syndrome (RESLES).

Results: Treatment was started with methylprednisolone and later with acetazolamide with complete recovery of the neurological symptoms and subsequent resolution of the papilledema and improvement of the MRI image.
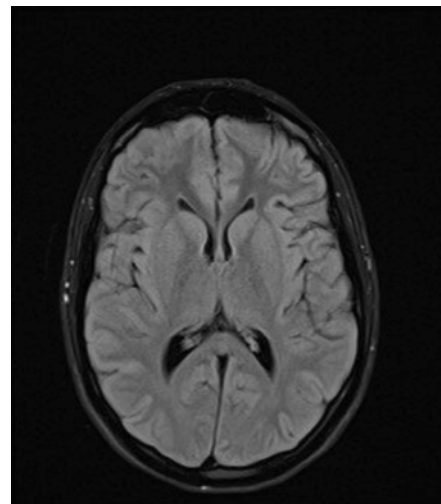
MRI FLAIR sequence shows improvment of the lesion.

Conclusion: CIPA syndrome can potentially mask serious pathologies due to insensitivity to pain; such as IH in the absence of headache, which is its main symptom. Gaining importance perform a thorough and exhaustive history and exploration.

Disclosure: Nothing to disclose.

MRI FLAIR sequence shows a lesion in the splenius of the corpus callosum, suggestive of reversible splenial lesion syndrome (RESLES).

EPO-517

Cerebellar vermian hypoplasia and retinal dystrophy : A genetic TMEM67/AHI1 linkage analysis

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Background and aims: AHI1 gene alteration is responsible of JBTS3 (MIM 608629) condition. Affected individuals with this gene mutation often have impaired vision due to retinal dystrophy. In the other hand, diseases associated with TMEM67 include Coach syndrome 1 which is a JS related disorder (JSRD) (MIM 216360). Here, we report a Tunisian child suspected to have an overlapping syndrome for who a linkage analysis was conducted.

Methods: Clinical, ophthalmic and radiographic examination as well as a linkage analysis with microsatellite markers for TMEM67 on and AHI1 genes were conducted for a child suspected to have an overlapping syndrome related to Joubert syndrome.

Results: The case report was a four-year-old female child born from Tunisian consanguineous parents, for who neonatal breathing abnormalities, hypotonia, developmental and psychomotor delays were, revealed in her clinical history. There was a delay in achieving motor milestones. Neuroradiologically, there were a cortico-subcortical atrophy as well as hypoplasia of the cerebellar vermis with the molar tooth sign. Ophthalmic examination showed bilateral retinal dystrophy. Linkage analysis with microsatellite markers for AHI1 and TMEM67 genes revealed homozygous/heterozygous haplotypes for respectively AH1 and TMEM67 genes.

Conclusion: Central nervous system involvement and retinal dystrophy associated to genetic variations in both TMEM67 and AHI1 may be a distinct form of JSRD.

Disclosure: Nothing to disclose.

EPO-518

Automated pupillometry to detect cognitive motor dissociation after acute brain injury

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Background and aims: Automated pupillometry is well-established in the clinical setting for quantifying pupil motility with great precision at the bedside. Mental tasks such as mental arithmetic leads to pupillary mydriasis in conscious persons and is considered a surrogate marker for cognitive and emotional processes. Using a paradigm of standardized stimuli to evoke pupillary dilation, we investigated if automated pupillometry could detect covert consciousness in patients with acute brain injury.

Methods: We established an automated pupillometry paradigm presenting patients and age- and sex-matched healthy volunteers to the following stimuli: 1) their own facial reflection in a mirror, 2) a series of three different sounds, and 3) a mental task based on mental arithmetic to produce cognitive load. Pupillary responses before and after stimuli were recorded by automated pupillometry.

Results: Automated pupillometry was performed on 91 patients (male 69%; median age 62; 45 neurological and 46 out-of-hospital cardiac arrest patients) and 25 volunteers. The total number of automated pupillometry recordings in patients was 688 (177 mirror; 174 auditory; 337 mental arithmetic) with 53 patients completing at least two series of stimuli. Data analysis is ongoing and will be presented at the congress.

Conclusion: Pilot data on healthy controls demonstrates the feasibility of automated pupillometry to record pupillary dilation as a measure of brain activity. We hypothesize that automated pupillometry also may contribute to the clinical evaluation of unresponsive patients with acute brain injury by detecting residual consciousness in a subset of patients with cognitive motor dissociation.

Disclosure: Authors have no conflict of interest to declare.

EPO-519

Acute toxic leukoencephalopathy induced by presumed synthetic cannabinoid intoxication – a case report

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Background and aims: Toxic leukoencephalopathy refers to a category of central nervous system disorders affecting the white matter structure potentially induced by acute or chronic exposure to exogenous neurotoxins such as (synthetic) drugs. We report here the case of a patient with acute leukoencephalopathy leading to neurological deterioration followed by an impressive functional recovery in the context of suspected synthetic cannabinoid intoxication.

Methods: A 29-year-old male patient was admitted in a United Arab Emirates hospital due to neurological deterioration in the context of high-dose synthetic cannabinoid consumption. No toxicology screening was performed. Given the absence of neurological evolution and concomitant impairments after 14 days, end-of-life decision was proposed by the medical team. However, the relatives decided to transfer the patient to a rehabilitation center in Germany 19 days after the intoxication. The patient underwent multimodal evaluations including clinical assessments with the Coma Recovery Scale-Revised, structural magnetic resonance imaging (MRI) and fluorodeoxyglucose positron emission tomography (PET).

Results: Clinical evaluations monitored the recovery of the patient from a diagnosis of coma to a diagnosis of emergence from minimally conscious state with functional recovery 50 days after intoxication. The reduction of hypometabolic areas and the increased global cortical metabolism between PET performed 50 days and 5 months after intoxication supported clinical signs of recovery (figure 1). However, bilateral white matter damage and subcortical necrosis persisted between the MRI performed 20 days and 5 months after intoxication (figure 2).
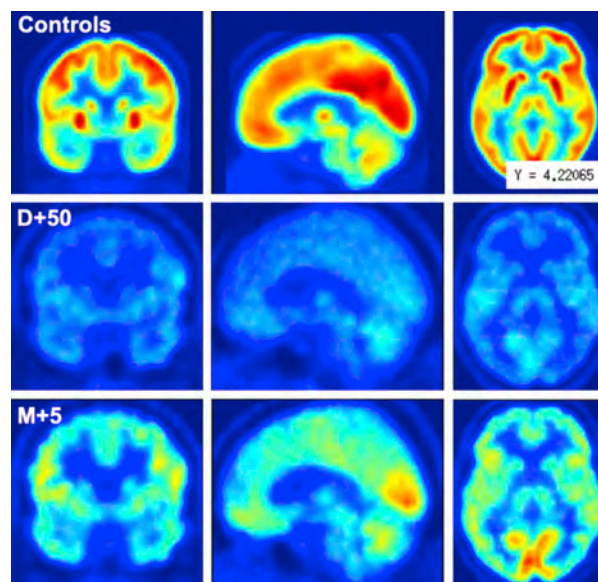
The bilateral hypometabolic areas in the frontal and parietal regions 50 days post-intoxication (global cortical metabolism decreased by 60%) regressed 5 months post-intoxication (global cortical metabolism decreased by 41%).
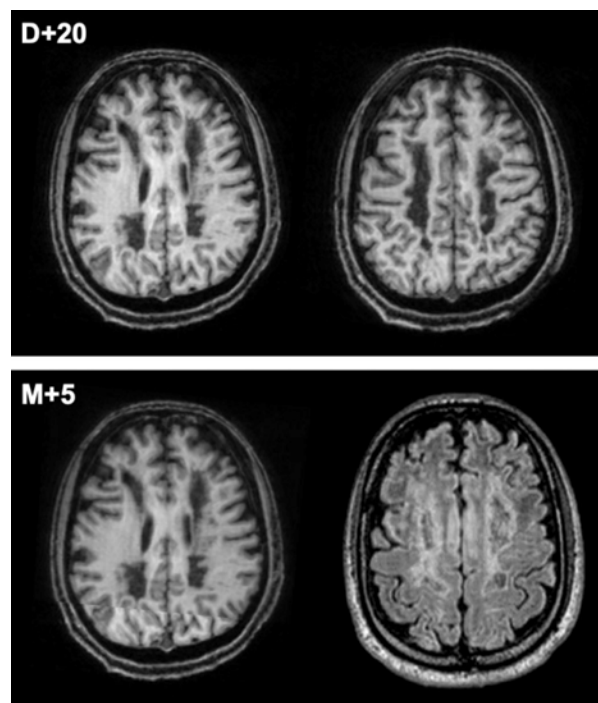
Structural MRI evidence of leukoencephalopathy revealing a diffuse, confluent and bilateral white matter damage involving subcortical necrotic tissue loss with no striking difference between the MRI performed 20 days and 5 months post-intoxication.

Conclusion: This patient presented the typical structural pattern of a toxic encephalopathy with severe but reversible cortical deafferentation.

Disclosure: Nothing to disclose.

EPO-520

Transauricular vagal nerve stimulation in patients with disorders of consciousness: a placebo-controlled clinical trial

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Background and aims: Patients with disorders of consciousness (DOC) are a challenging population prone to misdiagnosis and lacking effective treatment options. Among neuromodulation techniques, transcutaneous auricular vagal nerve stimulation (taVNS) may act through a bottom-up manner to modulate thalamo-cortical connectivity and promote patients' recovery. In this clinical trial, we aim to test the clinical and neurophysiological effects of taVNS in patients with DOC.

Methods: We will conduct the first prospective parallel randomized placebo-controlled double-blind trial in DOC patients with taVNS. 48 patients in the acute phase will randomly receive 5 days of either active bilateral vagal stimulation (45 min duration with 30s alternative episodes of active/rest periods; 3mA; 200–300μs current width, 25Hz.) or sham stimulation. Behavioural (i.e., Coma Recovery Scale-Revised) and neurophysiological (i.e., high density electroencephalography) measures will be collected at baseline and at the end of the treatment (see figure 1A & 1B). Primary and secondary analyses will seek for changes in the CRS-R and the EEG (i.e., alpha power spectrum, functional connectivity) at the group and individual levels.
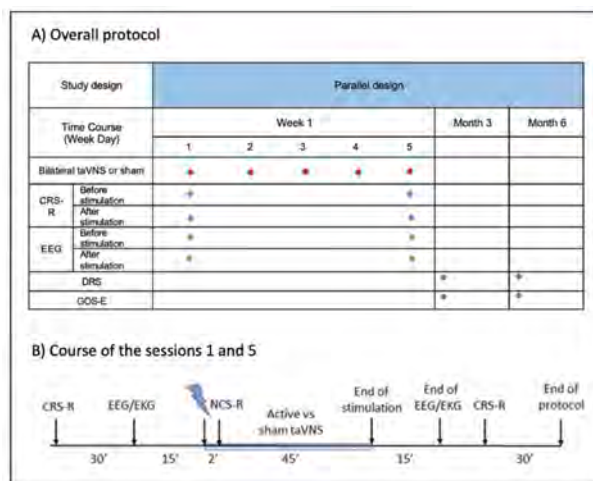
Figure 1. Study protocol. A) Overall 5-days protocol of the study. B) Detailed course of the first and last sessions.

Results: Preliminary results will be presented at the eventuell congres. Improvements in the CRS-R total score and in the subsequent index score will be our primary outcome. Such patients will be considered as responders. As secondary outcomes, we expect that the clinical changes in responders will be correlated with the EEG metrics.

Conclusion: These results will contribute to define the role of taVNS for the treatment of DOC patients, identify the neural correlates of its action and pave the way to targeted therapeutic strategy.

Disclosure: Nothing to disclose.

EPO-521

Pupillary constriction with brimonidine in awake volunteers and unconscious patients with brain injury

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Background and aims: Studies investigating unconscious individuals after blocking the alpha-1-adrenergic-receptor indicate that the parasympathetic nervous system dominates pupillary control during unconsciousness, suggesting that wakefulness is required for a sympathetic nervous system tone to affect pupillary innervation. We assessed the potential of brimonidine (an alpha-2-adrenergic agonist), which causes miosis in awake individuals, to distinguish preserved sympathetic pupillary tonus in consciousness from absence of sympathetic pupillary tonus in coma.

Methods: 15 unconscious patients were included and matched by age and sex with 15 awake controls. Inclusion criteria for unconscious patients were critical brain injury with EEG and/or neuroimaging indicating absence of residual consciousness. Pupil size was measured in both eyes via automated pupillometry under scotopic conditions. Measurements were done at baseline before administering brimonidine, and repeated at 5, 10, 20, 30, and 120 minutes after intervention. Pupillary size in comatose patients was compared individually and on the group level with those from matched controls.

Results: So far, 15 unconscious patients (7F, 8M, mean age 59 years, admitted for cardiac arrest (n=8) and stroke (n=7)) and 12 awake controls (7F, 5M, mean age 52 years) have been enrolled. Data analysis is ongoing and will be presented at the ventuell congres.

Conclusion: If miosis is induced in all healthy controls but not in comatose patients, a prospective trial might be warranted to test this bedside technique and investigate if pupillary constriction following brimonidine could serve as a biomarker for covert consciousness. We hence hypothesize that preserved pupillary sympathetic tonus might unravel residual consciousness in patients with cognitive motor dissociation.

Disclosure: Authors declare no conflicts of interests.

Cognitive neurology/neuropsychology

EPO-522

TMA-93 (Binding by Images): Extending the Spanish normative study on the elderly.

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Background and aims: TMA-93 examines relational binding by images. The test has been demonstrated discriminative for diagnosing early Alzheimer´s diseases. Norms for this test are available, but the very old people, at high risk for Alzheimer´s disease, have not been widely represented yet.

Methods: An extension of the cross-sectional, observational Spanish TMA-93 normative study focused on the elderly was undertaken. Only not-cognitively-impaired people aged 75 and over were included. Age, gender, and educational attainment were registered. By histograms analysis, median comparisons, and linear regression analysis, we selected variables that demonstrated influence on TMA-93 total scores and provided a percentile-base reference data according to combinations of those variables

Results: 431 new participants were included in this extension, resulting in a total sample of 657 individuals aged 75 and over (median age=78, interquartile range=76-81, range=75-93). A percentile-base reference data stratified by a combination of age ranges (75-79, n=428; and ≥80 y, n=229), and educational attainment (first grade, n=195) showed that TMA-93 total scores achieved a minimum of 26/30 at 50-percentile regardless of stratum. Considering the scores at 10-percentile, a maximum of 24/30 for the higher-educated strata contrasted with a minimum of 19/30 for the lower-educated strata.

Conclusion: TMA-93 may facilitate the discrimination of early Alzheimer's disease patients. Its ceiling effect is preserved in not-cognitively-impaired people aged 75 and over, although mitigated mainly by lower education.

Disclosure: This work was supported by Hoffmann-La Roche. Didier Maillet is the author of the TMA-93.

EPO-523

ApoE and recruitment profiles influence face-name associative memory task in subjective cognitive decline: a fMRI study

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Background and aims: Reduced performance at face-name associative memory (FNAM) task has been described in subjective memory decline (SMD) and APOE ε4 carriers, an Alzheimer's disease risk factor. In this study, we evaluated brain functional activity during FNAM task in SMD and explored its relationship with APOE ε4 and recruitment profiles.

Methods: Thirty-three SMD subjects stratified by APOE e4 (i.e. at risk – SMDε4+ or not – SMDε4-) and recruitment (i.e. from memory clinic – SMDclin or community centre – SMDcommu) profiles were enrolled. A fMRI FNAM task including three conditions with participants asked to learn and recall names associated with neutral, angry or fearful faces was performed. FNAM global performance and single emotion scores were computed.

Results: SMDε4+ and SMDε4- groups did not differ for demographic, clinical and cognitive features. Lower FNAM global and anger scores was found SMDε4+ with a significant combined effect of APOEε4 and recruitment profiles on anger performance. Analysis of functional brain activity showed a left-predominant activation of hippocampal structures, prefrontal and visual cortices. An activation of left temporoparietal junction and a deactivation of insula and subcortical network emerged in SMDclin/ε4+ subjects.

Conclusion: Functional and behavioral results suggest the presence of changes in functional memory network in SMD. Maladaptative mechanisms involving key regions of salience and attentional networks may be responsible of changes in FNAM performance in individuals at higher risk and with stronger complaints. Simultaneous consideration on both person-specific and task-specific factors is critical for identify SMD subjects more prone to be at risk.

Disclosure: Nothing to disclose.

EPO-524

Individual risk profile on word typicality in a semantic fluency task: an fMRI study in subjective memory decline

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Background and aims: Subjective memory decline (SMD) can be associated with an increased risk of cognitive decline. Semantic memory disturbances have been proved of extreme utility to identify individuals who will progress to Alzheimer's disease (AD). High typicality in word generation has been suggested as subtle marker of AD pathology. The study aims at evaluating the link between alterations in a semantic fluency task (SFT) and individual risk profile in SMD and exploring brain functional correlates.

Methods: We enrolled 34 SMD individuals (20 males; age: 67.5±4.84; education: 15.4±4.5) who performed a standardized SFT, evaluating the number of words and their typicality. Brain fMRI activity during a covert SFT was also recorded in each subject. SMD subjects were stratified by recruitment setting either from memory clinic (SMDclin) or community centre (SMDcommu) and presence of at least one ε4 allele of APOE gene (at risk: SMDε4+ and no risk: SMDε4-). Semantic performance and fMRI data were analysed according to recruitment and APOE profile.

Results: No effect of APOE profile and recruitment setting on number of words was found. A significant combined effect of APOE ε4 and recruitment grouping was found, with SMDclin/ε4+ generating words with higher typicality. The analysis of functional brain activity in the covert SFT showed an activation of the posterior cingulate cortex in SMDclin/ε4+ compared to SMDclin/ε4-.

Conclusion: Both genetic and individual risk profile may influence linguistic features on a SFT in SMD subjects, which could represent a valuable source in detecting SMD subjects more prone to be at risk of dementia progression.

Disclosure: Nothing to disclose.

EPO-525

Visual scanning patterns in patients with Alzheimer's disease dementia and mild cognitive impairment

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Background and aims: In this study, it was aimed to examine the visual scanning patterns of Alzheimer's disease (AD) dementia, mild cognitive impairment (MCI) and healthy controls (HC).

Methods: 30 AD (mean age, 72.70±7.83), 32 aMCI (mean age, 70.69±6.91), and 30 HC (mean age, 68.59±6.24) were include in this study. Neuropsychological tests evaluating general cognition, attention, memory, executive functions, visuospatial functions, and language were administered to all participants. Eye movements were recorded with an Eyelink 1,000 Plus. In this task consisting of two practice trials and 30 trials for 3,000 ms were presented. Participants were asked to view the pictures.

Results: AD, MCI and HC were not statistically different in terms of age, education, and gender (p>0.05). A statistically significant decrease was found in the number of fixations (p=0.005) and saccades (p=0.004) in AD than HC. The number of fixation and saccade in MCI were not statistically different compared to AD and HC (p>0.05). Number of mean fixation and saccade were significantly associated with general cognition (r=0.357, p<0.001), memory (r=0.278, p=0.007), executive function (r=0.263, p=0.011), visuospatial function (r=0.281, p=0.007) and language (r=0.242, p=0.020) domains.

Conclusion: This study shows that AD scan the visual world more superficially. This may cause patients to overlook or be unable to pay attention the visual stimuli around them.

Disclosure: Authors report no potential conflict of interests.

EPO-526

Abstract withdrawn

EPO-527

Abstract withdrawn

EPO-528

The gods' footprint: neuromythology

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Background and aims: Neurological eponyms usually make reference to the doctor who first described a disease. However, many others relate to different cultural aspects attributed to, for example, to mythology.

Methods: Herein, we present a review about neurological eponyms related to Greco-Roman mythology after the search in PubMed the terms "neurological eponyms", "eponyms mythology" and "Ulysses".

Results: The influence of Greek mythology is evident in neuroscientific eponyms. There are examples in neuroanatomy where we use hippocampus in reference to the mythological animal who is half horse half fish, we use arachnoid term in relation to the human who became a spider by virtue of Atenea and we use the word atlas in honor of the mythological giant that held the world. In the field of semiology we talk about the Achilles reflex (ankle reflex) with reference to the only weak point of the Trojan War hero. In pathology we allude to Hercules' disease as to epilepsy due to his characteristic strong movements, to Penelope's disease due to Ulysses' wife who unravel at night that which she have woven during the day. Ulysses syndrome in relation to the main Greek hero of the Odyssey and of the Elpénor syndrome in regard to the young man who fell deeply asleep and whose difficulty in awakening cost him his life in an accident.

Atlas. National Archeological Museum, Italy.

Thetis Riding Hippokampos. J Paul Getty Museum de Malibu, California, USA.
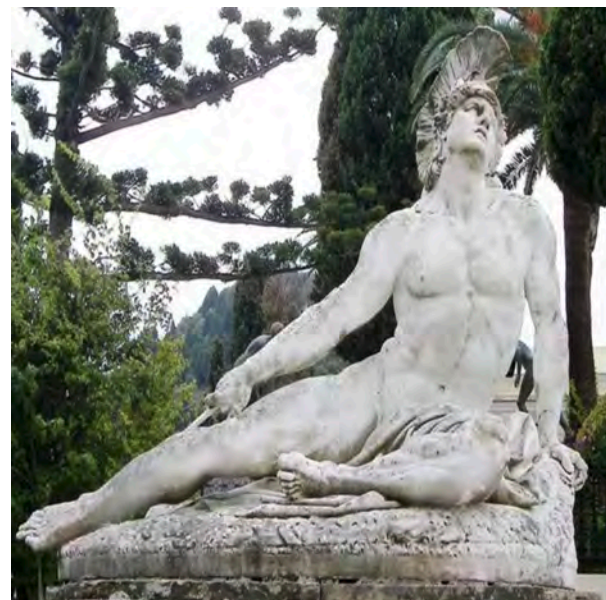
Achilles death. Aquileon, Corfú, Greece

Conclusion: Mythology has left its mark on neurological jargon. These are only a few of the many examples of the imprint that culture has on medicine, and especially on neurology.

Disclosure: Nothing to disclose.

EPO-529

Evaluating cognitive deficits in neurological conditions via Internet-based tools

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Background and aims: Cognitive deficits are present in many neurological conditions and greatly affect the quality of life of the patients. Despite this, they are hard to detect and evaluate in routine clinical practice. In person cognitive assessment does not offer a solution to this problem because it is unfeasible at large scale and impractical to be repeated over time. Conversely, Internet- and app-based tools for cognitive assessment offer superior sensitivity and can be easily scaled to reach a large population in a timely and cost-effective manner. Online registries offer ideal platforms to host these tools when monitoring large clinical populations over long periods of time.

Methods: In this study, we administered a superset of 23 brief internet-optimised cognitive tasks from the Cognitron platform to people with multiple sclerosis (PwMS) through the UKMSRegister. These tasks cover a wide range of cognitive domains and come with extensive normative data (n>400,000) collected during previous large-scale population studies.

Results: Our results show very high sensitivity of the online tasks to cognitive deficits in PwMS. We identify the cognitive domains that are most vulnerable and highlight how these vary with disease subtype and stage. We show how cognitive performance correlates with physical disability and mental health measures collected in the context of the UKMSRegister.

Conclusion: In this work we validate a set of cognitive tasks on PwMS and derive an optimal subset of these that can be used to monitor cognition over time via MS registers. We plan on extending this same approach to other registers and neurological conditions.

Disclosure: This work was supported by the UKRI CDT in AI for Healthcare http://ai4health.io (Grant No. EP/S023283/1)

EPO-530

To the issue of assessment of informational processing speed in persons with multiple sclerosis

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Background and aims: Symbol-to-digital conversion tests are commonly used to assess information processing speed (IPS) in persons with multiple sclerosis (pwMS). There is need to clear impacts of symbol modality, test duration, and cognitive switchability on IPS.

Methods: IPS assessments were performed by means of the Direct and Inverse Conversion Test (DICT) in 60 pwMS (mean age 38.68 ± 1.25 years) and 45 healthy control participants (HCp) (mean age 34.58 ± 2.07). DICT was consisted of 3 series of 15 conversions from letters to digits (DICT-LD) and then vice versa (DICT-DL).

Results: During 90 s, 23 pwMS (38.33%) and 5 HCp (11.11%) converted more efficiently with letters (L-group) than digits (D-group), 5 pwMS (8.33%) converted with equal efficiency in letters and digits (LD-group). The repeatability of the result was 0.95 in pwMS and <0.70 in HCp. D-group had 12 pwMS without cognitive impairments (CI) (37.50%), 20 pwMS with CI (62.50%); L-group had 6 pwMS without CI (26.09%), 17 pwMS with CI (73.91%). All pwMS from LD-group had CI. The pwMS without CI of D-group made 4.5 times fewer mistakes converting digits (0.42 ± 0.15) than letters (1.92 ± 0.34), p<0.01; in L-group, they made 3.6 times fewer mistakes converting letters (2.59 ± 0.36) than digits (0.67 ± 0.41), p<0.01. These differences were twice less for the pwMS with CI (Figure 1).
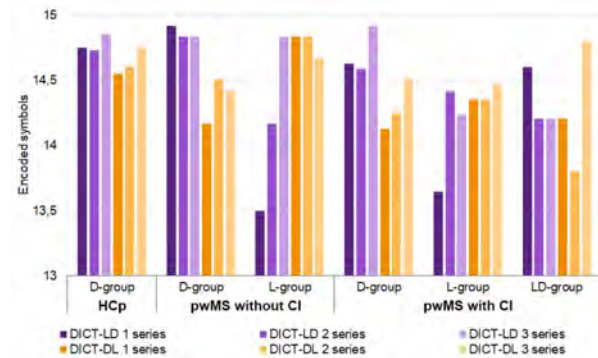
Figure 1: Amount of encoded symbols per series depending on the group in patients with MS

Conclusion: For one-third of pwMS, a decrease in the efficiency and speed of correct conversion in first 90 s might be associated not only with IPS but also with patient's perception of the type of a symbol.

Disclosure: Nothing to disclose.

EPO-531

Operationalization of proxies of cognitive reserve for prediction of post-stroke cognitive impairment

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Background and aims: Cognitive reserve (CR) accounts for the discrepancy between observed neuropathology and measured clinical outcomes in neurodegeneration. Several operationalizations of CR have been proposed in neurodegeneration, it is however unclear, if these can be applied to stroke equally well. We hypothesized to show the protective impact of CR for stroke outcome as well. We aimed to analyze the impact of different CR-proxies on post-stroke cognitive impairment.

Methods: 147 non-aphasic first-ever ischemic stroke patients with unimpaired pre-stroke cognition underwent a neuropsychological assessment 2.5 ± 1.9 days post-stroke. CR was operationalized through years of education (YoE), crystallized intelligence (IQ) and a standardized Cognitive Reserve Index Questionnaire (CRIq). We contrasted patient groups with high versus low CR in respect to cognitive performances.

Results: Compared to patients with low CR, those with high CR had comparable stroke severity as measured using NIHSS 24 h, but better performance in global cognition (MoCA), working memory and executive functions ($p<0.001$), independently of the chosen proxy. Despite their medium-to-strong correlation (Kendall-tau=0.32–0.43, $p<0.001$), CR-proxies impacted differently on other cognitive domains: after correcting for age and education effects, CRIq and YoE were protective for verbal learning and episodic memory, whereas IQ impacted on short-term memory and other executive domains (Fig. 1).
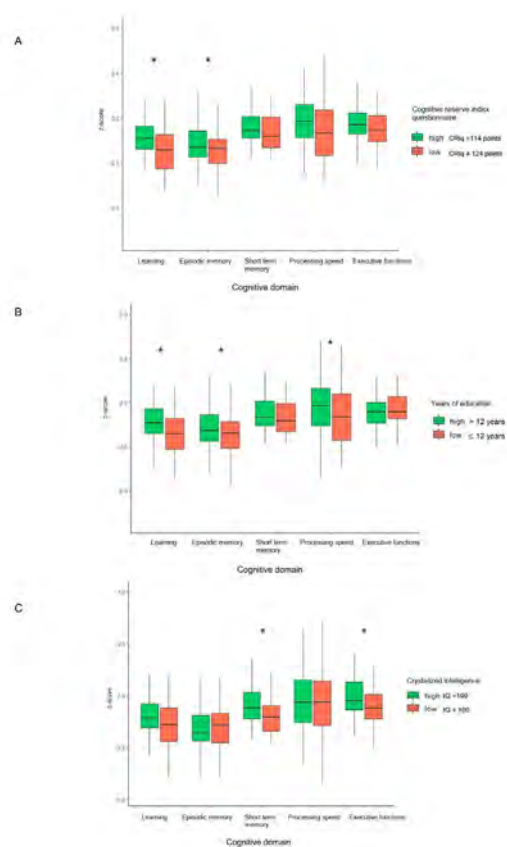
Figure 1. Specific impact of distinct CR-proxies on post-stroke cognitive performance in patients with high (green) versus low (orange) CR. The standardized normative values were stratified by age and educational level.

Conclusion: Even in the acute stroke phase, CR provides global protective impact on post-stroke cognition, and this impact goes beyond a simple additive effect of educational level. The specific impact of different CR-proxies might vary across cognitive domains. The data demonstrates that CR should be considered in the prediction of stroke outcome.

Disclosure: Nothing to disclose.

EPO-532

Informant-reported cognitive complaints reflect medial temporal lobe atrophy in subjective cognitive decline

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Background and aims: Cognitive complaints (CCs) are associated with normal aging, depressive symptoms and may also represent an early sign of Alzheimer's disease (AD). The aim was to compare CCs reported by patients with subjective cognitive decline (SCD) and their informants and analyse their relations to cognitive performance, depressive symptoms and atrophy of the medial temporal lobe structures.

Methods: In total, 72 SCD patients from the Czech Brain Aging Study were examined neuropsychologically and completed the Geriatric depression scale (GDS-15). The Questionnaire de Plainte Cognitive (QPC), a self-report 10-item yes/no questionnaire assessing the presence of specific CCs was completed by both patients (QPC-pat) and their informants (QPC-inf). 1.5T MRI and FreeSurfer 5.3. algorithm were used to measure left and right hippocampal volumes (HV) and parahippocampal cortical thicknesses (PHCT).

Results: Patients reported more CCs than their informants (p<0.001). The QPC-pat scores correlated with GDS-15 scores (r=0.39, p<0.001) but not with the Mini-Mental State Examination (MMSE) and the Rey Auditory Verbal Learning Test (RAVLT) scores or the brain measures (ps>0.15). The QPC-inf correlated with left and right HV and PHCT (range of r=-0.23 to -0.39, all ps<0.01) but not with GDS-15 or the MMSE and RAVLT scores (ps>0.10).

Conclusion: Self-reported CCs reflect depressive symptoms in SCD patients, while CCs reported by their informants are associated with atrophy of AD-related structures. Assessment of informant-reported CCs may be more valuable than the assessment of self-reported CCs in a clinical SCD population and we recommend the QPC-inf to be used as an integral part of the diagnostic workup.

Disclosure: The research leading to these results has received funding from the EEA/ Norway Grants and the Technology Agency of the Czech Republic - project number TO01000215 and by the Czech Science Foundation (GACR) registration number 22-33968S.

EPO-533

FKBP51-Hsp90 interaction inhibitors as new drug candidates for cognitive dysfunction in high-fat diet-induced obese mice

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Background and aims: Obesity increases the risk of several chronic diseases, such as type 2 diabetes mellitus, insulin resistance, and Alzheimer's disease. As one of the co-chaperones of Hsp90, FK506-binding protein 51 (FKBP51) is an important regulator of metabolic and cognitive dysfunction. FKBP51 knockout mice are resistant to diet-induced obesity, exhibit elevated glucose and insulin tolerance, and have less endogenous tau. FKBP51 overexpression preserves tau and impairs spatial reversal learning and memory. Our group has identified a new family of FKBP51 inhibitors that can disrupt FKBP51-Hsp90 interactions and penetrate the blood-brain barrier. This study aims to investigate the potential roles of our inhibitors on metabolic and cognitive dysfunction in a high-fat diet (HFD) model.

Methods: Male C57BL/6J mice were fed either the control diet or HFD for 4 weeks and then treated with vehicle or inhibitor E8 (20 mg/kg, s.c.) and their respective diets for another 4 weeks. Behaviors and glucose/insulin tolerance tests were performed during the last week. Hippocampus was collected for western blot.

Results: E8 can attenuate the impairment of locomotor activity and short-term memory induced by HFD. But it could neither reduce body weight gain nor improve glucose and insulin tolerance. In the hippocampus, E8 reduces the elevated p-tau (Ser214)/tau levels induced by HFD but does not show any effects on insulin signaling. It suggests that E8 reverses the behavioral impairments independently of metabolic regulation. The underlying mechanisms need further investigation.

Conclusion: We showed that inhibiting FKBP51-Hsp90 interactions with small molecules provides novel therapeutic targets on cognitive dysfunction in obesity.

Disclosure: The authors declare no conflict of interest.

COVID-19 2

EPO-534

Post-COVID Neurological Syndrome in a prospective cohort study

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Background and aims: COVID-19 patients frequently present acute neurological manifestations (NeuroCOVID). Such phenotypes can extend or emerge long after acute disease constituting the so-called Post-COVID Neurological Syndrome (PCNS).

Objective: Characterize PCNS longitudinal clinical profile in a consecutive cohort of COVID-19 patients.

Methods: We conducted a prospective study of COVID-19 patients diagnosed between March-June 2020. Clinical Information was obtained from e-Clinical records, face-to-face and/or telephone neurology consultations at 3-month and 12-month, including Neurological Examination, Sleep (ESS), fatigue (MFIS), and quality of life (QoL; SF-36) scales.

Results: We included 732 COVID-19 patients, 41.7% requiring hospital-based care. The COVID-19 fatality rate was 8.2%. A total of 519 patients completed 12-month follow-up. From these, 70.9% presented at least one neurological complaint at 3- and/or 12-month (56.8%/66.5%), with a median of 2. Sleep (27.7%/29.8%), headache (17.7%/21.6%), and sensitive (10.7%/12.2%) complaints increased slightly, while hyposmia (24.5%/15.3%) and hypogeusia (17.0%/9.7%) decreased close to half at 12-months. In contrast, cognitive, visual, and vertigo complains increased 2.7-fold (16.5%/44.5%), 1.6-fold (10.7%/17.2%), and 1.5-fold (6.0%/9.0%), respectively in post-COVID patients. Fatigue was present in 43.0% at 12-months. Previous migraine, acute disease severity, hyposmia, sleep, sensitive and visual complaints were independently associated with PCNS. Additionally, PCNS patients had lower physical and mental health QoL scores (p<0.001).

Conclusion: We found a very high frequency of PCNS in COVID-19 patients. Cognitive, sleep, headache, and fatigue are the most relevant PCNS complaints at 12-months, which may underlie the negative impact on patients' QoL. Our findings support the need for a long-term structured healthcare response for PCNS.

Disclosure: Supported by Bial Foundation Grant.

EPO-535

Impact of COVID-19 vaccine on patients with migraine: A cross-sectional study

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Background and aims: Background: Headache is a common adverse event of the Corona virus disease-19 (COVID-19) vaccination. Patients with migraine were concerned about their safety and worseninf of their headache. Aim of the work: to assess the interaction between migraine and COVID-19 vaccine.

Methods: Migraine patients who got COVID-19 vaccine were interviewed. Data of sociodemographic, vaccination type, doses, side effects and their impact on the migraine within three month post vaccine were collected.

Results: A total of 300 patients were identified in this observational cross-sectional study. Most of the patients were 40 years old or younger. 259 female patient represented 86.3% of our cohort. Post-vaccination, 83 (27.7%) reported worsening of their migraine headache. Headache frequency increased in 48 (57.8%) patient. Headache attack duration and headache attack severity had increased in 72 (86.7%) and 37 (44.6%) patients respectively. Mean duration of improving Worse migraine post vaccine was 21.34+1.06. Factor associated with post vaccination high migraine frequency were age (p=0.042), fever (p=0.014), diarrhea (p=0.022) and use prophylaxis (p=0.032). Factors associated with longer post-vaccination migraine attacks were age (p=0.033), disease duration (p=0.001), injection site pain (p=0.048), fever (p=0.026), diarrhea (p=0.037).

Conclusion: A considerable number reported worsening of their migraine headache post vaccination which resolve within one month. Migraine headache got worse in older age, longer disease duration and those who suffered fever and diarrhea post vaccine.

Disclosure: Nothing to disclose.

EPO-536

The Impact of COVID-19 infection on the Incidence of Cerebral Venous sinus thrombosis: An Observational Study

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Background and aims: COVID-19 has been associated with venous thromboembolism, including cerebral venous sinus thrombosis (CVT) in patients with confirmed COVID-19. From March 2020, there was a reduction in hospital admission rates for non-COVID-19 diseases. However, testing for COVID-19 was not routinely performed in the first half of 2020 for patients with no or mild respiratory symptoms. The aim of this study was to compare the number of CVT cases on imaging in 2019 and 2020 as a surrogate marker of COVID-19-related increased presentation in a patient population in Scotland.

Methods: Cases of CVT within Greater Glasgow and Clyde (GGC) were identified on neuroimaging studies between 1st January 2019 and 31st December 2020 using the Picture Archiving and Communication System (PACS) software. Patients aged below 18 years or diagnosed outside of GGC were excluded.

Results: A total of 14 CVT cases (21.4% male) were identified in 2019 with a mean age of 40 years (95% CI, 30.8–49.2) compared to 18 CVT cases (38.9% male) in 2020 with a mean age of 60 years (95% CI, 49.3–70). The CVT incidence was 1.45 per 100,000 person-years (PY) (95% CI, 0.86–2.46 per 100,000 PY) in 2019 and 1.87 per 100,000 PY (95% CI, 1.18–2.96 per 100,000 PY) in 2020.

Conclusion: Although the numbers do not reach statistical significance, this study demonstrates that CVT-related hospital admissions remained stable between 2019 and 2020, despite a reduction in the rate of admissions with non-respiratory symptoms which may provide indirect evidence of an association of CVT with COVID-19.

Disclosure: Miss Giulia Bankov is an undergraduate medical student at the University of Glasgow. Dr. Valentina Fenech is an ST3 neurology registrar based at the Queen Elizabeth University Hospital in Glasgow and Dr. Fozia Nazir is a stroke-neurology consultant based at the Queen Elizabeth University Hospital in Glasgow.

EPO-537

Abstract withdrawn

EPO-538

Neurological consequences of transferred SARS-CoV-2 in outpatient practice

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Background and aims: Neurological symptoms are a frequent manifestation of the post-COVID syndrome and common cause of outpatient visits.

Methods: We analyzed 53 patients who had COVID-19 between 2020 and 2021 and applied for outpatient care at the Delta Med clinic. Patients were grouped by age and based on the early and late post-COVID syndrome. The level of depression and anxiety were assessed with the HADS scale, cognitive impairment with the MoCA and MMSE scales.

Results: The share of early and late post-COVID syndromes was 37.7% and 62.3%, respectively. The following symptoms dominate in these patients: impaired sensitivity (34.0%), symptom of brain fog (37.7%), headache (32.0%), exacerbation of chronic pain (28,3%), fatigue (37,7%), memory impairment, including attention disorders (24,5%) and sleep disorders (20,7%). Dizziness and vertigo were also common (26.4%), usually manifested in combination with anxiety (24.5%). Three patients were diagnosed with post-infectious, COVID-19-induced demyelinating disease. A typical pattern of post-COVID neurological manifestations in the younger age group includes the symptom of "brain fog", anxiety, headaches and other pain syndromes. For the middle-age group - fatigue, memory impairment, "brain fog", sensitivity impairment were common. In the older age group, typical patterns consist of neurocognitive deficit, visual impairment, extrapyramidal disorders, and pain of various kinds.

Conclusion: Young patients are more prone to psycho-emotional changes, "brain fog " symptoms, and headaches. Symptoms of elderly patients have a predominantly relationship with deepening organic changes. Knowledge of these aspects will help practising doctors better diagnose and treat these patients, taking into account typical patterns of symptoms.

Disclosure: Nothing to disclose.

EPO-539

Cognitive dysfunction one year after COVID-19: evidence from eye tracking

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Background and aims: Persistent neurological, neuropsychiatric, and neuropsychological symptoms may arise after coronavirus disease (COVID-19) infection. In this study we aim to assess frontal lobe functions in patients with COVID-19 12 months after disease onset using a tailored eye tracking approach.

Methods: We recruited 55 COVID-19 patients and 23 healthy controls (HC). Patients were divided into those requiring hospital admission (n=38) and those who had milder symptoms and were managed as outpatients (n=17). We administered the Montreal Cognitive Assessment (MoCA) test to all participants and scales for the assessment of fatigue and depression symptoms in patients only. All participants performed an overlap pro-saccade, an anti-saccade, and a dual-task anti-saccade, while eye movements were recorded.

Results: There were no demographic differences between HC and patients (all p>0.1). COVID-19 patients made more directional errors in the anti-saccade task (p<0.001), in the dual-task anti-saccade (p=0.043), and more anticipatory errors in the pro-saccade task (p=0.002) than HC. A subgroup analysis revealed that inpatients made significantly more directional errors than outpatients and HC in both the anti-saccade and dual-task anti-saccade (p<0.03).

Demographic data of study population

Demographic data of study population			
	Covid Patients (n=55)	Controls (n=23)	P value
Sex M (%)	56,3	43,5	0,305
Age	54,4 ±11,2	57,1 ±8,0	0,387
MoCA	27,1 ±2,8	28,0 ±1,8	0,205
Education (years)	13,3 ±3,5	14,2 ±3,1	0,145
HADS-A	5,3 ±3,8		
HADS-D	3,4 ±3,1		
FAS	21,9 ±8,6		

Sub-Analysis of COVID-19 Patients			
	Outpatients (n=17)	Inpatients (n=38)	P value
Sex M (%)	23,8	71,0	0,001
Age	46,3 ±12,9	58,2 ±9,8	0,003
MoCA	28,43 ±1,31	26,5 ±2,7	0,023
Education (years)	14,4 ±2,5	12,7 ±3,4	0,104
Days since diagnosis	419,9 ±78,1	418,8 ±67,6	0,886
Fatigue (FAS)	18,5 ±6,9	22,0 ±8,9	0,100
HADS-A	4,3 ±3,6	5,6 ±3,9	0,613
HADS-D	2,6 ±3,6	3,8 ±3,6	0,304
FAS	19,6 ±6,5	22,9 ±9,0	0,100
Days hospitalized		18,7 ±11,7	

Abbreviations: MoCA Montreal Cognitive Assessment; HADS-A/D Hospital Anxiety Depression Scale; FAS Fatigue Assessment Scale.

Results and comparison of saccadic performance between patients and healthy controls

		Healthy Controls N=23	COVID Patients N=55	P
Saccadic tasks parameters				
Anti-saccade	Directional error	8,9 ±6,1	20,8 ±16,9	**<0,001**
	Saccade not performed	0,8 ±1,5	2,2 ±3,9	0,253
	Reaction time - Wrong	194,1 ±69,1	210,5 ±61,6	0,177
	Reaction time - Correct	275,6 ±80,4	289,3 ±62,3	0,248
Pro-saccade	Anticipatory error	11,6 ±9,7	26,7 ±23,7	**0,003**
	Reaction time	283,8 ±92,1	291,5 ±76,7	0,557
Anti-saccade Dual task	Directional error	21,4 ±9,7	34,0 ±22,1	**0,045**
	Saccade not performed	1,9 ±2,1	6,5 ±11,2	0,283
Dual task cost	Directional error	12,5 ±10,1	13,2 ±14,4	0,854
	Saccade not performed	1,1 ±1,9	4,3 ±11,0	0,854
	Reaction time - Correct	66,5 ±53,5	67,9 ±74,8	0,903

Significant p values (<0,05) are reported in bold text. Samples were compared using Mann Whitney U test. Errors are expressed as percentage, reaction time in milliseconds. Dual task cost is calculated with the formula: ((dual task-single task)/single task x 100).

Results and comparison of saccadic performance among subgroups

		Healthy Controls N=23	Outpatients N=17	Inpatients N=38	p	H/I	H/O	I/O
Saccadic tasks parameters								
Anti-saccade	Directional error	8,9 ±6,1	13,4 ±12,9	24,1 ±17,5	**0,001**	**0,001**	0,999	**0,026**
	Saccade not performed	0,8 ±1,5	0,9 ±2,4	2,8 ±4,6	0,084	-	-	-
	Reaction time - Wrong	194,1 ±69,1	211,7 ±85,2	210,0 ±50,0	0,293	-	-	-
	Reaction time - Correct	275,6 ±80,4	254,3 ±18,7	304,9 ±68,6	**0,004**	**0,090**	0,825	**0,005**
Pro-saccade	Anticipatory error	11,6 ±9,7	26,9 ±21,5	26,6 ±24,8	**0,013**	**0,024**	**0,040**	0,989
	Reaction time	283,8 ±92,1	261,7 ±43,9	302,4 ±83,5	0,226	-	-	-
Anti-saccade Dual task	Directional error	21,4 ±9,7	23,1 ±18,6	38,9 ±23,1	**0,006**	**0,003**	1,000	**0,022**
	Saccade not performed	1,9 ±2,1	0,9 ±2,1	5,8 ±12,9	0,429	-	-	-
	Reaction time - Wrong	243,7 ±93,2	235,1 ±64,2	239,8 ±57,4	0,220	-	-	-
	Reaction time - Correct	342,6 ±107,6	297,2 ±65,4	384,0 ±130,7	**0,014**	0,289	0,721	**0,014**
Dual task cost	Directional error	12,5 ±10,1	9,6 ±10,3	14,9 ±15,7	0,513	-	-	-
	Saccade not performed	1,1 ±1,9	1,8 ±4,1	8,7 ±12,7	0,429	-	-	-
	Reaction time - Correct	66,5 ±53,5	42,8 ±57,2	79,1 ±79,5	0,138	-	-	-

Significant p values (<0,05) are reported in bold text. Samples were compared using Mann Whitney U test. We report the adjusted significance using Bonferroni correction. Errors are expressed as percentage, reaction time in milliseconds. Dual task cost is calculated with the formula: ((dual task-single task)/single task x 100). Abbreviations: H Healthy Controls; I Inpatients; O Outpatients.

Conclusion: COVID-19 may lead to impaired inhibitory cortical control, particularly in those who require hospital admission, even up to one year after the infection. Our results broaden the knowledge on the COVID-19 sequelae that may have an important impact on patients' cognitive functioning and consequently their everyday activities.

Disclosure: There are no financial conflicts of interest to disclose.

EPO-540

Neurological syndromes following SARS-CoV-2 Vaccination: are medical unexplained symptoms the key players?

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Background and aims: Rare neurological syndromes have been associated with SARS-CoV-2 vaccination. Despite the growing number of cases reported, the characteristics of neurological diagnosis following SARS-CoV-2 vaccination and the underlying etiologic mechanisms still need further investigations. The aim of this study is to evaluate the association between specific neurological symptoms and syndromes and SARS-CoV-2 vaccination.

Methods: In this retrospective, single center cohort study, we included all adult inpatients consecutively admitted to the Department of Clinical and Experimental Sciences, Neurology Unit, of the ASST Spedali Civili Hospital, Brescia, from January 2021 to August 2021.

Results: Out of 871 consecutive patients admitted to Neurology Department, 102 and 61 subjects reported SARS-CoV-2 vaccination within 60 and 30 days, respectively. The most common neurological diagnosis following vaccination included cerebrovascular diseases (n=32), transient medical/neurological unexplained symptoms with negative instrumental tests (MUS, n=25), epileptic disorders (n=11) and demyelinating diseases (n=10). When compared to non-vaccinated cases, MUS emerged as the only diagnosis with higher prevalence in post-vaccine cases at 60 and 30 days (24,5% and 38% vs 7,2% of whole cohort).

Conclusion: Unexplained transient neurological symptoms appeared to be the most common neurological condition following SARS-CoV-2 vaccination in comparison to non-vaccinated cases.

Disclosure: The findings confirmed the safety of SARScoV-2 vaccination and argued against a prominent role in the pathogenesis of either cerebrovascular or inflammatory-mediated neurological disorders.

EPO-541

Predictors of subjective cognitive deficits one year after COVID-19 disease

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Background and aims: Cognitive symptoms have been described up to one year after SARS-CoV2 infection but their clinical significance and underlying mechanisms are still debated. In this study we aim at evaluate the prevalence and predictive factors of subjective cognitive complaints (SCC) reported at one-year follow-up in patients hospitalized for COVID-19.

Methods: Out of 246 COVID-19 patients, a sample of 137 subjects accepted to be evaluated at one year from discharge, though a neurological and psychological examination including the Montreal Cognitive Assessment (MoCA), impact of event scale (IES-R), Zung self-rating depression and anxiety scales (SDS and SAS) and fatigue severity scale (FSS).

Results: Out of the total sample, 22% of subjects presented SCC, described as 'brain fog' with difficulty focusing, confusion and forgetfulness. Patients with SCC were similar for age, premorbid conditions and severity of COVID-19, whereas they exhibit lower MoCA score (22.9+4.3 vs. 26.3 +3.1, p=0.002) and higher IES-R score (33.7+18.5 vs. 26.4 +16.3, p=0.050), SDS score (40.9+6.5 vs. 35.5+ 8.6, p=0.004) and Fatigue severity (FSS 33.6+16.1 vs. 23.7+ 12.5, p=0.001) compared to patients without cognitive complaints. Depression (p=0.02) emerged as the factor with strongest correlation with SCC adjusting for MoCA, fatigue and clinical variables.

	No Brain Fog (n=107)	Brain Fog (n=25)	p value
Demographic and clinical characteristics			
Age, years	64.6±12.4	68.5±11.1	0.157
Sex, female	32 (30.2%)	7 (29.2%)	0.921
mRS pre	0.31±0.6	0.39±0.5	0.587
CIRS severity index pre-hospitalization	1.3±0.3	1.3±0.4	0.571
NHS at admission (median value)	5.8±2.6	6.7±2.5	0.121
qSOFA at admission	1.05±1.3	1.88±1.9	0.118
BCRSS at admission (median value)	0.5±0.6	0.4±0.5	0.473
Low-flow oxygen treatment	52 (49.5%)	15 (62.5%)	0.268
Non-invasive ventilation	9 (8.5%)	4 (16.7%)	0.258
Total days of O2 therapy	5.3±8.6	6.9±5.9	0.383
MoCA score	26.3±3.1	22.9±4.3	0.002
IES-R	26.4±16.3	33.7±18.5	0.050
Fatigue severity scale	23.7±12.5	33.6±16.1	0.001
SDS (Zung)	35.5±8.6	40.9±6.5	0.004
SAS (Zung)	36.5±5.9	35.9±7.7	0.674

Table 1: Demographic and clinical factors associated with abnormal MoCA score. *p values were calculated by Mann Whitney test or Fisher's exact test, as appropriate.

Conclusion: Cognitive symptoms are commonly reported at one year of follow-up associated with depression, independently from premorbid conditions and COVID-19 severity. Larger longitudinal studies are warranted to investigate possible underlying mechanisms and future therapeutic strategies to reduce the burden of long-term neurological sequaleae.

Disclosure: All authors have no conflict of interest regarding the research related to the manuscript. The study was not financial supported.

EPO-542

COVID-19 – associated cerebral venous thrombosis in young and middle-aged patients

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Background and aims: During the COVID-19 pandemic the incidence of cerebral venous thrombosis (CVT) is increasing (0.5–1% vs 4.2%). Purpose: to study the clinical features of CVT, to determine the importance of neuroimaging methods, genetic risk factors of thrombosis in young and middle-aged patients associated with COVID-19.

Methods: 30 young and middle-aged patients with CVT associated with COVID-19 were examined: 22 (73%) women and 8 (27%) men. The age of the examined patients was 40.3±12.2 years. The analysis of the main clinical and neurological manifestations of CVT, laboratory, neuroimaging data and genetic risk factors for thrombosis were carried out.

Results: The interval between the clinical manifestations of COVID-19 and diagnosis CVT varied from 7 to 25 days. Most patients had leukocytosis, lymphopenia, increased levels of C-reactive protein and D-dimer. The course of CVT in 12 cases was acute and led to acute cerebrovascular events (hemorrhagic stroke - in 5 cases, ischemic stroke - in 7 cases), in other cases, subacute course of CVT was noted. The following polymorphisms were identified in patients: genetic polymorphisms of folate metabolism – 14 (46%), SERPINE1-4 (13%), F XIII (Val34Leu) – 6 (20%), ITGA2 C807T-3 (10%), FVII G10976A – 5 (16%), FGB (G455A) - 4 (13%), ITGB3(T1565C) – 3 (10%).

Conclusion: Verification of CVT during the COVID-19 pandemic is difficult. The presence of symptom characteristic of CVT – headache (90%) can be considered as a manifestation of COVID-19. Screening of thrombophilia may allow to administer anticoagulant treatment appropriately.

Disclosure: There not a conflict of interest.

EPO-543

Multiple sclerosis centers during COVID-19 pandemic: an italian multicenter patient-centered survey

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Background and aims: Multiple Sclerosis (MS) Centers experienced a significant disruption of their clinical activities during the first waves of COVID-19 pandemic. The aim of the present national multicentre survey was to collect the patient opinion regarding the quality of care and information received from MS Centers during the pandemic.
Methods: In April–May 2021, 16 Italian MS Centers sent a digital (35-item) survey by email to their patients. Statistical analyses were performed with SPSS, version 25.
Results: 1,670 pwMS (67.3% women) completed the survey. 82% of pwMS did not modify their disease-modifying drug (DMT) regimen, while 11% reported therapy discontinuation. 36% of pwMS contacted their MS Centers for getting information about the COVID-19 pandemic, while 30% were directly contacted from the healthcare personnel to provide information about pandemic and correct prevention behaviours. More than 80% of pwMS did not experience any difficulty in contacting their MS Center, with only 4% of users failing. The overall opinion on MS Centers during the pandemic was more than positive, with 32% of patients showing a significant increase in trust in their neurologists. Interestingly, more than 50% of patients suggested to invest more in telemedicine programs in order to expand contact channels with MS Centers.
Conclusion: Italian MS patients judged globally well the activity, the accessibility and the information received by their MS Centers during COVID-19 pandemic. Implementing telemedicine programs at MS Centers would further improve the taking charge of patients, particularly those with higher disability or living far from the Center.
Disclosure: Authors declare no disclosures.

EPO-544

Abstract withdrawn

EPO-545

To be or not to be vaccinated – The risk of MS or NMOSD relapse after COVID-19 vaccination and infection

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Background and aims: COVID-19 vaccination and infection are speculated to increase the likelihood of multiple sclerosis (MS) and neuromyelitis optica spectrum disorder (NMOSD) exacerbation. Our goal was to investigate this assumption.

Methods: Data were collected from March 1, 2020, to October 30, 2021. Primarily, we compared the proportion of patients with at least 1 clinical relapse in the 90 days following vaccination/infection to the proportion in the 90-day intervals during the year before.

Results: We identified 1,661 vaccinated MS (90.11% BNT162b2)/17 NMOSD (100.00% BNT162b2) patients without a history of COVID-19 and 469 unvaccinated MS/8 NMOSD patients who experienced COVID-19. A mild increase in the proportion of patients with at least 1 relapse (360 to -270 days: 4.27%; -270 to -180 days: 4.27%; -180 to -90 days: 3.85%; -90 to 0 days: 3.79% vs. 0 to +90 days: 5.30%) and annualised relapse rate increase (0.17 vs. 0.22) after vaccination in MS patients were observed. Also, a rise in the proportion of patients with at least 1 relapse after COVID-19 was observed (4.44%; 5.05%; 4.65%; 6.87% vs. 7.27%). Lower age was associated with clinical relapse after vaccination/infection. Trends in NMOSD patients were analogous.

Conclusion: There is a mild increase in the relapse incidence after the COVID-19 vaccination. The risks, however, need to be balanced against the risks of COVID-19 itself, also leading to the rise in relapse rate and particularly to morbidity and mortality.

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EPO-546

Abstract withdrawn

EPO-547

Small vessel disease in patients with post-COVID syndrome

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Background and aims: The aim of the study was to assess the prevalence of cognitive impairment in patients with post-COVID syndrome, depending on the degree of damage to small vessels.

Methods: The study was completed in 2020–2021. on the basis of PMC "Expert Health". We examined 68 patients with manifestations of post-COVID syndrome (PCS), including 25 with verified manifestations of small vessel disease (SVD) in the form of white matter changes due to damage to small cerebral arteries on MRI. Cognitive functions were assessed using the MMSE scale, TMT, GBP tests. Follow-up time is 3 months. Statistical processing was carried out by methods of dispersion analysis.

Results: The average age of patients was 57.5±7.1 years, with a slight predominance of men - 57.4%. Patients with post-COVID syndrome complained of deterioration in memory, concentration, brain fog. More pronounced decrease was found in patients with small vessel disease. Thus, the results of MMSE were 24.4±1.6 points in patients with SVD and PCS, and 25.3±1.0 points in patients without SVD. When performing the TMT-A subtest, patients with SVD and PCS spent an average of 62.2±7.8 s, patients without SVD – 43.7±7.3 s (p<0.05). When performing the TMT-B subtest, patients with SVD and PCS spent an average of 81.8±15.8 s, patients without SVD – 76.3±16.5 s (p>0.05). The GPB test took 71.6±5.2 s and 63.1±4.8 s, respectively (p>0.05).

Conclusion: The presence of small vessel disease significantly aggravates cognitive dysfunction in patients who have had a coronavirus infection

Disclosure: Nothing to disclose.

EPO-548

An evaluation of telemedicine for new outpatient neurological consultations

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Background and aims: The COVID-19 pandemic has broadened the use of teleneurology, how this compares to face-to-face (F2F) clinics is unclear. This study compared virtual with F2F new neurological consultations.

Methods: We retrospectively evaluated new outpatient consultations in neurology clinics in Aberdeen Royal Infirmary. We compared sociodemographic data, time to consultation, time to diagnosis, the need for reassessment and re-investigation between traditional F2F and virtual clinics using the web-based video platform (Near Me) or telephone into patients own homes (or chosen location) without a trained assistant. We calculated the relative risk of the need for reassessment and re-investigation over six-month periods by the suspected neurological diagnosis.

Results: 73% of consultations were virtual (Near Me or telephone) between June and October 2020, this was almost non-existent ($<0.1\%$) in June-October 2019. We analysed 352 F2F (June-July 2019) and 225 virtual consultations (June-July 2020). Compared to F2F clinics, virtual clinics had a longer time to diagnosis (p=0.019), were more likely to be re-assessed (RR: 2.2, 95% CI: 1.5–3.2; p<0.0001) and re-investigated (RR: 1.50, 95% CI: 0.88–2.54; p=0.133), this was likelier in those aged $\geq$60 years. Patients with headaches and suspected seizures were less likely to need reassessment or re-investigation following virtual clinics than multiple sclerosis & neuroinflammatory disorders, spinal cord disorders and functional neurological disorders.

Conclusion: This study demonstrates that virtual clinics have higher rates of reassessment and re-investigation than F2F clinics. As virtual clinics become a potential consultation alternative, this study should instruct the selection of patients for either consultation type.

Disclosure: We declare no conflict of interest.

Epilepsy 4

EPO-549

Cardiac dysfunction in SUDEP: insights from a probable near-SUDEP case rescued with extracorporeal membrane oxygenation

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Background and aims: Cardiorespiratory dysfunction plays a major role in sudden unexpected death in epilepsy (SUDEP); however, its exact pathophysiology remains elusive. We present the first reported case of probable near-SUDEP rescued with advanced life support (ALS) and venoarterial extracorporeal membrane oxygenation (VA-ECMO) and aim to detail the aspects of cardiac dysfunction in this setting.

Methods: Case-report

Results: A 44-yo former smoker man with past primary pneumothorax and without any known neurological disorder was admitted after two unprovoked bilateral tonic-clonic seizures. Neurological examination was normal. Prominent subconjunctival and periocular petechiae were apparent. Apart from mildly elevated myoglobin and D-dimer, investigation (including troponin, brain CT, EKG, and thoracic CT angiography) was unremarkable. Less than 24h after he had a witnessed prolonged bilateral tonic seizure followed by apnoea and asystole. Cardiorespiratory resuscitation was initiated followed by ALS requiring VA-ECMO. Post-arrest EKG revealed extensive ischemia. Echocardiogram unveiled severe left ventricular systolic dysfunction and akinesia of the mid- and apical segments of the anterior wall and septum. Coronary angiography was normal. Myocardial necrosis markers reached strikingly high levels (troponin up to 45,6521 ng/L). Hemodynamic stability was achieved with additional aminergic support. After reducing anesthetics, deep coma persisted along with facial myoclonus. Multimodal prognostic evaluation supported therapeutic futility due to severe hypoxic-ischemic encephalopathy. Treatment was withdrawn and he died soon after.

Conclusion: In this case of near-SUDEP, severe, presumably ischemic myocardial damage was seen, in the absence of coronary disease. This could partially be overtaken by VA-ECMO, but unfortunately severe, irreversible hypoxic-ischemic encephalopathy could not be prevented.

Disclosure: Nothing to disclose.

EPO-550

Epilepsy and ataxia: the hidden infection

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Background and aims: Whipple's disease is a rare entity caused by infection with the bacillus Tropheryma whipplei. In 20–40% of cases, neurological manifestations such as cognitive decline, epileptic seizures and ataxia may occur.

Methods: Presentation as a single case report.

Results: A 72-year-old patient with no relevant history, was initially admitted with frequent focal seizures characterized by speech impairment and eyelid myoclonus that progressed to bilateral tonic-clonic seizures. The EEG showed predominantly left temporal epileptiform activity. She was treated with levetiracetam, valproate, phenobarbital, midazolam and perampanel. The blood serum analysis revealed hypothyroidism and vitamin B12 deficiency. Lumbar puncture, brain MRI and search for occult malignancy were unremarkable. She was discharged with levetiracetam, perampanel and phenobarbital. In subsequent years, clonazepam and eslicarbazepine were introduced due to ineffective control of seizures. Four years after the first seizure, the patient returned to the ED due to gait imbalance and double vision. She also reported diarrhea and weight loss. Objectively, she presented vertical nystagmus, dysarthria, limb and gait ataxia. The brain MRI was normal. The investigation carried out resulted in the isolation of T. whipplei DNA in CSF. Thus, the patient started targeted antibiotic therapy, with significant clinical improvement. It was also possible to start slow weaning from antiepileptic drugs, without recurrence of seizures.
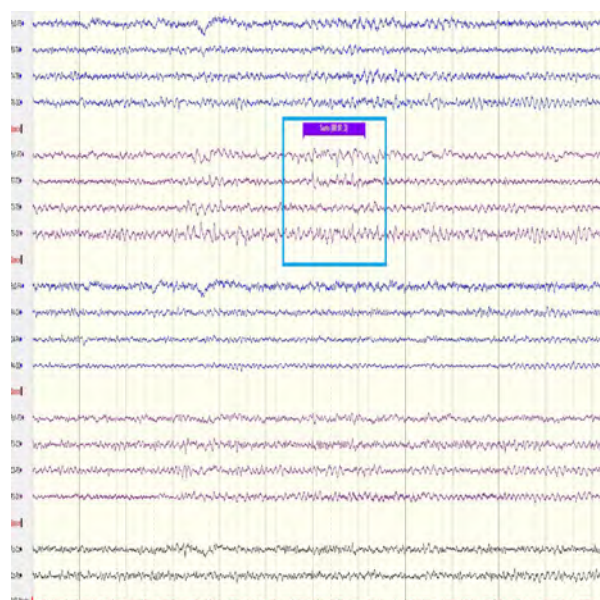
EEG showing anterior temporal epileptiform activity

Conclusion: This case constitutes an atypical presentation of Whipple's disease in which the absence of typical clinical manifestations at an early stage made the diagnosis challenging. It also highlighted the need to investigate systemic complaints in the evaluation of refractory epilepsies without identifiable cause.

Disclosure: Nothing to disclose

EPO-551

Epilepsy care during COVID-19 pandemic lockdown: how to get access to Epilepsy Clinic

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Background and aims: Wait-times for a neurologist in Almaty, Kazakhstan can range from 1–2 months. The COVID-19 pandemic has exacerbated wait-times, making it more difficult for patients with epilepsy to access timely medical care. The Special Group for Fast Access was developed in response to these situation. The clinic used a telemedicine: a multidisciplinary consultative model and an online referral way from GP that patients to be evaluated by an epilepsy specialist within 1 week from referral.

Methods: The special medical inform system is an online in clinic where appointments are conducted by video conference. Patients across Almaty obtain a referral and register on-line by site or messengers to receive an appointment. The Care Team consists of an epilepsy specialist, a physician assistant and a psychologist. Following every appointment, patients complete a survey based on their experience. In some cases video-EEG monitoring was performed at home with all sanitary requirements.

Results: Responders rate was 65% (62/96). Majority of the patients reported that the team members were empathetic, listened to their needs and explained treatment options "extremely well" (33/34,37%) or "very well" (51/53,1%). Majority of patients were "very likely" or "likely" 44/45, 83%) to use the online clinic due of COVID-19 limitations.

Conclusion: High feedback from the surveyed patients supports the patient-centred care model. Survey demonstrates doctors and patients are interested in adopting this model of telemedicine care for patients with epilepsy. It is our goal these experience catalyse the improvement of access to specialist care and reduce wait-times in Almaty and Kazakhstan.

Disclosure: The authors declare no conflicts of interest.

EPO-552

Two cases of the GRIN-associated epileptic encephalopathies with new data

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Background and aims: Last decade, different GRIN variants have been discovered in pediatric patients with the majority of mutations with the GRIN2A and −2B genes (46% and 38%, respectively). Pathogenic variants in GRIN genes cause severe encephalopathies, with complex and overlapping clinical pictures involving intellectual disabilities, neurodevelopmental delays, autism spectrum disorders, movement disorders, schizophrenia, seizures, epilepsy and more.

Methods: Cases reports.

Results: We have the 1st patient 17-months old boy with epilepsy onset at 3 months with bilateral tonic-clonic and focal seizures with eye deviation to the right side and mental retardation. He was treated with valproic acid, oxcarbazepine, clonazepam and steroids without any benefit. Video-EEG monitoring showed modified hypsarrhythmia with a burst suppression pattern. MRI showed brain malformation as polymicrogyria. DNA sequencing revealed heterozygous mutation in the GRIN2A gene (13 of 13 exons, p.Asp1115Glu). The 2nd one 22-months old girl with seizures onset at 3d day of life with eye deviation and dacrystic seizures about 120 per day. MRI showed hypothalamic hamartoma. Video-EEG monitoring – regional epileptic activity spike-wave (more in the left vertex region); registered dacrystic seizures; DNA sequencing revealed previously not described heterozygous mutation in the GRIN2B gene (14 of 14 exons, p. Ser1259Ala).

Conclusion: The mutations variants we identified have not been previously described. Some clinical features as dacrystic seizures were very rare described before.

Disclosure: The authors declare no conflicts of interest.

EPO-553

Relationship between zinc deficiency and activation of GPR39 receptor by TC-G 1008 in an animal model of epilepsy

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Background and aims: The G-protein coupled receptor 39 (GPR39) is unique among GPCRs as it may be activated by zinc ions. We demonstrated that the effects of TC-G 1008, GPR39 agonist, on pentyleneterazole (PTZ)-induced epileptogenesis are mediated by GPR39. Furthermore, TC-G 1008 aggravated PTZ-induced epileptogenesis in mice fed a diet containing adequate amount of zinc (ZnA) of 50 mg Zn/kg but not in mice fed a zinc deficient (ZnD) diet of 3 mg/kg. This data links the effects mediated by GPR39 with dietary zinc.

Methods: Male Albino Swiss mice received a ZnA or ZnD diet for 4 weeks. Then, PTZ-kindling model of epilepsy was initiated. Mice were divided into kindled or non-kindled mice, that received TC-G 1008 (10 mg/kg), zinc chloride (ZnCl2) (8 mg Zn/kg), valproic acid (VPA) (150 mg/kg) or vehicle (VEH). The diets were continued during this procedure. Serum zinc concentration was measured using Inductively Coupled Plasma Optical Emission Spectrometry. Data were analyzed by the three-way ANOVA and a Bonferroni post hoc test.

Results: Chronic treatment with VPA abolished the effects of the ZnD diet on serum zinc in non-kindled mice. Chronic treatment with Zn abolished the effects of the ZnD diet on serum zinc in both kindled and non-kindled mice. Chronic treatment with TC-G 1008 did not modify the effects of the ZnD diet on serum zinc in kindled or non-kindled mice.

Conclusion: Although the behavioral effects of TC-G 1008 may depend on dietary zinc supply, the compound did not significantly affect serum zinc concentration in either ZnA or ZnD mice.

EPO-554

Personalized predictive modeling of epileptic network dynamics

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Background and aims: Epilepsy research has recently undergone a paradigm shift: from epilepsy as focal cortical disease towards epilepsy as network disease. This is motivated by new evidence of widespread brain activity in seizure initiation and maintenance, and by promising results of brain stimulation for drug-resistant cases. However, a thorough understanding of the network-rooted epileptic dynamics is still missing, and the details of the stimulation procedures do not account for the variable brain network dynamics between patients.

Methods: We develop personalized dynamical models of epileptic networks, based on EEG in an entirely data-driven manner. A dynamic connectivity matrix, simultaneously capturing the dominant spatial and temporal modes in the epileptic network, is extracted for steady-state EEG dynamics. The considered population includes 30 patients with frequent epileptiform discharges ("active EEG"). The dynamical properties of the active and inactive EEG states are compared.

Results: Our model accurately reproduces the clinically relevant properties of the recorded EEG dynamics: spectral power, channel coherence and amplitude variation. We find the dominant coherent structures for each epileptic network state. In addition, the models allow to simulate the effects of external network stimulation. By comparing the two types of brain dynamics, the model is used to predict targeted interventions to transition from pathological to healthy states.
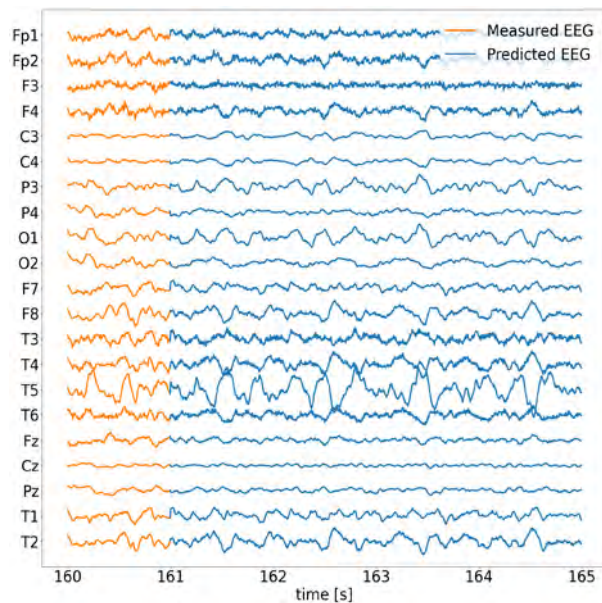
Example of status epilepticus EEG dynamics prediction by developed data-driven model: The model simultaneously captures the dominant spatial and temporal modes of the epileptic network dynamics, enabling the simulation of external network stimulation.
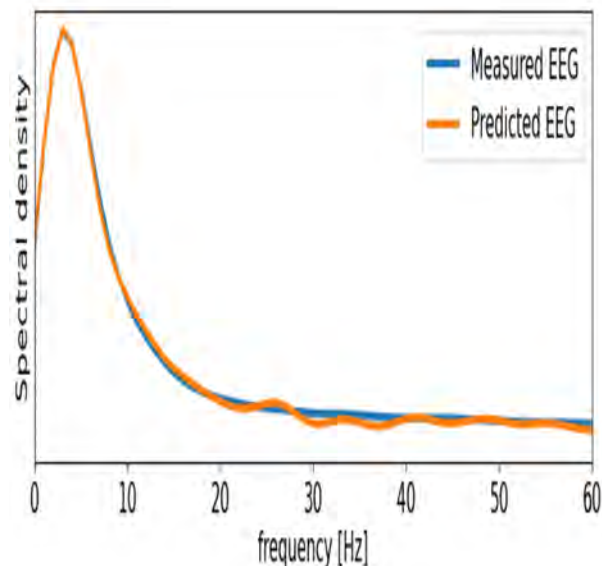
Power spectra of measured and predicted EEG dynamics: The model accurately reproduces the clinically relevant properties of the recorded EEG dynamics (spectral power, channel coherence and amplitude variation).

Conclusion: We developed personalized EEG-driven models of epileptic network dynamics. We demonstrated their accuracy for patients with active EEG. The models can be readily used to predict the optimal localization and stimulation parameters of patient-specific interventions and help resolve the pathological epileptic network states.

Disclosure: The authors declare no conflict of interest.

EPO-555

Sex differences in side effects of antiseizure medications in pediatric patients with epilepsy: a systematic review

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Background and aims: Sex differences in pharmacokinetic and pharmacodynamic of drug treatments have been highlighted since the first months of intrauterine life and become evident after puberty. Little is known about the differences in efficacy and safety of antiseizure medications (ASMs) between boys and girls with epilepsy. Aim of the study was to perform a systematic review searching for differences in the side effects of ASMs with respect to sex in pediatric patients with epilepsy.

Methods: We carried out a literature search of PubMed and all results up to April 2020 were included. Titles, abstracts and full texts were screened by two independent reviewers. We included all studies evaluating the side effects of ASMs in patients with epilepsy younger than 18 years, with reference to the two sexes.

Results: 5,164 studies were identified of which 68 studies were included. 18 studies identified sex as an influential variable for the occurrence of side effects. An overall higher frequency of adverse drug reactions in girls with different ASMs, a higher retinal toxicity in boys taking vigabatrin, higher BMI, leptin levels, hyperammonemia risk and carnitine deficiency in girls on valproic acid, a higher weight loss, more frequent acute psychosis and renal stones occurrence in girls on topiramate were reported.

Conclusion: Few studies analyzed sex differences in side effects of ASMs in pediatric populations. The findings of our study point to the presence of some sex differences, highlighting the need for a systematic evaluation of sex as a determinant variable influencing the response to medications in clinical research.

Disclosure: On behalf of the Epilepsy and Gender Commission of the Italian League Against Epilepsy.

EPO-556

Seizure frequency during preceding year may contribute to worse health-related quality of life in epilepsy

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Background and aims: Health-related quality of life (HRQOL) is used to reflect the burden of disease in adults with epilepsy (AWE). The objective of our study was to study the effects of yearly versus recent (monthly) seizure frequency on HRQOL in AWE.

Methods: AWE underwent an interview assessing seizure frequency during preceding month and year. The number of generalized tonic-clonic seizures and complex partial seizures was recorded. HRQOL was assessed using SF-36 inventory, represented by 8 domains: D1 – Physical Functioning, D2 – Physical Role-Limitations, D3 – Emotional Role-Limitations, D4 – Energy/Fatigue, D5 – Emotional Well-Being, D6 – Social Functioning, D7 – Pain, D8 – General Health. Spearman's correlation and Mann-Whitney U test were utilized.

Results: AWE (n=152, mean age 35.7, females – 48.1%) had on average 39.3 seizures per year, and 4.15/month. There was a negative correlation between all SF-36 domains and seizure frequency for preceding year and not for preceding month (p<0.05), shown as Y/M: D1 -0.194/0.046, D2 -0.255/0.032, D3 -0.241/-0.037, D4 -0.289/0.02, D5 -0.267/-0.027, D6 -0.340/0.066, D7 -0.38/-0.011, D8 -0.329/0.062. Interestingly, those who had only recent seizures but no seizures for the remaining year, showed higher HRQOL compared to those with seizures scattered throughout the recent year (month/year): D1 75/65, D2* 55/35, D3 54/38, D4* 66/48, D5* 64/49, D6* 79/60, D7* 80/58, D8* 55/45 (*p<0.05).

Conclusion: According to our study, more yearly seizures were associated with lower overall HRQOL. HRQOL was affected by seizure frequency per year, rather than per month, suggesting bigger role for the effect of yearly seizures.

Disclosure: Nothing to disclose.

EPO-557

Ictal yawning in an epilepsy monitoring unit: a review

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Background and aims: Yawning is rarely described as a peri-ictal phenomenon and in most cases is associated with temporal lobe epilepsy.

Methods: We performed a retrospective review of the patients who presented with ictal yawning during long-term video EEG monitoring in our Epilepsy Monitoring Unit (EMU). We included patients admitted between November of 2011 and December of 2021 who showed at least one episode of ictal yawning.

Results: Of a total of 426 patients, only 2 (~0.5%) showed ictal yawning. Case 1: 37-year-old male, with refractory epilepsy secondary to a right frontal malformation of cortical development (MDC). The seizure semiology included loss of consciousness, spasms with right cephalic version, vocalizations, followed by left upper limb myoclonus, automatisms, and yawning, sometimes evolving to generalized tonic-clonic seizures. Case 2: 33-year-old male, with focal refractory epilepsy of the right posterior quadrant of unknown etiology. Seizure semiology consisted of visual aura, loss of consciousness, vocalizations, automatisms and yawning, sometimes evolving to generalized tonic-clonic seizures.

Conclusion: The very low frequency of ictal yawning in our review is in accordance with the few case reports found in the literature. We highlight that we present the only case of ictal yawning known to be associated with right frontal lobe epilepsy

Disclosure: The authors declare no financial or other conflicts of interest.

EPO-558

Improving semiological seizure classification through structured interviews and video tutorials

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Background and aims: Seizure semiology is one of the corner stones in the diagnosis and classification of epilepsy syndromes. Structured interviews about the semiology are quite challenging as recollection by the patient and their relatives may be inconsistent and flawed by subjectivity. We aimed to investigate whether semiological teaching and structured interviews of the caregivers and family improves diagnostic accuracy of seizure semiology and epilepsy syndrome diagnosis.

Methods: 56 patients with epilepsy (generalized and focal), whose seizures were observed by their relatives, were included from the Liga Chilena de Epilepsia. Interviewers were blinded to the diagnoses. A structured interview focused on seizure semiology was performed with patients and their relatives. A second interview was conducted after training with annotated video recordings of typical epileptic seizures, including lateralizing and localizing signs.

Results: The structured interview improved semiological signs of focal epilepsy from 19.6% to 46.4%. Lateralizing signs were detected in 39.3% and localizing signs in 42.9% not documented before the interview. Video training improved lateralization in 17.9% and localization in 3.6% of the patients.

Conclusion: Structured interviews on seizure semiology resulted in statistically significant improvement of lateralizing and localizing signs compared with the patient records. The video training added even more information. Taken together with other information, this may improve the triage of patients towards presurgical epilepsy monitoring.

Disclosure: Nothing to disclose.

EPO-559

Long-term results with the novel anti-seizure medication, cenobamate, in a single centre in Hungary

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Background and aims: Cenobamate (CBM) is approved in Europe as adjunctive anti seizure medication (ASM) therapy for adults with drug-resistant focal-onset seizures. This study reviews the early clinical experience of CBM at the National Institute of Mental Health, Neurology and Neurosurgery, Budapest.

Methods: 61 adult patients were included treated with CBM for inadequately controlled focal seizures being enrolled in the double blind controlled phase III (YKP3089-C017) and open label safety (YKP3089-C021) studies between 2014 and 2017. Efficacy outcomes were obtained from cases continued CBM treatment in the extended access program (EAP) up to present. Pertinent data points (seizure diary based seizure control data, medications, side effects) were extracted retrospectively for analysis.

Results: 40 patients was identified in EAP taking CBM for 5–8 years. 11 (27,5%) patients were rendered seizure free taking 100–400mg/day CBM, and 23 (57,5%) patients experienced significant (more than 50%) seizure reduction. The other 6 (15%) experienced non-significant seizure reduction. Adverse events included dizziness, nystagmus, fatigue, elevation of liver enzimes, hair loss, bacteriuria, hypercholesterinaemia, anaemia, hypertension, psychosis (one case, treatable with concomitant medication), suicidal thoughts (one case, resolved after dose reduction), in the order of the frequency of appearance. One case had eosinophilia and was discontinued early during up titration in the safety study.

Conclusion: We found that CBM is a highly effective, well-tolerated ASM over long periods of time. Real world data is concordant to previous reports of efficacy in controlled studies.

Disclosure: Analyses supported by Angelini S.p.a.

EPO-560

Cognitive adverse events of adjunctive eslicarbazepine acetate in children with refractory focal seizures

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Background and aims: Cognitive impairment in children can lead to poor psychosocial outcomes, impacting learning, social behaviour, and school performance. We aim to evaluate cognitive adverse events(AEs) of adjunctive eslicarbazepine acetate(ESL) in children with focal seizures(FS).

Methods: Safety data were collected and analysed from two randomized, double-blind(DB), placebo-controlled studies(BIA-2093-208(phase II) and-305(phase III)) of adjunctive ESL in children. Data from 8–12 week maintenance DB part, and subsequent 1-year open-label extension(OLE) in children(2–17 years) with refractory FS were analysed. Treatment Emergent Adverse Events(TEAE) affecting any aspect of cognition were tabulated.

Results: During DB(238 patients in ESL group vs 189 in placebo), the following cognitive TEAEs were identified: agitation(2.1% of ESL subjects vs 0.5% in placebo), irritability(1.3%vs1.1%), abnormal behaviour (0.8% vs 0.5%), mental retardation (0.8% vs 0.5%). The remaining TEAEs occurred in one patient each in ESL group(0.4% of subjects): memory impairment(vs 0% in placebo), speech disorder (vs 0.0%), bradyphrenia (vs 0.0%), dyslogia (vs 0.0%), psychomotor hyperactivity (vs 1.1%). No TEAE led to discontinuation of subjects. During the 1-year OLE (372 subjects), the following cognitive TEAE were identified: irritability (1.6% of subjects), abnormal behaviour (0.8%), agitation (0.5%). The remaining TEAEs occurred in one patient each (0.3% of subjects): cognitive disorder, mental impairment, psychomotor hyperactivity, aggression, attention deficit/hyperactivity disorder, conduct disorder. Two cases of abnormal behaviour and one case of conduct disorder led to the discontinuation of study medication.

Conclusion: Cognitive TEAEs observed in children with FS treated with adjunctive ESL were relatively infrequent, during the double-blind and 1-year OLE, and rarely led to discontinuation.

Disclosure: This study was supported by BIAL.

EPO-561

Electrophysiological analysis and clinical follow-up in two siblings with action myoclonus- renal failure syndrome

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Background and aims: Action Myoclonus - Renal Failure Syndrome (AMRF) is a rare form of progressive myoclonic epilepsy (PME). Tremor, cerebellar findings, polyneuropathy, and hearing problems are also seen in AMRF caused by the SCARB2 gene mutation. Detailed electrophysiological analysis of patients including analysis of C reflex or somatosensory evoked potentials were generally lacking in previous reports. Here, we aimed to present the clinical and electrophysiological findings of two siblings with AMRF.

Methods: Clinical evaluation, electroencephalography (EEG), EEG- electromyography (EMG) polygraph, long-loop reflexes (LLR), and somatosensory evoked potentials (SEPs) according to the standard techniques were performed.

Results: Case 1 (25-year-old, female) had stimulus-sensitive, irregular jerks of arms and hands enhanced upon action preventing daily living activities, hyperactive deep tendon reflexes, cerebellar findings. Case 2 (20-year-old, male) had a high-frequency tremor in both hands that does not affect his daily routine. He had a history of renal transplantation. Both of the siblings have positive and negative myoclonus in polygraphic analysis. There was no C reflex, but LLR obtained during the action was high in amplitude. The latency of SEPs was minimally prolonged, however, amplitudes were normal. The R1 and R2 latencies of the blink reflex were prolonged. There was no auditory or somatosensory startle response. Case 1 had 5–6 Hz spike/ poly-spike wave paroxysms in the occipital lobes during photic stimulation accompanying myoclonic jerks. Case 2 had irregular and rare sharp waves in the left temporal lobe.

Conclusion: The prognosis of AMRF can be variable. New electrophysiological markers could help to distinguish AMRF from other PME syndromes.

Disclosure: Authors have nothing to disclose.

Headache 4

EPO-562

Idiopathic Intracranial Hypertension and its management in an increasingly obese population

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Background and aims: Idiopathic Intracranial Hypertension (IIH) is caused by elevated cerebrospinal fluid pressure of unknown aetiology predominantly affecting obese women of childbearing age. This study looked into the management of this patient population in a country with a rising obesity rate.

Methods: Patients diagnosed with IIH were identified through the national Maltese database and further data was retrospectively collected from patients' files.

Results: 59 patients were identified with an average age of 34 (14–68yr), and BMI 36.3 (26.7–49.1). Most underwent repeated lumbar punctures (Graph 1). The average opening pressure was 31.71cm of water (17–72cm of water). Visual field testing (75%), fundal photos (44%) and optical coherence tomography (21%) were often employed to assess papilledema. MRI showed typical IIH changes in 75% (Table 1). All patients were started on acetazolamide. Magnitude and specific strategies for weight loss were not routinely documented. 17% were offered surgical management; including shunt insertion (15%), and dural venous sinus stenting (5%).
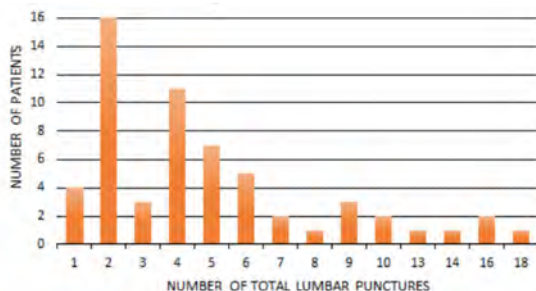
Number of lumbar punctures per patient.

MRI Study Findings	Number of Patients
Normal	12 (20.3%)
Typical IIH Changes	44 (74.6%)
Venous Sinus Stenosis	12 (20.3%)
No MRI	1 (1.7%)
Other Abnormalities	2 (3.4%)

Table 1: MRI Findings

Reported MRI findings for IIH patients.

Conclusion: With rising obesity rates, this has become an increasingly prevalent disorder. Moreover, several patients either presented or relapsed following weight gain at the beginning of the COVID-19 pandemic. This study confirmed that more focus should be employed towards weight loss, which was often poorly documented and not aggressively targeted. Patients were undergoing frequent lumbar punctures rather than repeat, non-invasive ophthalmological investigations – this was tackled locally by involving an ophthalmologist with a special interest in the disorder. A multidisciplinary task force and new local guidelines have been instrumental in standardising and optimising management for these patients.

Disclosure: Nothing to disclose.

EPO-563

Acute Herpes Zoster Infection presenting with SUNCT: an uncommon presentation

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Background and aims: Although SUNCT has previously been considered a primary trigeminal autonomic headache, there is increasing evidence in the literature for secondary SUNCT-like headaches.

Methods: Retrospective review of a patient's clinical file.

Results: An 80-year-old man was admitted to the Emergency Department with complaints of sudden, very brief (seconds of duration) attacks of extremely severe, sharp, unilateral pain affecting the right periorbital region. The attacks occurred several times a day and the patient did not identify any specific trigger. Physical examination showed right eye conjunctival injection, ptosis and eyelid redness. The patient had no prior history of headaches. A diagnosis of SUNA was made and the patient was then discharged with a prescription of Lamotrigine. Two days later the patient returned, presenting with right eye conjunctival injection, right eyelid edema and vesicular desquamation affecting the right eyelid and frontal region. The paroxysmal periorbital sharp pain had eased, and after ophtalmologic evaluation, he was diagnosed with herpes zoster ophtalmicus and treated accordingly with acyclovir.

Conclusion: Varicella zoster virus is well known to be associated with headache and facial pain, due to the trigeminal involvement, but this happens usually under the form of postherpetic neuralgia. A SUNCT-like headache as the form of presentation of the infection is a very rare phenomenon, but our case shows that it should be considered in cases of SUNCT with atypical features, such as onset in later life.

Disclosure: The authors have nothing to disclose.

EPO-564

Side Effects and Discontinuation Risk of Prophylactic Medication in Headache Outpatients

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Background and aims: Primary headaches can be disabling and impair quality of life. A decisive factor in headache treatment is drug discontinuation, either by lack of effectiveness or an often disregarded intolerance to treatment. The aim of this study is to determine the safety profile of these drugs in headache outpatients.

Methods: Data about demographics, diagnosis, treatment, side effects, and patient history were retrospectively collected from adult headache patients under prophylactic treatment who attended headache consultation in a local hospital, from January 2020 to July 2021.

Results: We analyzed a total of 126 patients, 106 females, mean age 51.8 years (19–87). 61.1% had migraine. A total of 14 different prophylactics were used, 46% of the patients took topiramate and 26.2% amitriptyline. 44,4% of the patients had side effects, which led to discontinuation in 7.9%. The most common were cognitive complaints (11.9%), somnolence (5.6%) and paresthesia (5.6%). Side effects had a tendency to correlate with sex, being less frequent in males (p=0.056); a tendency to correlate with topiramate use (p=0.06; mean dose 104.7mg) and an inverse correlation with amitriptyline use (p=0.021; mean dose 25.2mg). After the exclusion of patients under amitriptyline, side effects correlated with an age superior to 65 years (p=0.023).

Conclusion: This study portraits the need for careful consideration of side effects before initiating a new prophylactic treatment, especially in the elderly. We found side effects in almost half the patients, which led to treatment discontinuation in one-fifth. The safety profile favored the use of amitriptyline, disfavored topiramate, and was worse in the elderly.

Disclosure: The authors have nothing to disclose.

EPO-565

Machine-learning based approach to predict CGRP response in patients with migraine: multicenter Spanish study

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Background and aims: Monoclonal antibodies targeting calcitonin gene-related peptide (CGRP) used as preventive treatment for episodic high-frequency episodic migraine (HFEM) and chronic migraine (CM). The main objective of the present study is to predict anti-CGRP response at 6 months using a machine-learning approach.

Methods: We performed a retrospective multicenter study nested in a prospectively collected cohort of patients with migraine anti-CGRP therapies. Demographic and headache variables were collected. 50% responder rate defined as a 50% reduction in the number of headache days per month at 6 months. 30% and 75% response rates were also evaluated. Machine-learning approaches were used for features selection to generate a prediction model of 30%, 50% and 75% response to anti-CGRP therapies at 6 months.

Results: 720 patients were included in the study, 93% were women, and the mean age of all patients was 48 years (SD: 11.6). At baseline, 83.1% of patients had chronic migraine. 50% response rate was achieved by 43% at 6 months, 30% response rate was achieved by 60% and 75% response was achieved by 17% at 6 months. Variables included in the prediction model were the change in headache days per month at 3 months compared to baseline, the number of headache days at 3 months and HIT 6 score at 3 months.

Conclusion: According to our study, anti-CGRP response at 6 months in patients with migraine can be predicted based on machine-learning approaches in a real-world setting.

Disclosure: Nothing to disclose.

EPO-566

Efficacy and safety of Fremanezumab in patients with episodic and chronic migraine in a real-life setting

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Background and aims: Fremanezumab is a recent gene–related peptide (CGRP) monoclonal antibody to treat both chronic and episodic migraine prevention. We aim to describe efficacy and safety outcomes in a very well defined cohort of patients with migraine and Fremanezumab.

Methods: We collected a prospective longitudinal cohort of patients with episodic and chronic migraine receiving Fremanezumab. Demographic characteristics and headache variables were collected at baseline and every 3 months at 3, 6 and 9 months including safety, tolerability, and outcome measures such as adverse events, discontinuation, partial (30% improvement), standard (50% improvement) and optimal (75% improvement) response regarding monthly headache days (MHD).

Results: 14 patients, 52 (SD: 11) mean age, 84% women, 85% chronic migraine, 15% episodic migraine, age of onset 14 (SD: 3) years, time from migraine diagnosis 38 (SD:10) years, time with chronic migraine 48 (SD:54) months, average number of prior preventive treatments 8 (SD:3), medication overuse at baseline 61%. At 3 months, partial response was achieved by 30% of patients, standard response by 30% and optimal response by 50% of patients. Adverse events occurred in 60% of patients. most commonly constipation (50%). At 6 months, partial response was achieved by 28%, standard response by 14% and optimal response by 28% of patients. 85% of patients had any adverse events, mostly local reactions (42%). At 9 months, one patient achieved optimal response and another patient standard response. None of them had any adverse events.

Conclusion: In this real-world study, Fremanezumab was an overall effective and safe treatment in patients with migraine.

Disclosure: Nothing to disclose.

EPO-567

Elevated calcitonine-gene related peptide in syndrome of headache, neurologic deficits and CSF lymphocytosis (HaNDL)

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Background and aims: We report 3 subsequent cases of a rare clinical syndrome of headache, neurologic deficit and cerebrospinal fluid lymphocytosis (HaNDL). Patients with HaNDL present with recurring migraine-like episodes of severe headache with transient neurologic deficit. The localization and lateralization of the deficit can change with each episode. Furthermore, we report a novel observation of elevated serum calcitonine gene-related peptide (CGRP) in two of three reported cases.

Methods: Medical records of 3 patients with the diagnosis of HaNDL were reviewed. In addition, stored cerebrospinal fluid and serum samples of 3 patients and 20 controls were analysed using commercially available enzyme-linked immunoassay (ELISA) CGRP kit.

Results: Of the 3 reported patients, each had 3–7 episodes with neurological deficit and headache over 4–5 weeks, each patient had at least one hemiparetic episode and one with hemiparesthesias. Two had visual auras. CSF lymphocytosis (116–217 cells/microliter) was seen in all cases, no pathogen or imaging abnormity was found. Measurable levels of CGRP were detected in in 2 of 3 cases and only in 2 of 20 controls (p=0.015%; chi-squared test, 75 vs 39 pg/ml); In the remaining serum samples (1 patient, 18 controls) the CGRP concentration was below detection limit (10pg/ml), all CSF samples were negative for CGRP.

Conclusion: HaNDL is a rare syndrome with features of acute stroke, migraine and meningitis, which can easily mimic stroke and present a diagnostic conundrum in the acute stroke clinic. Our observation of elevated CGPR levels adds further support to a shared pathophysiology of HaNDL and migraine.

Disclosure: Supported by Ministry of Health, Czech Republic – conceptual development of research organization (NHH, 00023884).

EPO-568

Alternative diagnostic criteria for headache attributed to ischemic stroke and new criteria for sentinel headache

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Background and aims: The current diagnostic criteria of the ICHD-3 for acute headache attributed to ischemic stroke are based primarily on the opinion of experts rather than on published clinical evidence based on extensive case-control studies in patients with first-ever stroke. Diagnostic criteria for sentinel headache do not exist. The present study aimed to cover these gaps.

Methods: This prospective case-control study included 550 patients (mean age 63.1, 54% males) with first-ever ischemic stroke and 192 control patients (mean age 58.7, 36% males). Standardized semi-structured interview forms were used to evaluate past and present headaches during face-to-face interviews by a neurologist. To test and develop new criteria, we tabulated the onset of headaches and their type (new type, the previous headache with altered and unaltered characteristics) before a first-ever ischemic stroke and at the time of onset of stroke.

Results: Headache at the onset of ischemic stroke was present in 82 (14.9%) of 550 patients, and 81 (14.7%) patients had sentinel headache within the last week before a stroke. Only 60% of the headaches at stroke onset fulfilled the diagnostic criteria of ICHD-3. Therefore, we proposed alternative criteria with a sensitivity of 100% and specificity of 97% (Figure 1). Besides, we developed diagnostic criteria for sentinel headache for the first time with a specificity of 98% and a sensitivity of 100% (Figure 2).

Figure 1. Alternative diagnostic criteria for acute headache attributed to ischemic stroke

A. Any headache fulfilling criteria B and C.

B. Acute ischaemic stroke has been diagnosed.

C. Evidence of causation demonstrated by the following:

　1. a new headache has developed within 24 hours of other symptoms and/or clinical signs of ischaemic stroke

　2. a previous headache with altered characteristics has developed within 24 hours of other symptoms and/or clinical signs of ischaemic stroke

D. Either of the following:

　1. headache has resolved within three months

　2. headache has not yet resolved but three months have not yet passed

E. Not better accounted for by another ICHD-3 diagnosis.

Figure 1.

Figure 2. New diagnostic criteria for sentinel headache before ischemic stroke

A. Any headache fulfilling criteria B and C

B. Acute ischaemic stroke has been diagnosed

C. Evidence of causation demonstrated by least one of the following:

　1. a new headache never experienced before developed within one week before ischaemic stroke

　2. a previous headache with altered characteristics (severe intensity, increased frequency, prolonged duration, development of new accompanying symptoms, absence of effect of drugs for pain relief) developed within one week before ischaemic stroke

D. Not better accounted for by another ICHD-3 diagnosis.

Figure 2.

Conclusion: We suggest alternative diagnostic criteria for acute headache attributed to ischemic stroke and new diagnostic criteria for sentinel headache with high sensitivity and specificity.

Disclosure: Nothing to disclose.

EPO-570

Botulinum Toxin A in the management of Refractory Trigeminal Neuralgia: a case-series

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Background and aims: Botulinum toxin A (BoNT) has been described as useful in Trigeminal Neuralgia (TN) patients that are refractory or intolerant to conventional medical therapies. Our aim was to study the short and long-term efficacy and safety of BoNT in these patients.

Methods: We included TN patients treated quarterly with BoNT in our center, between April 2021 and December 2022. We applied the brief pain inventory (short form) to assess pain before BoNT and at 3, 6 months (mo) and at the moment of data collection (median 8mo) after the first treatment with BoNT.

Results: 12 out of 16 patients agreed to participate in the study [response rate 75%; 6 males, median 70 (IQR 56–75) years old, median 25 U/treatment]. Significant differences were found between baseline and the three moments post-BoNT in maximum pain [8.75 ± 1.42 vs. 5.58 ± 2.75 3mo, 5.17 ± 2.92 6mo, 5.25 ± 2.73 currently (cu)], daily living activities impact (7.67 ± 2.15 vs. 3.92 ± 2.64 3mo, 3.08 ± 2.47 6mo, 3.42 ± 2.27cu), mood (7.83 ± 2.55 vs. 3.92 ± 2.68 3mo, 3.17 ± 2.12 6mo and 3.33 ± 1.92cu) and social relationships (6.50 ± 3.50 vs. 2.25 ± 3.36 3mo, 2.75 ± 2.86 6mo and 2.75 ± 2.96cu). Pain impact at work was significantly lower after 6mo (2.42 ± 2.35) and at the moment of data collection (2.42 ± 2.35) compared to baseline (6.17 ± 3.49). The greatest reduction in post-BoNT pain impact was found for walking (69%) and mood, work, and social relationships (58%). No adverse-effects were reported besides facial edema in three patients (25%).

Conclusion: In our cohort, BoNT was a safe and effective method in the management of TN. This effect seems to be consistent and longstanding.

Disclosure: The authors have no conflict of interest to disclose.

EPO-571

Abstract withdrawn

EPO-572

Headache and COVID-19 Vaccination: data from online questionnaire in patients with migraine

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Background and aims: Vaccines represented the breakthrough in the fight against COVID-19 allowing a reduction of COVID-19 related hospitalizations and deaths. Based on high frequency of headache attacks reported in the days following vaccination, both in randomized controlled trials and in our clinical experience, we focused on the effects of COVID-19 vaccine administration in migraine population and we speculated on the putative pathophysiological mechanisms.

Methods: An on-line questionnaire was published on Italian Facebook groups oriented to headache patients to collect demographics data, information about previous COVID-19 infection and vaccination and clinical parameters of putative headache attacks occurring after vaccination.

Results: Of 841 migraine patients filling-in the questionnaire, 66% and 60% experienced a headache attack within 7 days after, respectively, the first and the second vaccine dose. Over the half of patients perceived the headache attacks as more severe, long-lasting, resistant to symptomatic treatment compared to usual experienced episodes.

Conclusion: Headache worsening following COVID-19 vaccination could be related to the production of inflammatory mediators such as type Iβ-interferon known to be involved in migraine occurrence or worsening, along with IL-6, NO pathway activation and cortical dysexcitability, altogether recognized as critical moments of migraine pathophysiology. Considering the high prevalence of migraine in the general population, the awareness of the possibility of headache worsening following COVID-19 vaccine administration in these patients could make a reduced waste of resources employed in an inappropriate health-care.

Disclosure: I have no disclosure.

EPO-573

Disconnectome of the migraine brain: a model of migraine as "connectopathy"

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Background and aims: Graph analysis allowed to explore the - so-called - human brain connectome, in neurological disorders. We hypothesized that a connectivity mismatch between 'integration' and 'segregation', as well as changes in hubs and edges organization, may represent the neural correlates of migraine brain.

Methods: We investigated, using high angular resolution diffusion-weighted MRI imaging tractography-based graph analysis, the graph-theoretic indices of brain connectome, in 94 patients with migraine without aura compared to 91 healthy controls.

Results: We observed in migraine patients when compared to healthy controls: i) higher local and global efficiency (p<0.001) and ii) higher local and global clustering coefficient (p<0.001). Moreover, we found changes in the hubs topology in migraine patients with: i) posterior cingulate cortex and inferior parietal lobule (encompassing the so-called neurolimbic-pain network) and ii) fronto-orbital cortex, involved in emotional aspects, and the visual areas, involved in migraine pathophysiology. Finally, we demonstrated a higher connection probability (edges) between cortical nodes involved in pain perception and modulation as well as in cognitive and affective attribution of pain experiences, in migraine patients when compared to healthy controls (p=0.0002).
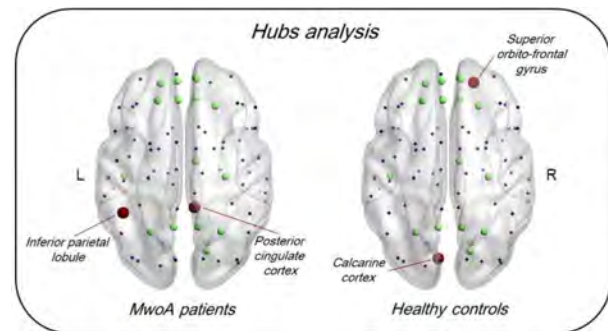
Hubs regions with groups betweenness centrality scores in the 80th percentile displayed on brain on MNI template surface.

Conclusion: Our findings support an imbalance between the need of investing resources to promote network efficiency and the need to minimize the metabolic cost of wiring in migraine. The abnormal distribution of strategical hubs may represent a mechanism of susceptibility to migraine trigger factors. In conclusion, we identified a connectome disconnectivity pattern that could represent the migraine brain landscape, proposing an intriguing pathophysiological model of migraine as brain "connectopathy".

Disclosure: Nothing to disclose.
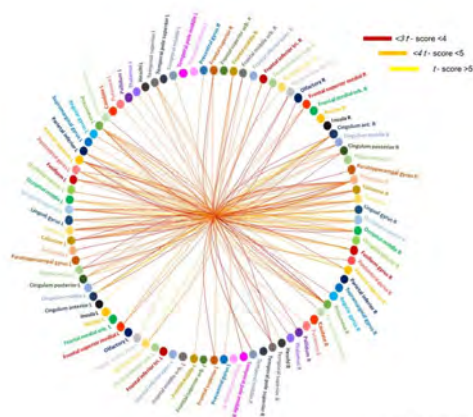
Fig. 4

Connectogram of nodes and edges showing significantly higher connection probability (t score) in MwoA patients compared to HC data sets (p

EPO-574

Response to galcanezumab in chronic migraine patients with daily headache. Results in a series of 47 cases

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Background and aims: Daily headache was an exclusion criterion in the clinical trials that led to the approval of anti-CGRP monoclonal antibodies as a preventive treatment for chronic migraine. However, it is common in real life to treat these patients and, in our country, the presence of daily headache does not exclude reimbursement. We aimed to analyze whether the presence of daily headache predicts the response to galcanezumab in a population of patients with chronic migraine.

Methods: We considered patients treated with anti-CGRP monoclonal antibodies during the first year after its approval in a headache unit of a tertiary hospital. During this time the only monoclonal available in our hospital was galcanezumab. The patients recorded on a calendar the number of headache and migraine days during the 2 months prior to the start of treatment and throughout it. We defined response as a decrease in the number of monthly headache days of at least 50% during third month after starting treatment.

Results: We included 47 patients. Mean age was 45.3 ± 10.2 years and 44 (93.6%) were women. They had 26.2 ± 12.3 years of migraine before galcanezumab treatment and received 4.6 ± 1 prior preventive treatments. At baseline, 19 (40.4%) presented daily headache. Response was achieved in 26 (55.3%) cases. There was no difference in response among patients with (47.4%) and without (60.7%) daily headache ($p=0.39$).

Conclusion: The presence of daily headache does not predict a lack of response to treatment with galcanezumab in patients with chronic migraine.

Disclosure: I have no conflict of interests related to the publication of this poster .

Infectious diseases 2

EPO-575

Spinal Cord Schistosomiasis: Case series and review of treatment options and response to treatment

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Background and aims: Spinal Cord Schistosomiasis is a serious form of neuroschistosomiasis that is often neglected in the differential diagnosis of myelopathies. With the advancing Urbanization, the endemicity of Schistosomiasis in previously noted endemic areas is changing, consideration of this tragic complication of parasitic infestation has been more challenging specially with the lack of definitive diagnostic tools.

Methods: Four cases of probably Schistosoma myelitis are evaluated for their clinical presentation, environmental exposure and risk factors, demographic characteristics and imaging criteria. Duration from onset to antiparasitic treatment and response to other modalities of treatment.

Results: Four cases of myelitis, two children and two adults presenting with subacute myelopathy as follows. One with early suspicion due to history of work in the agricultural field and early introduction of praziquantal, two relatives with one previously operated on with histopathological evidence of recent Schistosoma myelitis and concomitant occurrence of subacute myelitis involving the conus medullaris in a child relative with positive serological tests and partial response on Praziquantal and marked improvement on plasma exchange. The fourth case of probable Schistosoma myelitis with delayed suspicion and late introduction of Praziquantal with minimal improvement on both antiparasitic drug and plasma exchange.
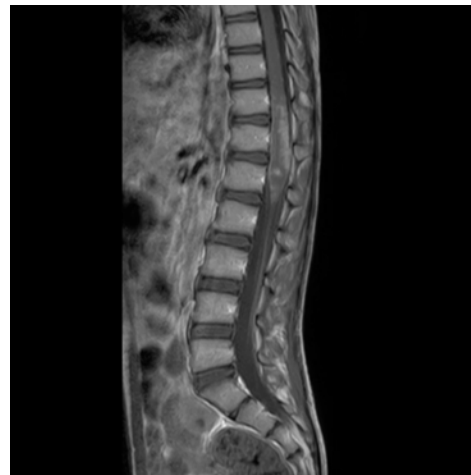
Dorso-Lumbo-Sacral MRI, Sagittal T1 post contrast

Dorso-Lumbo-Sacral MRI, Sagittal T2

Conclusion: Keeping a high index of suspicion of Spinal Schistosomiasis in cases of subacute myelitis with suggestive imaging and clinical features and early introduction of Praziquantal is needed and more extensive work on prognostic factors for good response to antiparasitic treatment and the role of plasma exchange and surgical intervention in refractory cases.

Disclosure: No conflict of interest, no funding received.

EPO-576

Acanthamoeba encephalitis in an immunocompetent patient: A case report

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Background and aims: Acanthamoeba species are the most common free-living amoeboid organisms in nature. They usually cause chronic sinusitis, otitis, cutaneous lesions, chronic amoebic encephalitis in immunocompromised individuals.

Methods: A 43-year-old male patient with congenital deafness was admitted because of headache and right hemiparesis.

Results: The patient's brain MRI revealed multiple hyperintense, circumferentially enhanced, and edematous lesions (Figure 1). Cerebrospinal fluid (CSF) analysis revealed 49/mm^3 lymphocytes, 2/mm^3 polymorphonuclear cells. Viral-bacterial CS PCR was negative, there was no growth in fungal and mycobacterial cultures, and no parasites were observed in the microscopic inspection. Histopathological examination of the excisional brain biopsy revealed foci with histiocytic infiltration containing PAS-positive granules and perivascular inflammation (Figure 2). A follow-up brain MRI showed a contrast-enhancing collection in the operation lodge that was aspirated. The analysis of this fluid revealed 1,333/mm^3 polymorphonuclear leukocytes, 80/mm^3 lymphocytes, and a total protein level of 2,848 mg/dL. In the microscopic examination, Acanthamoeba spp. trophozoites and cysts were observed (Figure 3). The patient was treated with trimethoprim-sulfamethoxazole, azithromycin, fluconazole, and metronidazole.
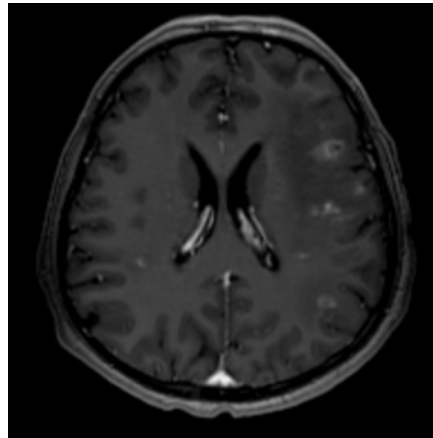
The patient's brain MRI revealed multiple hyperintense, circumferentially enhanced, and edematous lesions.
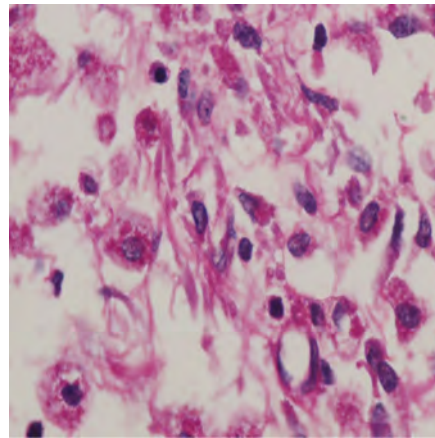
PAS+ granular staining in macrophage cytoplasm in PAS stain.
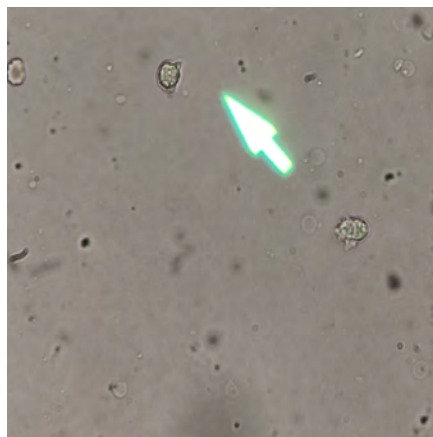
Trophozoites of Acanthamoeba spp. (15–45 μm) with pseudopodia in CSF direct microscopy of wet mount 40 x objective lens.

Conclusion: The Acanthamoeba cysts are common in nature that may cause encephalitis also in immunocompetent individuals. The delay in the diagnosis may result in a fatal disease course.

Disclosure: There is no disclosure.

EPO-577

Abstract withdrawn

EPO-578

Histoplasmosis of central nervous system presenting as a brain tumor

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Background and aims: CNS infection occurs in 5 to 10% of patients with disseminated histoplasmosis. The recognition, diagnosis, and treatment of CNS histoplasmosis is not well-characterized. Over one third of cases reported, have occurred in immunocompetent individuals. Morbidity, and mortality appear to be high in patients with CNS histoplasmosis with high rates of relapse. Despite prolonged courses of treatment, the case fatality was 39% with half of the survivors relapsing in a prior study.

Methods: 30-year-old male presented with chief complaints of ataxia, headache in the occipital region for 2 years. Patient also gave recent history of blurring of vision in right eye. Patient tested positive for retroviral disease (CD4 count -44). MRI brain was suggestive of peripherally enhancing lesion in cerebellar vermis and right middle cerebellar peduncle with effacement of 4th ventricle leading to hydrocephalus (Figure 1).
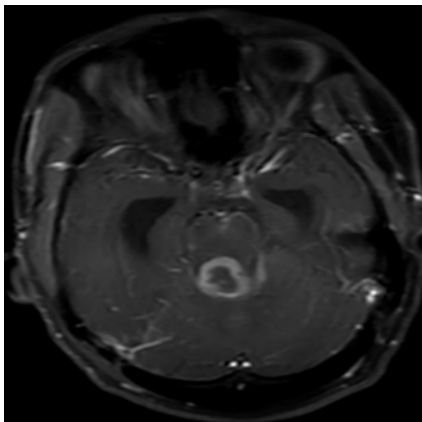
MRI brain suggestive of peripherally enhancing lesion in cerebellar vermis and right middle cerebellar peduncle with effacement of 4th ventricle leading to hydrocephalus

Results: We performed a midline suboccipital craniotomy with decompression of 4th ventricle tumor. HPE of tumor biopsy revealed necrotizing histoplasma infection. Patient was managed with 8 weeks of IV Amphotericin B followed by long term oral Itraconazole. Patient made significant recovery with the treatment. His condition remains stable 4 years later, and no recurrence of histoplasmosis has been observed.

Conclusion: Clinicians should have a low threshold for considering histoplasmosis as a cause for meningitis, brain lesions, vascular events, or hydrocephalus in immunocompromised, and non-immunocompromised patients who reside in endemic areas, and for whom an alternative diagnosis has not been established.
Disclosure: Nothing to disclose.

EPO-579

Early fascicular nerve biopsy in suspected leprosy

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Background and aims: Pure neuritic leprosy has constantly been a paradox due to its clinical and management uncertainties. Pure neural leprosy (PNL) is tricky to diagnose due to absence of skin lesions.
Methods: A 26-year-old Indian male presented to our hospital with gradually progressive hypoesthesia on the inner aspect of right hand and mild difficulty in holding objects with right hand. It worsened in severity and extended gradually upto the inner aspect of distal forearm over next 1 year. He developed an unnoticed burn on inner aspect of his right wrist which resolved on his own with some over the counter medications. Right ulnar nerve thickening was palpable at the elbow joint. Patient's NCV revealed peripheral neuropathy. The criteria for diagnosing PNL are as follows- (1) Clinically, the patient presents with peripheral neuropathy. (2) The patient is from endemic area or has a family history of leprosy. (3) Peripheral nerve thickening on palpation. (4) Typical ENMG abnormalities. (5) Absence of other co-morbidities including diabetes mellitus, autoimmune diseases, paraproteinemia or other systemic disorders. (6) Absence of any skin manifestation.
Results: Due to high index of suspicion, we performed fascicular nerve biopsy. Nerve biopsy revealed, well- to ill-formed epithelioid cell granulomas, neural fibrosis, lymphocytic inflammation, and foam cells; suggestive of pure neuritic leprosy (PNL) (Figure 1). Patient was started on leprosy treatment and he responded well to treatment.
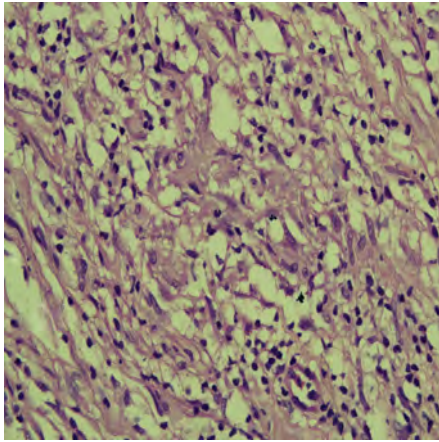
Fascicular nerve biopsy revealed, well- to ill-formed epithelioid cell granulomas, neural fibrosis, lymphocytic inflammation, and foam cells; suggestive of pure neuritic leprosy (PNL)

Conclusion: • The gold standard for confirmation of pure neuritic leprosy is by nerve biopsy. • Early identification of pure neuritic leprosy and its treatment is of great benefit.
Disclosure: Nothing to disclose.

EPO-580

Cerebral Whipple's disease presenting with an epileptic seizure: reminder of a rare disease with variable manifestations

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Background and aims: Whipple's disease is a rare infectious disease caused by the actinomycete T. whipplei that can involve the central nervous system in addition to other organs, predominantly the gastro-intestinal tract. Neurological signs and symptoms vary greatly and are often subtle while brain imaging can show non-specific features, likely delaying diagnosis and treatment.
Methods: We report the case of an otherwise healthy 31-year old female patient who was referred to our hospital after presenting with a first epileptic seizure. The clinical neurological examination was unremarkable. She reported a two-month episode of persistent diarrhea two years prior.
Results: Brain MRI showed multiple FLAIR and T1 gadolinium-enhancing lesions surrounded by vasogenic edema (Fig. 1). Cerebrospinal fluid analysis showed a monocytic pleocytosis ($18/\mu L$) but initial extensive microbiological analysis remained negative. Histological examination of brain tissue obtained via stereotactic biopsy demonstrated a meningoencephalitis with granular PAS-staining within histiocytes, thereby indicating the diagnosis of cerebral Whipple's disease. Gastroduodenoscopy demonstrated an atrophic gastritis but PAS-positive histiocytes were not present in the duodenal biopsies. Intravenous treatment with ceftriaxone during two weeks followed by oral doxycycline combined with hydroxychloroquine resulted in a progressive reduction of the lesions on brain MRI at 1, 3 and 6 months after treatment initiation (Fig. 2). Her clinical neurological status remained unaffected, without recurrence of epileptic seizures.
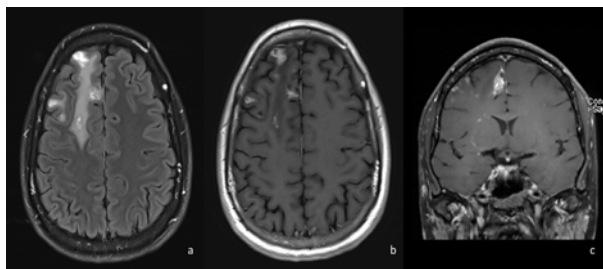
Initial brain MRI showing multiple gadolinium-enhancing lesions surrounded by vasogenic edema in the right frontal lobe on axial FLAIR (a), axial T1 TSE (b) and coronal 3D T1 (c) images. FLAIR: fluid-attenuated inversion recovery; TSE: turbo spin echo.
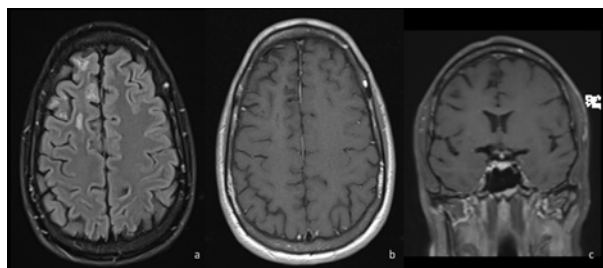
The follow-up MRI of the brain at 6 months shows a decrease in gadolinium-enhancing lesion load, with areas of parenchymal destruction and residual gliosis being evident. Axial FLAIR (a), axial T1 TSE (b) and coronal 3D T1 (c) images with gadolinium.

Conclusion: This case clearly shows the clinical subtleness and the clinico-radiological paradox by which cerebral Whipple's disease can present itself.

Disclosure: The authors declare no conflicts of interest.

EPO-581

A "smoldering" case of HSV-2 encephalitis in an immunocompetent patient with mild cognitive impairment

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Background and aims: We describe a case of herpes simplex virus-type 2 (HSV-2) encephalitis (HSE) in a immunocompetent patient with MCI.

Methods: N/A

Results: A 75 years-old woman was admitted for an acute altered mental status. Her medical history was remarkable for amnestic mild cognitive impairment and cardiovascular problems. Ten days earlier, she presented worsening of memory loss and slowness of cognition. The day before, she complained a headache. At the admission, she was afebrile, disoriented, amnesic for the last hours, aphasic. Blood and urine tests excluded metabolic disorders, signs of infection, autoimmune and paraneoplastic diseases. Imaging studies including brain CT, CT angiography and CT perfusion were all normal. Electroencephalogram was not specific. CSF examination showed normal WBC, mild elevated protein (64 mg/dl) and a positive PCR test for HSV-2. She was then treated with acyclovir intravenous for 10 days with clinical improvement during the hospitalization but residual memory difficulties. Brain MRI, performed 4 days after the therapy started, showed no acute lesions.

Conclusion: HSV-2 encephalitis is uncommon and represents less than 10% of HSE. Subtle clinical and radiological signs occur more frequently than in HSV-1 encephalitis, especially in immunocompetent with normocellular CSF, leading to diagnostic mistakes and delays in treatment with prognostic consequences. Our case is an example of such "smoldering" forms, for the absence of fever, pleocytosis, typical EEG and imaging findings. Clinicians should consider HSE in the differential diagnosis of acute altered mental status and memory deficits otherwise unexplained, also in elderly patients with prior cognitive impairment.

Disclosure: Nothing to disclose.

EPO-582

Longitudinal extensive transverse myelitis as a manifestation of Neurosyphilis – a rare but treatable cause

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Background and aims: Tabes dorsalis associated with late Neurosyphilis is well established, however spinal cord involvement in the meningovascular phase is rarely reported and poorly characterized.

Methods: Case report. Pubmed literature search, for articles published up to December 2021 using the terms "syphilitic myelitis" or "meningovascular syphilis". We reviewed the characteristics of patients with probable (reactive CSF non-treponemal test) and possible (reactive serum treponemal test and pleocytosis or high CSF protein count) syphilitic myelitis (except for tables dorsalis).

Results: We reviewed 28 patients (20 probable and 8 possible syphilitic myelitis). The majority (68%) were males with a median onset age of 41 (range 17–69) years. Twelve presented with a complete picture of transverse myelitis; the median time to nadir was 30 days. CSF studies revealed pleocytosis in 96% (median 90 cells/mm^3) and high protein count in 93% (median 91.7 mg/dL). All patients had a high intensity T2 lesion in spine MRI, mainly involving the thoracic (50%) or cervicothoracic cord (46%), 86% involving more than 3 segments, 43% with gadolinium enhancement, and 5 with "flip-flop sign". The majority (79%) improved with treatment.

Fig. 2: MRI after treatment showing (C) significative resolution of abnormal high intensity signal on T2-weigted image, now limited to T4-T7, and reduction of oedematous aspect of spinal cord, and of (D) gadolinium enhancement (now only T6-T7).

Conclusion: This case and literature review demonstrates that neurosyphilis should be considered in the differential diagnosis of acute/subacute longitudinally extensive transverse myelitis. As a rare but treatable cause, a high level of suspicion is needed.

Disclosure: Nothing to disclose.

Fig. 1: Initial MRI showing (A) a T2-weighted high signal intensity from C4 to T11, with a moderately swollen spinal cord, and (B) patchy gadolinium enhancement.

EPO-583

Paraparesis and encephalopathy in a previously heathy man

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Background and aims: Since the introduction of combined antiretroviral therapy (cART) there has been a dramatic decrease in the incidence of AIDS-defining neurological diseases.

Methods: A previously healthy 44-year-old man presented with progressive lumbar pain, lower limb weakness, gait disturbance and urinary symptoms for 4–5 months. Patient denied fever or unprotected sex. A month later, he also had slow speech and comprehension impairment. Complete blood test only showed anemia and a brain Magnetic Resonance Imaging (MRI) without contrast showed confluent multifocal white matter lesions in T2 sequence, suggestive of leukopathy (Figure 1).

Axial T2-weighted image shows bilateral increased diffuse T2 signal affecting subcortical white matter, corpus callosum and brainstem, suggestive of leukopathy.
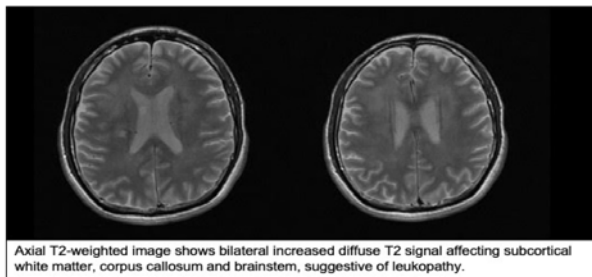
Figure 1: Brain MRI

Results: Neurological examination revealed signs of encephalopathy and asymmetric motor paraparesis. A lumbar puncture showed mildly elevated cell count and protein. As part of the initial screening for infectious causes of encephalopathy, HIV antibodies and p24 antigen were tested positive being diagnosed with AIDS. An MRI contrast was performed, showing findings compatible with toxoplasmosis (Figure 2). Despite negative results in serologic test for toxoplasma and PCR signal for T. gondii-DNA in CSF, patient was diagnosed with probable cerebral toxoplasmosis (Table 1). He was treated with pyrimethamine, sulfonamide and cART with a spectacular clinical and radiological response with near complete recovery (Figure 2).

Brain contrast MRI showing diffuse leukopathy suggestive of HIV encephalopathy. Focal lesion with postcontrast enhancement in right cerebral hemisphere, to rule out the possibility of cerebral toxoplasmosis.

Brain contrast MRI after 14 days of treatment proven cerebral toxoplasmosis due to unequivocal radiological response to treatment with clinical and radiological follow up

Brain contrast MRI after 2 months of treatment showing almost complete resolution of focal lesion in right cerebral hemisphere and no changes in diffuse leukopathy.

Figure 2: Radiological diagnosis and follow-up

Histology-confirmed cerebral toxoplasmosis	Laboratory-confirmed cerebral toxoplasmosis	Probable cerebral toxoplasmosis	Possible cerebral toxoplasmosis
- Compatible clinical syndrome	- Compatible clinical syndrome	- Compatible clinical syndrome	- Compatible clinical syndrome
- Identification of one or more expansive focal brain lesions by imaging	- Identification of one or more expansive focal brain lesions by imaging	- Identification of one or more expansive focal brain lesions by imaging	- Identification of one or more expansive focal brain lesions by imaging
- Brain biopsy showing evidence of T gondii.	- Evidence of T gondii DNA in cerebrospinal fluid (CSF) by PCR	- Unequivocal radiological response to 10 to 14 days of empiric antitoxoplasma therapy	- Presence of serum T gondii IgG antibodies, and no other alternative diagnosis

Table 1: Diagnostic categories of cerebral toxoplasmosis

Conclusion: Cerebral toxoplasmosis presents a wide spectrum of clinical and neuroradiological manifestations and a high rate of early suspicion is vital, because it is a treatable and reversible cause of leukopathy. Despite the lack of potential risk factors in the anamnesis, in a patient with diffuse leukopathy and one or more expansive brain lesions, HIV associated toxoplasmosis must be ruled out.
Disclosure: Nothing to disclose.

EPO-584

Neurological manifestations of Lyme borreliosis and tick borne encephalitis coinfection: case series

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Background and aims: A single tick bite has the potential to transmit both tick-borne encephalitis (TBE) and Lyme borreliosis. Despite their different clinical courses, TBE and Lyme borreliosis have common neurological features: lymphocytic meningitis, flaccid or spastic limb weakness, and cranial nerve involvement [1]. Thus, differentiating between these disorders is important, given different approaches to treatment.

Methods: This is case series of 3 patients diagnosed with a coinfection of Lyme borreliosis and tick-borne encephalitis (TBE) between 2021 and 2020 in PSCUH, Latvia.

Results: Patients' data summarized in table 1.

Age, sex	Male, 64	Male, 51	Male, 43
Main complaints	Fatigue, followed by high fever and pain in the lower back radiating to the left leg. Despite adequate analgetic therapy no pain relief.	Biphasic fever, weakness in the legs and headache.	Fever, joint pain, fatigue.
Neurological assessment	Pain in the left gluteal region, bilaterally in sacroiliac joints. Hypesthesia in the left leg's external and back surface.	No focal neurological symptoms.	Disoriented in time and place, with altered mental state, no other focal neurological symptoms.
Known tick bite	No	Yes	No
Vaccination against TBE	No	No	No
Time from admission to performed lumbar puncture	2 days	0 days	0 days
Cerebrospinal fluid analysis	Cell count 9/microL Protein 1.3	Cell count 34 /microL Protein 0.876 g/L Granulocytes 88%	Cell count 45/microL Protein 1.2 Agranulocytes 91%,
	Anti-TBE IgG 7641, IgM (PI 21.84) positive. Anti- borrelia IgG negative (<0.2 AU/ml), IgM dubious (2.5 AU/ml), rechecked with Western-blot IgM -positive.	Anti-borrelia IgM positive (6.1 AU /ml), IgG negative (0.2 AU/ml), rechecked with Western-blot - Positive. Anti-TBE IgM positive.	Anti-TBE positive IgM (PI 2.08) and IgG, Anti-borrelia positive IgM and IgG (32.6 AU/ml)- rechecked with Western-blot.
Specific treatment	S.Ceftriaxon i/v (for 21 days).	S.Ceftriaxon i/v (for 14 days).	S.Ceftriaxon i/v (for 21 days
Other investigational tools	CT and MRI for lower back Head CT Neurography	Head CT	Head CT

Table 1

Conclusion: Both Lyme borreliosis and TBE should be investigated if neuroinfections are suspected in endemic regions. Patients with either TBE or neuroborreliosis can present with nonspecific neurological symptoms. With high suspicion of neuroinfections established by lumbar puncture, both TBE and neuroborreliosis should be tested in endemic regions, even if patients do not report tick bite. Patients with unexplained fever or severe radicular pain should undergo lumbar puncture, since such unspecific symptoms can be the only manifestation of both TBE and neuroborreliosis.

Disclosure: Nothing to disclose.

EPO-585

Varicella-Zoster Vasculopathy: A diverse clinical and radiological entity.

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Background and aims: Vasculopathies and intracranial hemorrhage are rare but known entities caused by varicella zoster virus (VZV).

Methods: We present a rare case of VZV associated subarachnoid hemorrhage and vasculopathy in an otherwise immunocompetent adult.

Results: A 35-year-old man presented with transient episodes of weakness and aphasia. Neurological examination was negative. Brain magnetic resonance imaging and angiography (MRI/MRA) revealed an isolated cortical subarachnoid hemorrhage, increased T1/T2-signal in the left head of the caudate and a marked stenosis at the M1 segment of the left middle cerebral artery (MCA). Computed tomography angiography (CTA) and digital subtracted angiography confirmed the above finding and did not indicate vasculitis. Routine blood work was normal, whereas cerebrospinal fluid (CSF) testing revealed lymphocytosis, elevated albumin and normal CSF/blood glucose ratio. Serology revealed high levels of VZV IgG in the serum and CSF was positive for VZV genetic material. Treated with antivirals, the patient improved and was discharged. 1 month later, while exercising, he developed right-side hemiparesis for 30 minutes. Repeat MRI/MRA/CTA showed improvement in the caudate lesion, with no new findings. Nevertheless, the stenosis of the left MCA remained and the patient was treated with dual antiplatelet therapy for 3 months as a symptomatic intracranial stenosis. At 4-months follow-up the patient remains asymptomatic and repeat DSA revealed improvement of MCA stenosis.
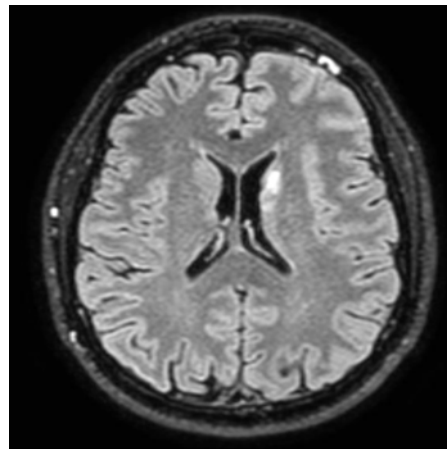
Axial FLAIR MRI: Increased signal in the head of caudate nucleus
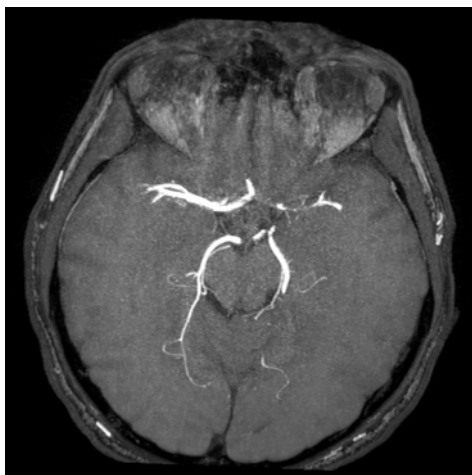
Axial CTA: Narrowing of M1 segment of MCA.

Digital Subtracted Angiography: M1 stenosis of left MCA

Conclusion: VZV vasculopathies can complicate zoster or varicella and are caused by productive viral infection in cerebral arteries. Clinicians must keep in mind that unlike most cases of acute viral encephalitis, VZV vasculopathy is often chronic and protracted.

Disclosure: Nothing to disclose.

EPO-586

Analysis of hospitalizations due to central nervous system tuberculosis and BCG vaccination in the State of São Paulo

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Background and aims: This paper aims to correlate the hospitalizations for central nervous system tuberculosis (CNS-TB) (ICD-10: A17) in the State of São Paulo, Brazil, and the levels of vaccination by Bacillus Calmette-Guérin (BCG).

Methods: The temporal analysis was based on the hospitalizations for CNS-TB in the State of São Paulo from January 2010 to November 2021, gathered from the Hospitals' Information System of the Unified Health System, and the information about BCG vaccination was collected from the Information System of the National Immunization Program. The statistical modelling was executed in gretl and Stata/MP 14.0 software. We used the X-13-ARIMA-SEATS tool to analyze hospitalizations and the Prais-Winsten regression to analyze vaccination coverage. We also checked the influence of decreasing BCG coverage on the dynamics of hospitalizations due to CNS-TB.

Results: The best ARIMA modeling was (0,1,1)x(0,1,1), showing a seasonal component of hospitalizations. The model proved to be more efficient than the naive prediction (MASE <1; Theil's U <1), it obtained an R^2 of 85% and a positive Portmanteau Q for residuals with white noise (Table 1). The trend of hospitalizations remains stable. However, vaccination coverage is decreasing (Table 2). Least squares regression showed that the drop in the vaccine coverage has not yet had a statistically significant impact on hospitalizations for CNS-TB.
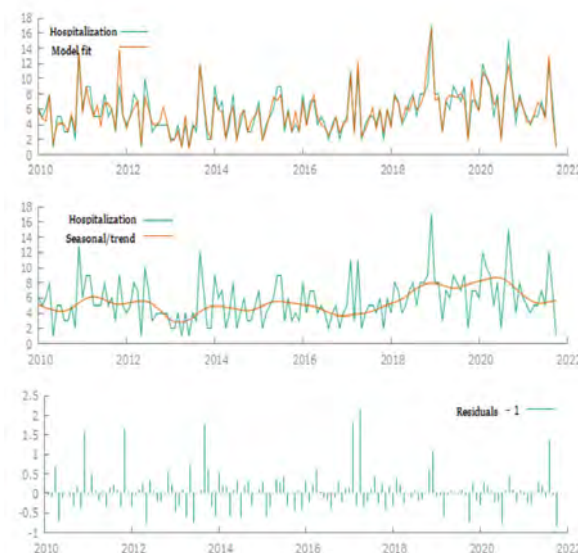
Table 1

Time series		Hospitalizations due to CNS-TB
Optimal model		$(0,1,1) \times (0,1,1)$
Goodness-of-fit	MASE	0.27
	RMSE	0.07
	R²	0.85
	Theil's U	0.29
	AIC	665.8381
	BIC	674.4176
	Portmanteau (Q)	0.8019

*MASE: mean absolute scaled error; RMSE: root mean square error; AIC: Akaike information criterion; BIC: Bayesian information criterion.

Table 2: Adjustment of the X-13 ARIMA model to analyze the historical series of hospitalizations due to CNS-TB in São Paulo over the last decade

Table 2: Adjustment of the X-13 ARIMA model to analyze the historical series of hospitalizations due to CNS-TB in São Paulo over the last decade

Prais-Winsten AR(1) regression		
β		-0.021
SD		0.008
p-value		0.031
Average annual increment (%)		-0.046
CI95%	LL	-0.085
	UL	-0.006
R²		0.976
Interpretation		Decreasing

Table 2: Analysis of the time series of BCG vaccination in São Paulo over the last decade

Table 3: Analysis of the time series of BCG vaccination in São Paulo over the last decade

Conclusion: Although hospitalizations for CNS-TB have been stable in this period, other infectious diseases suggest that the drop in vaccination may lead to an increase in hospitalizations.

Disclosure: Nothing to disclose.

EPO-587

Optic neuropathy secondary to Herpes Zoster virus

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Background and aims: Herpes Zoster Ophtalmicus is secondary to the reactivation of latent Varicella Zoster Virus (VZV) involving the ophtalmic branch of trigeminal nerve (V1). It has diverse presentations that include both anterior and posterior segment pathology. Herpes Zoster optic neuropathy (HZON) has been reported in 1.9% HZO-affected eyes.

Methods: A 62-years-old man, without relevant medical history, presented to the emergency department with left red eye symptoms and vesicules in left V1 territory. He was diagnosed of herpetic keratoconjunctivitis by ophtalmologist and started treatment with oral aciclovir and topical corticosteroids. One week later he was derivated to the neurologist because of left papilledema. Visual acuity was normal in both examinations.

Left herpetic vesicules in V1 territory

Results: Brain CT was normal. Cerebrospinal fluid (CSF) analysis: 131 leukocytes (98% lymphocytes), mild hyperproteinorrhachia (66.7mg/dl) without glucose consumption. Polymerase Chain Reaction (PCR) was positive to VZV. Orbital and brain MRI were normal. He completed 2 weeks of intravenous aciclovir without visual impairment.

Conclusion: HZON is a rare complication of HZO that may present either in papillitis or retrobulbar form and habitually occurs simultaneously with other ocular complications. It develops with a mean of 14 days after initial rash. Visual recovery is variable and MRI-restricted diffusion of the optic nerve can predict a poor recovery. In our case, there was an excellent visual outcome because of the fast

diagnosis of papilledema with positive PCR to VZV in CSF (which is exceptional). We remark the importance of the early diagnosis to start a prompt treatment with both systemic acyclovir and topical or systemic corticosteroids.
Disclosure: Nthing to disclose.

EPO-588

The intestinal epithelium is one of the loci where primary HIV occurs

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Background and aims: The intestinal epithelium is one of the loci where primary HIV occurs.
Methods: 746 children under the age of 18 were studied. The children were divided into 3 groups: the 1st group included 261 HIV-infected children with acute diarrhea, the 2nd group included 238 HIV-infected children without diarrhea, and the 3rd group included 247 children with acute diarrhea without HIV infection. The diagnosis was made on the basis of clinical, serological, bacteriological, immunological, virological research methods.
Results: Violation of the intestinal microbiocenosis was noted in all children of the 1st group, in 94.1% of the 2nd and in 88.7% of the 3rd group. Bacteroides spp., <1010cfu/g in most cases was observed in the 1st group, compared with the 1st group in the 2nd group by 1.5 times, and in the 3rd group 1.5 times less often (68, 6%, 57.9% and 38.8%, respectively, p<0.05). Indicators of Bifidobacterium spp. <109CFU/g, Lactobacillus spp.<107CFU/g and E. coli lac+ <107 CFU/g in comparable groups, there were no significant differences, only among the 1st and 3rd groups there were significant differences (p>0.05) .
Conclusion: In all HIV-infected children with acute diarrhea, a violation of the microbiocenosis of the intestine develops and profound changes are noted in the indicators of the obligate microflora.
Disclosure: Nothing to disclose.

EPO-589

Three-dose Pembrolizumab Treatment for Progressive Multifocal Leukoencephalopathy: a case report

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Background and aims: We report a case of Progressive Multifocal Leucoencephalopathy (PML) on a background of primary lymphopenia, treated with Pembrolizumab, a humanized monoclonal anti-programmed cell death protein 1 (PD-1) antibody.
Methods: A 67-year-old gentleman, previously independent, presented with rapid-worsening cognitive decline, bulbar weakness with severe dysarthria and dysphagia and marked upper and lower limb ataxia. His MRI-brain showed a confluent area of signal abnormality involving the posterior fossa structures, with marked low T1 signal, and without any mass effect, which were atypical for a neoplastic process. The patient received extensive diagnostic work up with CSF analysis including flow-cytometry. Paraneoplastic and autoimmune screen was negative in the CSF and bloods. He was found to be pan-lymphopenic attributed to a primary immunodeficiency. There was no lymphadenopathy or malignancy in the PET scan. Infective screen including HIV screen was negative. CSF was positive for JC-virus with low viral load (623 copies/ml).
Results: The patient continued to deteriorate despite prolonged treatment with steroids. To guide the diagnosis of PML, his CSF was tested for JCV antibodies, which were positive. The patient was diagnosed with PML and was treated with 3 doses of Pembrolizumab 1mg/kg with 6 weeks intervals. He had significant subjective and objective improvement 6 months in total after the first dose especially involving his finger-to-nose dysmetria and his dysarthria.
Conclusion: This is a case of PML in the context of idiopathic pan-lymphopaenia. Our results show that pembrolizumab is a promising treatment for PML and it should be further evaluated with randomised-controlled trials.
Disclosure: Nothing to disclose.

Miscellaneous 2

EPO-590

Neuroprotective Effect of L-Theanine against Tramadol Induced Parkinson's Like Symptoms in Experimental Rats

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Background and aims: Parkinson's disease (PD) is a chronic neurodegenerative disorder triggered by degeneration of dopaminergic neurons in substantia nigra pars compacta (SNpc).

Methods: Experimental procedure: The animals were divided into 7 groups. Group 1 served as Normal control. Group 2 received Tramadol (50 mg/kg, i.p.) daily for 28 days. Group 3, 4 and 5 received L-theanine (25, 50 and 100 mg/kg; p.o.) from 14 to 28 day prior to the tramadol administration. Group 6 received Sinemet [Levodopa and Carbidopa] (36 mg/kg; p.o.) from day 14 to day 28 prior to the tramadol administration. Group 7 received Naloxone (0.4mg/kg; i.p.) from day 14 to day 28 prior to the tramadol administration. Behavioral observations were done on 1, 7, 14, 21 and 28 day after tramadol treatment. On 29 day, animals were sacrificed and striatum was isolated for biochemical, neuroinflammation, histopathological and neurotransmitters analysis.

Results: Administration of tramadol (50 mg/ kg, i.p.) for 28 days in rats produces impaired motor functions and locomotor activity. In addition, there was increased oxidative stress (MDA, nitrite) and neuroinflammatory markers and decreased levels of catecholamines, GABA and glutamate. The treatment drug L-theanine at dose (25, 50, 100 mg/kg) significantly and dose- dependently improved alterations in motor impairments and locomotor activity, attenuated oxidative stress, neuroinflammatory markers and restored catecholamines, GABA and glutamate level in striatum

Conclusion: Chronic tramadol administration produces impaired motor functions, increased oxidative stress, neuroinflammation and altered neurotransmitters level was significantly ameliorated by L-theanine.

Disclosure: There is no any conflict of interests

EPO-591

Brainstem Raphe Hypoechogenicity is associated with Depressive Symptoms in Long-COVID Patients

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Background and aims: Long coronavirus disease (Long-COVID) syndrome is a poorly understood phenomenon with a range of symptoms, including depression and anxiety. Beforehand, depressive symptoms have been associated with brainstem raphe (BR) hypoechogenicity in transcranial sonography (TCS) which might reflect dysfunction of the serotonergic system. Primary aim of this study was to investigate an association of BR hypoechogenicity with depressive and anxiety symptoms in Long-COVID patients.

Methods: Using a cross-sectional study design, we included outpatients fulfilling the criteria of Long-COVID syndrome. All patients were examined for BR hypoechogenicity. Symptoms of anxiety and depression were investigated by the Hospital Anxiety and Depression Scale (HADS), with a cut-off of 8 points indicating relevant depressive or anxiety symptoms, respectively. Outcomes between hypoechogenic versus normoechogenic patients were compared using nonparametric tests. Predictor independence was assessed by an adjusted logistic regression model.

Results: We included n=70 patients with Long-COVID syndrome. 28.6% showed a BR hypoechogenicity in the TCS examination. Hypoechogenic patients scored higher in the subscores for anxiety (median 9 versus 6.5, p=0.006) and depression (median 8 versus 5.5, p=0.006) compared to normoechogenic patients. Adjusted OR for relevant depressive symptoms was higher among Long-COVID patients with hypoechogenic raphe (3.884, 95% CI 1.244 –12.123).

Conclusion: Compared to previous studies reporting the frequency of BR hypoechogenicity in patients with primary depression, this finding is less common in Long-COVID patients, but independently associated with depressive symptoms in this population. Further research should question whether this finding is a direct consequence or whether it reflects a higher susceptibility to depressive symptoms after COVID-19.

Disclosure: The authors report no relationships/activities/ interests related to this manuscript.

EPO-592

Brain Parenchyma Sonography is useful in identifying Parkinson's Disease in Essential Tremor patients: a case report

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Background and aims: Essential tremor (ET) is the most common cause of action tremor. ET patients have an increased risk of developing Parkinson's Disease (PD) during their lifetime. Single-photon emission computed tomography (SPECT) with DaT has high specificity and sensitivity, but in early stage of disease can be negative. Brain Parenchyma Sonography (BPS) have been shown to be a useful tool in detecting patients with ET who have developed or are at risk to develop PD.

Methods: Case report

Results: A female 76-years-old patient, suffering from ET from childhood developed tremor dominant PD, in the last year. Neurological examination revealed head and voice tremor, kinetic postural and rest tremor of upper limbs, greater on the left, bilateral bradykinesia and reduction of synkinesis. Dopaminergic treatment was started with resolution of bradykinesia and improvement of tremor at rest. Brain MRI showed only mild brain atrophy; a DaT SPECT was apparently normal; a BPS revealed a bilateral hyperechogenicity of the Substantia Nigra (SN, right 0,46 cm^2, left 0,33 cm^2) (Figures 1–2).

The butterfly-shaped hypoechogenic midbrain surrounded by the highly echogenic basal cisterns. Left acustic window. SN hyperechogenicity (0,33 cm^2)

Conclusion: The clinical presentation leaded to a diagnosis of PD, that is more frequent in long-standing ET. The DaT SPECT was apparently negative and seemed to exclude a consistent damage of DaT presynaptic basal ganglia receptors. BPS revealed SN hyperechogenicity, detectable in more than 90% of patients with PD or at risk to develop it but not in ET. BPS may be a sensitive non-invasive diagnostic tool in doubtful clinical cases or in early stages of PD, as in this case.

Disclosure: Nothing to disclose.

The butterfly-shaped hypoechogenic midbrain surrounded by the highly echogenic basal cisterns. Right acustic window. SN hyperchogenicity (0,46 cm^2)

EPO-593

Understanding Research Data Sharing and Use by Early-career Neurologists

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Background and aims: While responsible publishing of medical data sets is increasingly promoted, there is little empirical data regarding its adoption by Neurologists. We surveyed the European Academy of Neurology's (EAN) early career members in order to understand their motivations, training, and experiences with data-sharing and (re)use.

Methods: n=1,370 Resident and Research Fellows Section (RRFS) members were invited to participate in a Web-based survey, which included questions about publication-related data as well as research data management (RDM). n=142 participants (10.37%) answered at least one question.

Results: 125 respondents are ≤35 years old, indicating a long Neurological career ahead of them. 93 participants believe that data should be published along with publications and more than 80% believe that published data can help other researchers with designing experiments and validating outcomes (fig. 1). Despite these views, only about 30% have experience with sharing data and most of these have done so on publishers' portals (75%) or institutional servers (60%). Few researchers have received formal (10%) or informal (20%) training in research data management practices and fewer still are trained to reuse others' data (22%). 57% of the participants also reported having no institutional RDM support. While only 20% have shared their research data publicly, about 37% have downloaded public datasets, indicating a broader interest in using available data.

Figure 1. Data sharing - support and perceived value

Conclusion: Our findings demonstrate interest in data-related issues among RRFS members and a need to train and support early career neurologists so that they can engage in data-enabled research practices by publishing and reusing data.

EPO-594

The use of the Spinal Cord Independence Measure III interchangeably among rehabilitation professionals

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Background and aims: The Spinal Cord Independence Measure (SCIM) III has been reported its reliability in rehabilitation professionals who are responsible in a particular domain. With myriad components of the SCIM III items, the researchers also hypothesized that the outcomes would reflect essential components for independence of individuals with spinal cord injury (SCI). This study investigated the rater reliability of SCIM III among rehabilitation professionals, along with its concurrent validity as compared to standard measures covering wheelchair-bound (WB) and ambulatory (AM) individuals with SCI.

Methods: Participants (39 WB and 43 AM individuals) were assessed using SCIM III items. The data of 30 participants were video recorded for rater reliability assessments by rehabilitation professionals, including nurses, occupational therapists and physical therapists. All participants were also assessed using standard measures.

Results: The SCIM III showed excellent rater reliability when analysed for overall items (ICCs > 0.90) and separately for each subscale (kappa values > 0.80). The SCIM III scores of WB participants and the mobility scores of AM participants showed significant correlation with standard measures used to indicate muscle strength, limit of stability, balance control, functional endurance and walking ability of the participants (rs = 0.343 - 0.779; p < 0.05).

Conclusion: The present findings are important for current healthcare situations with limited hospital beds and in-patient services for individuals with SCI as they enable the use of SCIM III for community-based rehabilitation and home healthcare services that might not have all the professionals needed for a particular domain of the SCIM III.

EPO-595

Title: Acute lumbosacral radiculitis with myelitis related to recent herpes virus infection (Elsberg Syndrome)

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Background and aims: We report a 37-year-old female who presented to the emergency department with acute painful urinary retention, constipation, imbalance, and sensory loss in the perinium and lower limbs. There were no motor symptoms, rash or fever. One week prior she developed dysuria and ano-genital ulceration.

Methods: Neurological examination showed a T9 sensory level, impaired vibration and proprioception, clonus, upgoing plantars and brisk knee and ankle jerks bilaterally. Gynaecological exam showed ano-genital ulceration.

MRI thoracic spine T2 axial sequence demonstrating area of high signal in the central cord at the level of T10

MRI thoracic spine T2 sagittal sequence demonstrating area of high signal in the central cord at the level of T10

Results: Genital swabs were positive for herpes simplex virus type 2 (HSV-2). CSF showed a lymphocytic pleocytosis. CSF viral PCR was negative. MRI spine showed high T2 signal in the central cord in the lower thoracic spine around T10 level. Neurophysiology studies were normal. The patient met clinical definite criteria for a diagnosis of HSV-2-related Elsberg Syndrome and was treated with IV acyclovir for 21 days with almost complete resolution of pain and sensory loss but ongoing urinary retention requiring a long-term catheter.

Conclusion: Elsberg syndrome is an under-recognised syndrome commonly presenting with an acute lumbosacral radiculomyelitis with variable signs of spinal cord dysfunction and a CSF pleocytosis. It is most commonly associated with reactivation of HSV-2 from spinal ganglia or primary HSV-2 infection. Elsberg Syndrome can result in permanent neurological deficit and should therefore always be considered in the differential diagnosis of patients presenting with a cauda equina. If there is a clinical suspicion of Elsberg syndrome then treatment with acyclovir is recommended, even in the absence of definite intrathecal detection of the viral pathogen.

Disclosure: Nothing to disclose.

EPO-596

Prevalence of sleep disturbances following mild traumatic brain injury: a pilot cross-sectional survey.

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Background and aims: Patients who underwent a mild traumatic brain injury, or concussion, may present chronic symptoms such as headaches, attentional disorders or sleep disturbances that can last for months. While sleep is a key factor for recovery, it is still poorly investigated in the literature.

Methods: We developed an online survey to evaluate the prevalence of sleep disturbances in patients who had suffered from at least one concussion based on validated questionnaires (i.e., Pittsburgh Sleep Quality Index – PSQI & Epworth Sleepiness Scale – ESS). The Rivermead Post-Concussion Symptoms Questionnaire, demographic data and additional clinical information were also collected (e.g., number of concussions, concussion management, treatments).

Results: Out of 230 participants who started the survey, 89 (39%) completed it and their answers were analysed. 59/89 (66%) of respondents were women. 61% of respondents had a PSQI above 5 and 33% a ESS above 10, corresponding to the presence of sleep disturbances and daytime sleepiness. 58% of respondents reported one concussion, 24% two, 11% three and 7% more than 3 concussions; 17% had their (last) concussion less than a year ago and 83% between one and five years. The main post-concussion symptoms were sleep disturbances (61%), troubles to stay focused (54%), light sensitivity (48%), irritability (47%), headaches (42%), and memory impairments (42%). 57% received pharmacological treatments and 25% non-pharmacological interventions (e.g., neuropsychology) following their concussion.

Conclusion: This preliminary data highlights a majority proportion of self-reported sleep disturbances in concussed patients. Prospective longitudinal studies should be conducted to confirm this finding and optimize patients' management.

Disclosure: Nothing to disclose.

EPO-597

Brain infarction in a young patient associated to a vertebral artery fenestration

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Background and aims: Fenestration is a congenital abnormality, frequently asymptomatic, of the vessels and consists of a division of the vessel into parallel segments which end up re-emerging in one. It is supposed to be caused due to a malformation during embryogenesis. We discuss a case of a 43 years-old woman with a stroke associated to a contralateral vertebral artery (VA) fenestration

Methods: 43 years-old female, with history of hypertension, a single episode of lupus mediated nephropathy and practice of kickboxing and weight-lifting on a regular basis, was admitted to the Emergency room due to symptoms and signs of stroke in the vertebrobasilar territory: multidirectional nystagmus, hypophonia, soft palatal deviation, and XII nerve palsy.
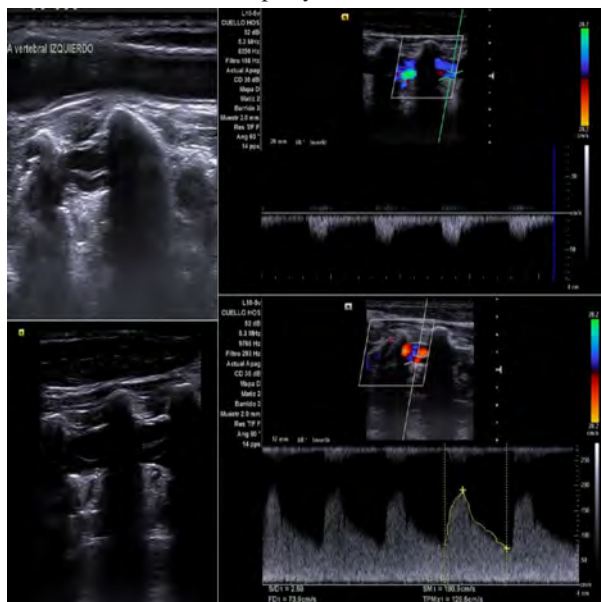
Ultrasound view of VA fenestration

Results: Urgent brain-CT showed a hyperdense right VA and the angio-CT showed a defect in the right VA, identifying it as an occlusion, and contralateral VA double lumina. The vertebrobasilar duplex showed an intimal flap in V2 segment suggestive of left VA dissection and occlusion of the right VA, the echocardiography, a patent foramen ovale (PFO).The patient was diagnosed with right laterobulbar infarction due to a dissection of the right VA and, furthermore, an asymptomatic dissection of the left VA. The six-months angio-CT and duplex showed the same abnormalities in the left VA, which was not compatible with the usual outcome of an arterial dissection. The patient was finally diagnosed with left VA fenestration.
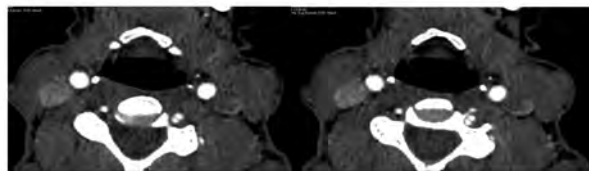
Angio-CT VA fenestration

Conclusion: The differential diagnosis between VA dissection and fenestration may be challenging, especially in the emergency room.
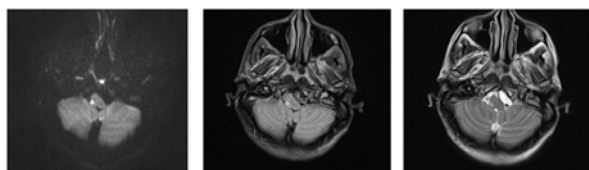
Brain MRI laterobulbarinfarction

Disclosure: Nothing to disclose.

EPO-598

Withdrawal of life-sustaining treatment in ALS patients: a Multicenter Italian Survey

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Background and aims: In Italy, recent significant juridical and social developments led to the entry into force of Law 219/2017, providing possibility of life-sustaining treatment suspension. However, no practical guidelines about life-sustaining treatment suspension are available in Italy.

Methods: To investigate the current status in Italy of clinical management for life-sustaining treatment suspension in ALS patients and to evaluate the impact of Law 2017/219 on italian Neurologists involvement and Advanced Care Planning (ACP) discussion in ALS patients.

Results: 38 forms were completed, from 33 Italian ALS Centers. Results of the present Survey show that the entry into force of Law 219 was followed by an increase of vital treatment suspension, percentage of DAT discussion and Neurologists involvement in this procedure. However, we also noticed an extreme variability in some aspects of practical management of the procedure, particularly concerning timing, Health professionals involved and Palliative Care Service participation.

Conclusion: The present Survey shows that the entry into force of Law 219 resulted in a higher frequency of invasive ventilation treatment suspension, a more consistent involvement of Neurologists in the procedure and an increase in frequency of ACP discussion. However, decisional steps, Health professionals and PCS involvement were variable

Disclosure: The authors have nothing to disclose.

EPO-599

CYGNET: A Prospective Multicenter Observational Study of Disease Progression in Patients with Adrenomyeloneuropathy

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Background and aims: Adrenomyeloneuropathy (AMN) is the spinal cord disease of adults with the rare disease Adrenoleukodystrophy (ALD), characterized by a predominately progressive dying-back axonopathy leading to lifelong disability. Symptoms include progressive stiffness and leg weakness, impaired vibration sensation, and bowel and bladder disturbances. There are no approved treatment options available. The natural history of AMN is poorly understood. Substantial phenotypic and individual variability makes quantifying disease progression during a clinical trial challenging. One solution to address this variability is to instrument traditional functional motor tasks (TFTs) using technology such as wireless motion sensors in order to characterize disease progression and define clinical relevance for the outcome measures in the AMN population.

Methods: The study (NCT05008874) will enroll approximately 80 patients with AMN who will be followed for a minimum of two years with annual clinic visits and quarterly remote visits.

Results: Gait and balance assessments will include postural body sway parameters, TFTs such as 2- and 6-minute walk tests, Timed-Up-and-Go, and 5 times sit to stand. Wireless motion sensors will allow quantification of the temporal–spatial components of gait assessments such as stride velocity, stride length, and trunk range of motion. The clinical relevance of TFTs in AMN will also be assessed using patient-reported outcome measures. Baseline characteristics for the first 20 patients will be presented.

Conclusion: This ongoing study is designed to obtain a better understanding of AMN's natural history and disease progression, and to inform upon the design of future clinical trials of potential therapeutics, including gene therapy, for AMN.

Disclosure: This study is sponsored by SwanBio Therapeutics.

EPO-600

Patient-centered migraine treatment options: clinical personas models using data clustering

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Background and aims: Patient compliance is the key to successful treatment of most chronic conditions, such as migraine. Currently, there are a lot of prophylactic options, each of which has benefits and disadvantages that can influence the patient's willingness to continue treatment. In this study we attempt to group patients based on personal features related to migraine. This study is a framework for designing a more patient-centered migraine treatment approach.

Methods: 212 patients were assessed using a questionnaire consisting of 28 questions regarding their habits, lifestyle, previous compliance history, etc. In addition, 7 questions from HADS anxiety subscale and 21 questions from Beck's depression inventory were included to screen for mental health abnormalities. Divisive data clustering was performed in RStudio. A focus group of neurologists (n=10) was conducted to assess clinicians' perspective.
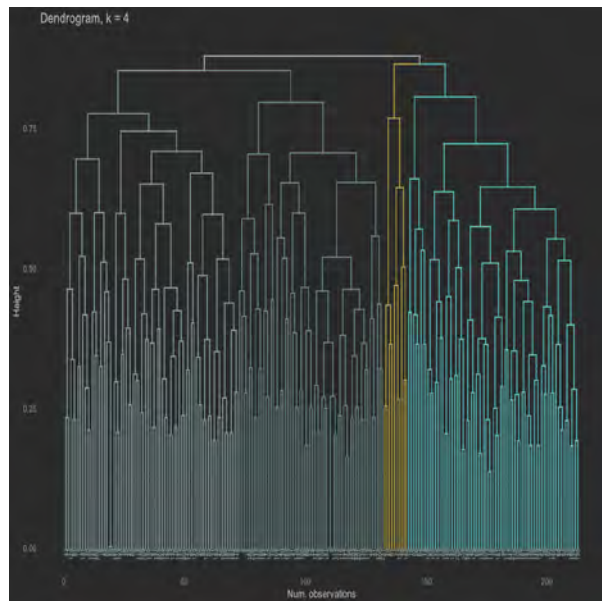
Determining the optimal number of clusters: the 'elbow' method

Results: Four distinct clusters were identified, with the following characteristics of the patients (on average): (1) male, overweight, have mild anxiety and depression scores, poor sleep routine and spend more than 8 hours using a computer; (2) female, younger, normal both on HADS and Beck's scales, most incompliant, most educated and hold leadership positions; (3) abnormal HADS scores, as well as very irregular sleep patterns, also the highest Beck's scores. (4) little to no anxiety and depression symptoms, most compliant; The existence of these groups is confirmed by the results of the focus group, however, clinicians tend to distinguish more groups.
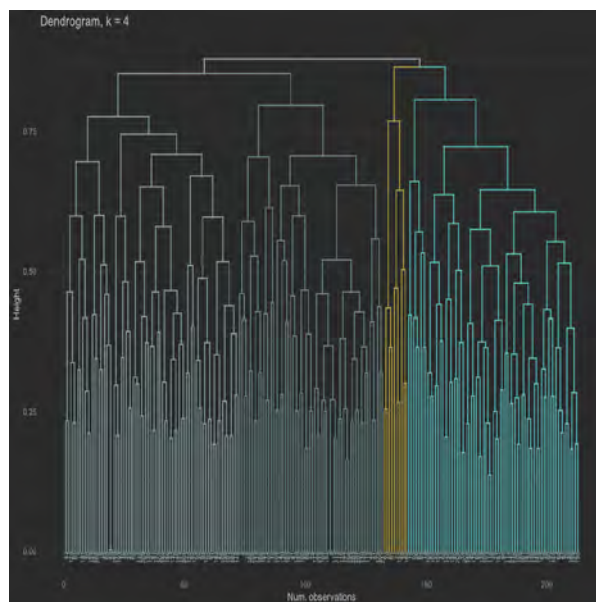
Dendrogram depicting the clusters
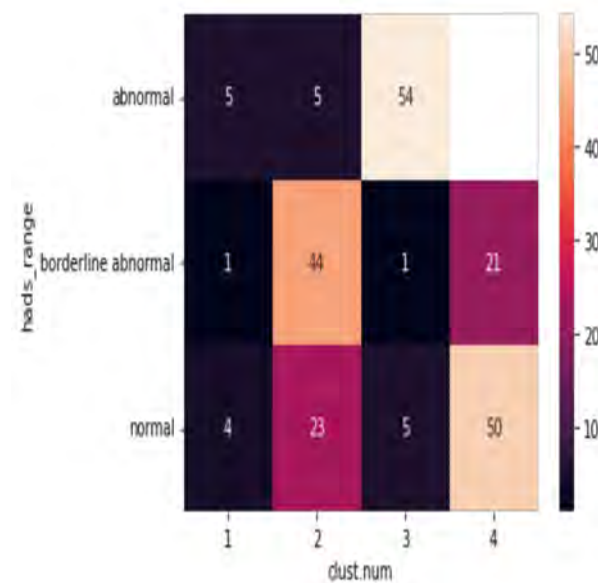
A heatmap plot illustrating the distribution in HADS anxiety subscale scores between clusters

Conclusion: The consideration of described differences could prove to be useful for more personalized prophylaxis prescribing.
Disclosure: Nothing to disclose.

EPO-601

Minding the skin examination in an unusual case of progressive spastic paraparesis

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Background and aims: The differential diagnosis of an adult patient with progressive spastic paraparesis is wide, requiring extensive investigation. It is often secondary to a myelopathy.

Methods: Clinical Case

Results: A 42-year-old male, with unremarkable personal or family background, presented to a Neurology Outpatient Clinic with one-year progressive asymmetric bilateral lower limb weakness, starting in the right and progressing to the left in months, leading to increasing disability. He denied sensory complaints, pain, sphincter, and sexual dysfunction. Upon examination, spastic paraparesis (grade 4 in the MRC scale) with bilateral lower limb hyperreflexia and Babinski sign were observed. He also had right upper limb hyperreflexia. He had a right cervical painless mass and occasional cutaneous nodular lesions in the neck, thorax, and dorsum. «Café-au-lait» macules (≈5) were identified in the armpits and lower limbs. Given the possible spinal cord involvement, a neuroaxis magnetic resonance imaging was performed, displaying multiple spinal root plexiform neurofibromas, mainly at a cervical and lumbar level, causing spinal cord compression at C2 and C6. Due to progressive worsening, both lesions were surgically removed. Genetic testing confirmed the likely diagnosis of neurofibromatosis type 1 (NF1).

Conclusion: NF1 is a genetic autosomal dominant disorder, often recognised by an early cutaneous presentation. These manifestations were scarce in our patient and the diagnosis was performed due to progressive spastic paraparesis resulting from a severe nervous system involvement. NF1 should be considered in the workup of an adult with progressive spastic paraparesis, and skin examination can provide details that allow an early diagnosis and intervention.

Disclosure: Nothing to disclose.

EPO-602

Health professional involvement in the formulation of the clinical questions: the Guideline on PC in Adults with Glioma

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Background and aims: In 2017, the European Association for Neuro-Oncology (EANO) published the guideline for palliative care (PC) in adults with glioma. The Italian Society of Neurology (SIN), the Italian Association for Neuro-Oncology (AINO), and the Italian Society for Palliative Care (SICP) joined forces to update the guideline, and adapt it to the Italian context. To obtain this, we involved patients, caregivers and health professionals (HPs) in the formulation of the clinical questions.

Methods: Online survey of HPs experienced in the care of patients with glioma. HPs rated the importance of 10 pre-specified intervention topics on a 0/10 scale, and gave their free comments.

Results: Of 244 participants, 149 (61%) were PC HPs and 95 other HPs. Their mean age was 48.9 years, 63% were women, and 48% had over 12 years of experience in the care of glioma patients. Physicians were 68%, followed by nurses (28%), psychologists (7%), therapists (3%), and social workers (2%). All HPs rated each pre-specified intervention topic as important (score ≥7) or critical (score ≥9). The proportion of PC HPs rating the topic as critical was significantly higher for six: spiritual/existential support, advance care planning, end-of-life, bereavement, HP psychological support, and HP training in PC. There were 43 free comments: 25 (58%) on 9 of the pre-specified topics, and 18 on 5 new topics.

Conclusion: Participation in the survey was high, and information-rich. The differences between the two HPs groups in scoring reflect their background. These data will inform the formulation of the guideline clinical questions.

Disclosure: Nothing to disclose.

EPO-603

Automatic thresholding methods for muscle ultrasound evaluation in amyotrophic lateral sclerosis: a pilot study

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Background and aims: Neuromuscular ultrasound (NMUS) is an increasingly implemented technique for early diagnosis and long-term monitoring of patients with amyotrophic lateral sclerosis (ALS). Objective of this pilot study was to investigate feasibility of automatic thresholding methods when quantifying muscle echogenicity in ALS.

Methods: 15 patients diagnosed with ALS and 15 sex-, age- and body mass- matched healthy controls were assessed by ultrasound imaging of biceps brachii, rectus femoris and tibialis anterior muscles. A manually drawn region of interest was studied by grayscale histogram analysis and automated thresholding. The 17 thresholding methods implemented in ImageJ (Default, Huang, Intermodes, IsoData, IJ_IsoData, Li, MaxEntropy, Mean, MinError, Minimum, Moments, Otsu, Percentile, RenyiEntropy, Shanbhag, Triangle and Yen) were applied in each image. Mean hyperechoic fraction and mean grayscale value were compared as echogenicity parameters between patients and controls. Correlation between hyperechoic fraction and Medical Research Council (MRC) muscle strength score was calculated in patients.
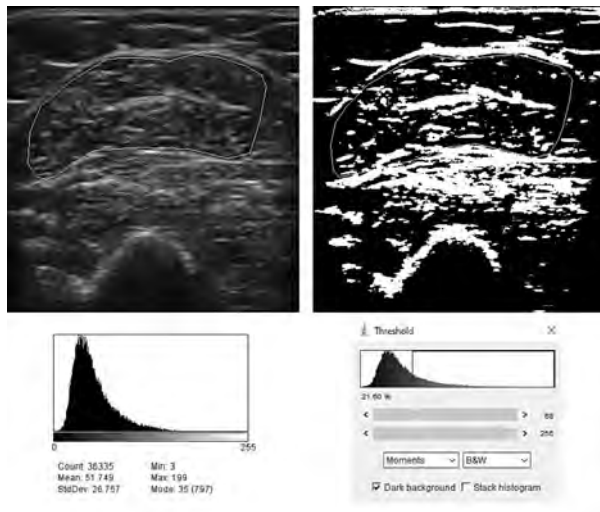
Ultrasound imaging of biceps brachii in a 60-year-old female ALS patient. Grayscale analysis of the acquired image (left) and automatic thresholding with the 'Moments' method (right), applied in a manually drawn region of interest.

Results: Statistically significant difference between patients aesults: Statistically significant difference between patients and healthy controls was shown in grayscale analysis (p<0.05) and 10 of 17 automatic thresholding methods (p<0.05). Mean hyperechoic fraction of IsoData, Li, Moments and Otsu methods were significantly different in all evaluated muscle groups between ALS patients and healthy subjects. Moments was the only method of echogenicity evaluation that correlated significantly with MRC score in all muscles (p<0.05).

Mean hyperechoic fraction ± SD	Biceps brachii		p-value	Rectus femoris		p-value	Tibialis anterior		p-value
Default	29.11 (±4.81)	20.40 (±6.44)	0.000	31.21 (±6.57)	27.07 (±4.65)	0.056	36.05 (±6.20)	28.95 (±3.23)	0.001
Huang	43.41 (±2.95)	34.91 (±6.37)	0.000	40.73 (±4.44)	39.89 (±3.66)	0.436	43.96 (±3.33)	41.09 (±2.58)	0.013
Intermodes	N/A	N/A		N/A	N/A		N/A	N/A	
IsoData	27.95 (±4.85)	19.51 (±6.27)	0.000	30.14 (±6.81)	25.47 (±4.65)	0.037	34.83 (±6.56)	27.65 (±3.34)	0.001
IJ_IsoData	29.24 (±4.86)	20.40 (±6.44)	0.000	31.21 (±6.57)	27.07 (±4.65)	0.056	36.05 (±6.20)	28.94 (±3.23)	0.000
Li	35.86 (±4.33)	27.91 (±5.87)	0.000	36.09 (±5.58)	32.29 (±4.07)	0.043	40.91 (±5.09)	35.25 (±2.98)	0.001
MaxEntropy	5.67 (±3.43)	5.88 (±2.64)	0.849	7.96 (±4.90)	7.17 (±3.23)	0.607	6.33 (±5.25)	4.62 (±2.25)	0.512
Mean	41.45 (±1.76)	37.63 (±2.46)	0.000	42.04 (±2.51)	40.46 (±1.97)	0.065	43.87 (±2.83)	41.12 (±1.19)	0.002
MinError	N/A	N/A		N/A	N/A		N/A	N/A	
Minimum	N/A	N/A		N/A	N/A		N/A	N/A	
Moments	23.05 (±5.01)	16.72 (±3.20)	0.000	27.46 (±6.11)	22.53 (±3.92)	0.014	29.26 (±6.32)	22.90 (±2.00)	0.001
Otsu	26.92 (±4.86)	19.17 (±6.32)	0.000	29.24 (±6.47)	24.44 (±4.53)	0.026	33.40 (±5.80)	26.59 (±2.91)	0.000
Percentile	49.92 (±0.55)	50.00 (±0.64)	0.567	50.11 (±0.46)	49.82 (±0.53)	0.116	50.11 (±0.46)	49.90 (±0.51)	0.239
RenyiEntropy	7.30 (±3.99)	6.78 (±3.10)	0.697	10.91 (±6.38)	8.17 (±3.67)	0.161	7.05 (±5.60)	5.21 (±2.32)	0.486
Shanbhag	30.34 (±6.65)	14.75 (±9.29)	0.000	31.22 (±6.96)	27.73 (±6.11)	0.155	35.83 (±6.07)	29.63 (±3.95)	0.003
Triangle	8.12 (±2.18)	9.60 (±2.99)	0.133	11.07 (±3.74)	10.23 (±4.05)	0.559	5.13 (±2.58)	7.43 (±3.35)	0.044
Yen	7.10 (±4.66)	6.81 (±3.25)	0.846	10.12 (±6.17)	7.98 (±4.12)	0.274	6.84 (±5.44)	5.11 (±2.53)	0.436
Mean grayscale value	57.96 (±7.80)	43.10 (±6.21)	0.000	70.55 (±10.23)	58.64 (±8.05)	0.001	64.42 (±14.20)	54.91 (±6.46)	0.025

SD: Standard Deviation, N/A: not applicable

Table: Mean hyperechoic fraction and mean grayscale value measurements of ALS patients and healthy controls in the three scanned muscle groups.

Conclusion: Muscle echogenicity assessment using automatic thresholding methods is an objective, measurable and easy to perform technique for the investigation of motor neuron disease.

Disclosure: Nothing to disclose.

EPO-604

Effect of serotonin antagonists on an experimental serotonin syndrome model: comparing asenapine and cyproheptadine

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Background and aims: Serotonin syndrome (serotonin toxicity) is a clinical condition that occurs as a result of a drug-induced increase in intrasynaptic serotonin levels. In the mechanism of SS development, 5-HT1A and 5-HT2A receptors are thought to play a key role in both animals and humans, mediating most of the manifestations. Hyperthermia and its inadequate treatment are the most common causes of life-threatening forms of SS. The aim of the present study is to investigate the effect of the atypical antipsychotic asenapine classified as a multi-acting receptor-targeted antipsychotic and to compare its effect with cyproheptadine acting only as a 5-HT2 receptor antagonist on the development of SS in an experimental rat model.

Methods: An experimental model of serotonin syndrome was induced by co-administration of fluoxetine and tranylcypromine, injected intraperitoneally in male Wistar rats. Their body temperature was measured rectally, at intervals. Specific behavioral and autonomic manifestations of serotonin syndrome were observed.

Results: In the experimental model examined, administration of fluoxetine and tranylcypromine caused development of hyperthermia (Fig. 1). Pretreatment with asenapine and cyproheptadine not only inhibited the development of the hyperthermic reaction but also reversed the thermal response to hypothermic (Fig.2). The hypothermic response was more pronounced with asenapine pretreatment.

▲ fluoxetine (10 mg/kg i.p.) + tranylcypromine (3.5 mg/kg i.p.)

◆ 0.9% NaCl (control)
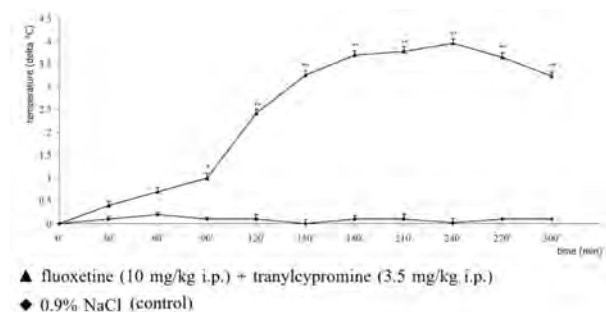
Figure 1: Change in body temperature in a serotonin syndrome model induced by co-administration of fluoxetine and tranylcypromine.

▲ asenapine (0.6 mg/kg i.p.) + fluoxetine (10 mg/kg i.p.) + tranylcypromine (3.5 mg/kg i.p.)

■ cyproheptadine (10 mg/kg i.p.) + fluoxetine (10 mg/kg i.p.) + tranylcypromine (3.5 mg/kg i.p.)
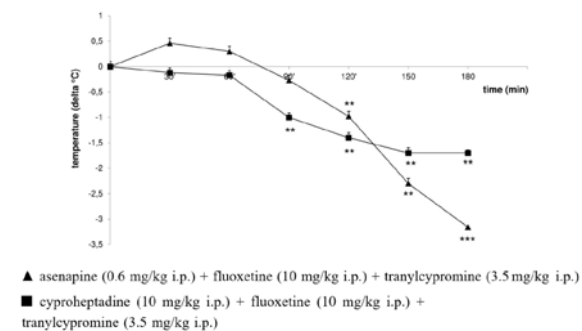
Figure 2: Effect of asenapine and cyproheptadine on the hyperthermic response in a serotonin syndrome model induced by co-administration of fluoxetine and tranylcypromine.

Conclusion: Our study found that asenapine and cyproheptadine effectively attenuated the hyperthermic response. The more pronounced hypothermic response observed with the asenapine pretreatment may be explained with its more complex pharmacodynamic profile, indicating a possible involvement of other receptors in maintaining thermoregulation.

Disclosure: This work is supported by the Bulgarian Ministry of Education and Science under National Program for Research "Young Scientists and Postdoctoral Students".

Movement disorders 5

EPO-605

Insertion of interphase gaps in symmetric biphasic pulses decreases the therapeutic window in Vim-DBS Introduction

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Background and aims: Symmetric biphasic pulses enlarge the therapeutic window in deep brain stimulation (DBS) in patients with essential tremor (ET)1. Animal studies have shown that an interphase gap can decrease the current needed to elicit action potentials[2].

Methods: 9 patients (16 hemispheres) were included in this study. Biphasic pulses (anodic phase first) with interphase gaps of 0, 10, 20, 50 and 100 μsec were tested, in a random order (Figure 1). The outcome parameters were the therapeutic threshold (TT) and side effect threshold (SET). The difference between the SET and TT is the therapeutic window (TW; Figure 2). The TT was the minimal amplitude needed to elicit tremor arrest. The lowest amplitude at which a permanent side effect was reported (e.g. muscle contraction), was the SET. All pulses were tested three times. Stimulation of the non-tested hemisphere was turned off. Patient and evaluator were blinded.
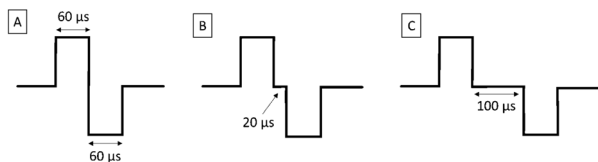
(A) Biphasic pulse with anodic-phase first. Both phases have a pulse width of 60 μsec. (B) Interphase gap of 20 μsec. (C) Interphase gap of 100 μsec. In the experimental setup interphase gaps of 10 and 50 μsec were tested as well.
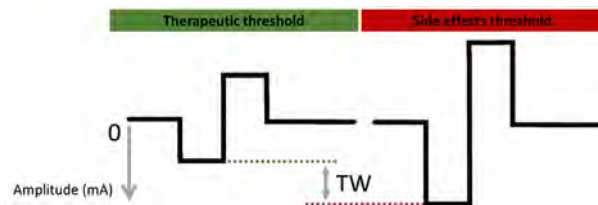
Visualization of the therapeutic window, defined as the difference between therapeutic threshold and side effect threshold.

Results: Both the TT and the SET were lowered by an increasing interphase gap (linear mixed-effects model), with the decrease of the SET being more pronounced than the TT, leading to smaller therapeutic windows for longer interphase gaps (Figure 3).
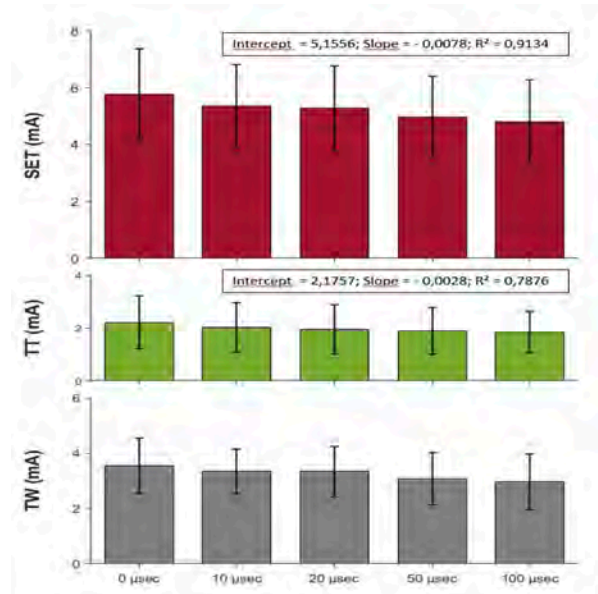
Bar graph showing on the x-axis the different interphase gaps tested. Red bars represent the corresponding SET in milliamperes (mA). Green bars show the TT in mA. Grey bars represent the TW in mA. Error bars represent mean ± standard deviation.

Conclusion: Introducing an interphase gap in a symmetric biphasic pulse lowered the SET more profoundly than the TT, leading to smaller therapeutic windows. This exploratory study highlights that the interphase gap influences target fibers (therapeutic threshold) differently than non-target fibers (side effect threshold). Thus, initial results indicate that to maintain a larger therapeutic window biphasic pulse with a zero interphase gap are optimal.

Disclosure: A. Boogers has received consultancy fees from Abbott. P. De Vloo received a grant from the Helaers Foundation. Bart Nuttin holds the Chair Neuromodulation an endowment from Medtronic, and Boston Scientific Chair Neuromodulation for Stroke.

EPO-606

Effects of opicapone in Parkinson disease as assessed by kinematic techniques

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Background and aims: By increasing L-dopa bioavailability, catechol-O-methyl transferase inhibitors are currently used as first-line add-on therapy to L-dopa to treat end-of-dose motor fluctuations in Parkinson's disease (PD) advanced stages. Here we objectively investigated the effects of Opicapone on bradykinesia in PD by kinematic analysis.

Methods: We studied 13 patients with PD and motor fluctuations being treated with dopaminergic drugs. Bradykinesia was measured by recording repetitive finger tapping. Patients were tested in two separate and randomized sessions (with and without Opicapone), at least one week apart. In each session, patients were assessed before and after their usual L-dopa morning dose (and the motor performance was followed up to 3.30 hours after L-dopa intake). Data were analyzed by analysis of variance (ANOVA) using the factor SIDE (two levels: more vs. less affected), SESSION (two levels: without vs. with Opicapone), and TIME POINT (four levels: baseline, 30 min, 1 hour and 30 min and 3 hours and 30 min after L-dopa intake).

Results: inger tapping velocity and amplitude were lower in patients without Opicapone than in patients with Opicapone [$F(1,12)=9.11$, $p=0.01$ and $F(1,12)=4.91$, $p=0.04$, respectively]. Opicapone intake, however, did not modify the sequence effect. Finally, as expected, we observed velocity and amplitude improvement related to L-dopa (both $ps<0.05$) while no changes of the sequence effect.

Conclusion: We provided the first objective assessment of Opicapone effects on bradykinesia in PD. The study results confirm that bradykinesia features (i.e., velocity, amplitude, and sequence effect) have different sensitivity to change after administration of dopaminergic drugs.

Disclosure: Nothing to disclose.

EPO-607

Safinamide as add-on to low doses of levodopa in non-advanced Parkinson disease

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Background and aims: A review of 75 patients with Parkinson disease is made in general neurology appoinment, in order to assess the stability and even reduction of levodopa dose established in the patient by combining with a new MAOB-I, as Safinamide.

Methods: 75 patients with H&Y stage II Parkinson disease (50 males and 25 women) between 55 and 80 years with a clinical follow-up of 3 to 36 months are analyzed to assess the need for levodopa dose adjustment in their treatment or the need to add another adjuvant therapy after add safinamide at doses of 50 or 100 mg.

Results: In all patients, in the review carried out, we did not have the need to increase the doses of levodopa with which patients are found before administering safinamide, neither was it required to add another adjuvant therapy type Dopaminergic agonist therapy or ICOMT. Even in 23 patients, the dose of levodopa is reduced due to the improvement in clinical motor and non-motor and so we consider this decrease as a long-term clinical benefit.

Conclusion: By administration Safinamide in the treatment of patients with non-advanced PD we can benefit from not having to increase the doses of levodopa previously scheduled and thus avoid secondary motor complications. Even the reduction in levodopa doses in some patients give us clinical control stability of motor symptoms in these patients.

Disclosure: Safinamide is a safe and well-tolerated drug, and by using it together with ldopa from the early stages of the disease, the patient can benefit greatly, as well as saving ldopa and resources, which we can use in more advanced stages of the disease.

EPO-608

Long-term efficacy of segmented and non-segmented leads for subthalamic deep brain stimulation in Parkinson's disease

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Background and aims: Deep brain stimulation (DBS) of the subthalamic nucleus (STN) is an established treatment for Parkinson's disease (PD). Recently commercialized segmented electrodes enable directional current steering and broaden the therapeutic window. This study compares the efficacy of segmented and non-segmented leads in motor symptom alleviation in PD patients undergoing STN-DBS.

Methods: Medical records of all PD patients implanted with segmented leads for STN-DBS at our centre between 02/2016 and 12/2019 (Boston Scientific) were collected. Demographic data, motor scores before surgery and at 12-month follow-up (12MFU) as well as stimulation parameters at 12MFU were assessed and compared with patients who received non-segmented leads (01/2015 to 12/2019; Medtronic and Boston Scientific). Directional current steering corresponded to an asymmetrical activation of the segmented contacts (min. 5% mismatch).

Results: Motor scores at 12MFU were available for 63/96 and 30/41 patients implanted with segmented and non-segmented leads, respectively. DBS-induced improvement in motor scores (OFF-DBS_OFF-Medication vs. ON-DBS_OFF-Medication) did not differ between groups (segmented 45.27% vs. non-segmented 44.74%, t-test p=0,9). One-way ANOVA comparing mean improvement in UPDRS-III revealed no significant difference between directional segmented (n=34; 41.86%), non-directional segmented (n=29; 49.27%) and non-segmented groups (n=30; p=0.4). There was a lower proportion of poor responders (improvement <30%) in the segmented group comparing with the non-segmented group (23.8% vs. 30%).

Conclusion: Segmented and non-segmented electrodes demonstrate comparable efficacy in motor symptom alleviation in PD patients undergoing STN-DBS. Even though the use of segmented leads accounted for a reduced number of poor responders, superiority of directional steering against ring-mode stimulation could not be shown.

Disclosure: Ana Luísa de A. Marcelino is supported by the BIH-Charité Clinician Scientist Program funded by the Charité-Universitätsmedizin Berlin and the Berlin Institute of Health. Andrea Kühn is on the Advisory Board of Medtronic and Boston Scientific.

EPO-609

Dyskinesia Signs and Symptoms, and Quality of Life in Parkinson's Disease: Post Hoc Analysis From the DYSCOVER Study

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Background and aims: This study assesses correlations of "On" time without troublesome dyskinesia (TSD) and dyskinesia with health-related quality of life (HRQoL), activities of daily living (ADL), and Clinical Global Impression of Severity (CGI-S) and Change (CGI-C) among patients with advanced Parkinson's disease (aPD).

Methods: In the phase 3b, multicenter, randomized, open-label DYSCOVER (DYSkinesia COmparative interventional trial on Duodopa VERsus oral medication) study (NCT02799381), patients with levodopa-responsive aPD and a Unified Dyskinesia Rating Scale (UDysRS) Total Score ≥30 received 12 weeks of optimized medical treatment or levodopa-carbidopa intestinal gel (randomized 1:1). This post hoc analysis combines data from both groups using Pearson correlation coefficients for baseline and change to week 12.

Results: Among patients (n=60), there were significant moderate positive correlations between UDysRS and HRQoL (8-item Parkinson's Disease Questionnaire [PDQ-8]), ADL (Unified Parkinson's Disease Rating Scale part II [UPDRS II]), CGI-S (baseline), and CGI-C (week 12) at baseline and for change to week 12 (Table). There were significant moderate negative correlations between changes to week 12 in "On" time without TSD and PDQ-8, UPDRS II, and CGI-C, and a weak negative correlation with PDQ-8 at baseline. Baseline "On" time without TSD was not correlated with baseline UPDRS II or CGI-S. All change from baseline correlations were stronger than baseline correlations. Safety was consistent with the established LCIG safety profile, as reported previously.

Correlations Between Dyskinesia Signs and Symptoms, and HRQoL, ADL, CGI-S and CGI-C

Variables	Pearson Correlation Coefficient (P Value)	
	Baseline	Change From Baseline at Week 12
UDysRS and PDQ-8	0.4548 (<.001)***	0.5401 (<.001)***
UDysRS and UPDRS II	0.4469 (<.001)***	0.5713 (<.001)***
UDysRS and CGI-S	0.4076 (.001)**	—
UDysRS and CGI-C	—	0.4700 (<.001)***
"On" time without TSD and PDQ-8	−0.3159 (0.016)*	−0.4976 (<.001)***
"On" time without TSD and UPDRS II	0.0066 (0.961)	−0.4484 (<.001)***
"On" time without TSD and CGI-S	−0.0602 (0.653)	—
"On" time without TSD and CGI-C	—	−0.5235 (<.001)***

Shading indicates correlations that are statistically significant and weak (light green), or moderate (medium green).

Significance level: ***P <.001; **P<.01; *P<.05.

ADL, activities of daily living; CGI-C, Clinical Global Impression of Change; CGI-S, Clinical Global Impression of Severity; HRQoL, health-related quality of life; PDQ-8, 8-item Parkinson's Disease Questionnaire; TSD, troublesome dyskinesia; UDysRS, Unified Dyskinesia Rating Scale; UPDRS II, Unified Parkinson's Disease Rating Scale part II.

Correlations Between Dyskinesia Signs and Symptoms, and HRQoL, ADL, CGI-S and CGI-C

Conclusion: Dyskinesia signs/symptoms were moderately correlated with ADL, HRQoL, and CGI, while "On" time without TSD was mostly negatively correlated, indicating a relevant impact on patients with high dyskinesia burden.

Disclosure: AbbVie funded the research for this study and provided writing support for this abstract. No honoraria or payments were made for authorship. Medical writing assistance, funded by AbbVie, was provided by Alicia Salinero, PhD, CMPP, of JB Ashtin.

EPO-610

Effects of Dopamine and Motivation on Motor and Cognitive control

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Background and aims: Fine-tuning dopaminergic tone is crucial for managing movement disorders while also mitigating neuropsychiatric consequences. Impulsivity and reward hypersensitivity have been associated with ventral striatal D2 receptor (D2R) stimulation inhibiting the "no-go pathway", the pathway that suppresses undesirable actions triggered by the environment. However, D2Rs, also inhibit dopaminergic reward signalling. Here we measured rewarded eye movements to quantify effects of motivation on motor and cognitive control, and how they are altered in different dopaminergic states.

Methods: 30 healthy participants received a single dose of Levodopa, Haloperidol or Placebo. They had to move their eyes towards a target, while ignoring a salient distractor. Crucially, auditory cues announced the reward available. On reaching the target they received reward depending on speed and accuracy.

Results: As expected, motivation improved speed and accuracy. Haloperidol increased distractibility, demonstrating impaired cognitive control. This resulted from faster reaction times, indicating early, error-prone responses. Levodopa reduced error rate without slowing reaction time, indicating a true cognitive improvement. Surprisingly, neither drug affected reward sensitivity.

Conclusion: Blockade of D2Rs traded off accuracy for speed. This impulsive pattern is in keeping with paradoxical inhibition of no-go pathway striatal neurons, permitting distractors to elicit action. Increasing dopamine improved performance without a speed cost – mimicking the effect of motivation by reward. This suggests that stimulating both "go" and "no-go" pathways together could energise action while preventing unwanted actions. Hence, better-targeted drugs may help manage the balance between apathy and impulsivity in PD.

Disclosure: Nothing to disclose.

EPO-611

Neurophysiological assessment of juvenile parkinsonism due to monoamine neurotransmitters disorders

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Background and aims: Juvenile parkinsonism is a rare condition due to various causes, including inherited monoamine neurotransmitters disorders, a group of potentially treatable inborn errors of metabolism. Only few studies, however, investigated motor abnormalities, including bradykinesia, in inherited monoamine neurotransmitters disorders. Also, little is known on possible excitability and plasticity changes of the primary motor cortex (M1) in patients.

Methods: Eight patients with inherited monoamine neurotransmitters disorders and 16 age-matched healthy subjects were enrolled. Objective measurements of repetitive finger tapping were obtained using a motion analysis system. The excitability of M1 was assessed by recording the input/output curve of the motor-evoked potentials and using a conditioning-test paradigm for the assessment of short-interval intracortical inhibition (SICI). Plasticity-like mechanisms of M1 were indexed according to the amplitude changes in motor-evoked potentials after the paired associative stimulation (PAS) protocol.

Results: Patients tapped more slowly (p<0.001), with a smaller amplitude (p<0.001), and an irregular rhythm (p<0.001), as compared to controls. However, they did not show any decrement in movement amplitude and velocity during the finger tapping task (no sequence effect). Patients also showed a flattened input/output curve (p=0.042) and a reduced intracortical inhibition of M1 (p<0.001), as assessed by SICI, compared to controls, whereas the response to the PAS protocol was normal in patients.

Conclusion: We here provided the first objective assessment of bradykinesia features and we also demonstrated some excitability changes of M1 in patients in patients with inherited monoamine neurotransmitters disorders. Our results may be interpreted for a better understanding of juvenile parkinsonism pathophysiology.

Disclosure: Nothing to disclose.

EPO-612

Opicapone in German Parkinson's disease patients with motor fluctuations: Results on WOQ-9, QoL and non-motor symptoms.

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Background and aims: Opicapone (OPC) proved to be effective in treating end-of-dose motor fluctuations in Parkinson's disease (PD) patients [1,2]. The OPTIPARK study evaluated OPC 50-mg in a heterogeneous population of patients treated in real-world conditions [3].

Methods: OPTIPARK was a prospective, open-label, single-arm, multicentre trial conducted in Germany and the UK. Patients with motor fluctuations received OPC 50-mg in addition to current antiparkinsonian treatment. Primary efficacy endpoint was Clinician's Global Impression of Change. Secondary endpoints included WOQ-9 (Wearing-off Questionnaire), PDQ-8 (quality of life) and NMSS (non-motor symptoms scale). Safety assessments included evaluation of treatment-emergent adverse events (TEAEs). Here Germany-only data is reported.

Results: 363 patients took one OPC dose and 291 completed three months' treatment. In the 349 patients with post-baseline efficacy data (Full Analysis Set), the presence of symptoms on WOQ-9 decreased from baseline to 3 months, with similar improvements observed already after one month. PDQ-8 improved by (mean ± SD) by -3.1±12.5 points and NMSS improved by -7.7±18.6 points. TEAEs considered at least possibly related to OPC were reported for 37.7% of patients, the most frequently reported being dyskinesia (5.8%). 91.7% of TEAEs were of mild or moderate. Serious TEAEs were reported for five (1.4%) patients.

Conclusion: OPC 50-mg was effective, Patients improved in WOQ-9, PDQ-8, NMSS and generally well tolerated in German PD patients with motor fluctuations treated in clinical practice.

Disclosure: 1. Ferreira et al., Lancet Neurology 2016;15 (2):154-165; 2. Lees et al., JAMA Neurol. 2017;74(2):197–206; 3. Reichmann et al., Transl Neurodegener. 2020;9(1):9

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EPO-613

Cannabinoids for painful dystonia in corticobasal syndrome: a report of three patients.

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Background and aims: The clinical phenotype of corticobasal syndrome (CBS) includes limb dystonia, which may be associated with intense pain that is often difficult to treat despite numerous therapeutic attempts. Cannabinoids are increasingly used to treat pain and some reports suggest a potential benefit in dystonia. We aimed to assess the efficacy of cannabinoids in painful dystonia of CBS patients.

Methods: Three patients with CBS complained painful limb dystonia. All three patients were treated with different pain medication, without achieving satisfactory pain relief. Therefore, we added cannabis-based oily solutions to the therapy, collecting Numeric Rating Scale (NRS) values for pain before and after three months from the start.

Results: Case 1 presented main involvement of the right arm. Her therapy included botulinum toxin injections, amitriptyline, clonazepam and baclofen. She started Bedrolite® oil (THC 1%, CBD 9%, 20 drops/die) therapy, and the NRS value changed from 8 to 3. Case 2 presented main involvement of the left arm. Her therapy included botulinum toxin injections, amitriptyline, clonazepam, baclofen and oxycodone. She started Bediol® oil (THC 6.5%, CBD 8%, 25 drops/die) therapy, and the NRS value decreased from 10 to 1. Case 3 presented main involvement of the right leg. His therapy included botulinum toxin injections, clonazepam, pregabalin, baclofen and oxycodone. He started Bedrolite® oil (60 drops/die) therapy, and the NRS value decreased from 9 to 2. The therapy was well tolerated in all patients.

Conclusion: Cannabinoids should be considered as a useful add-on therapy for painful dystonia in CBS patients.

Disclosure: Nothing to disclose.

EPO-614

Longitudinal progression of Parkin associated Parkinson's disease

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Background and aims: Mutations in Parkin is the most frequent cause of autosomal recessive, early onset, Parkinson's disease (PD). Parkin associated PD is characterized by a relatively 'pure' motor disease with progression described as slower than idiopathic. However, studies directly comparing the progression of Parkin-PD to genetically undefined PD (GU-PD) are lacking.

Methods: We compared the progression of motor symptoms and complications in Parkin-PD vs GU-PD. Parkin-PD patients underwent clinical evaluation including MDS-UPDRS and retrospective assessment of motor complications onset chronology. MDS-UPDRS scores and motor complications chronology were compared to GU-PD patients followed in a prospective cohort.

Results: 21 Parkin-PD and 415 GU-PD were included (see Table 1). GU-PD were older at symptoms onset (Median [first quartile, third quartile]: GU-PD 60 [53, 66], Parkin-PD 25 [18, 36], p<0.001), had shorter disease duration (3 [2, 5] versus 30 [20, 38], p<0.001), but were comparable for motor severity (MDS-UPDRS-III: 29 [19, 38] versus 32 [22, 43], p=0.38), while motor complications were less severe than Parkin-PD (MDS-UPDRS-IV: 1 [0, 5] versus 5 [1, 7], p=0.01). Cox proportional-hazards models adjusted by age at onset showed that motor complications progression was slower in Parkin-PD than GU-PD with respect to dyskinesia (Hazard Ratio [95% Confidence Interval (CI)]: 2.7 [1.1–6.5], p=0.027), motor fluctuations (9.6 [3.9–24], p<0.001) and falls (4 [1.1-14], p=0.031), but not freezing of gait (2.2 [0.6–7.4], p=0.218) (see Figure 1).
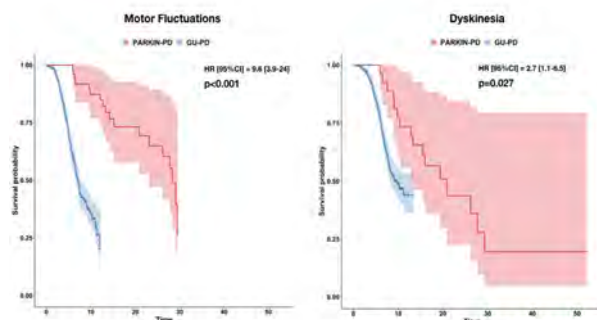
Figure 1: Symptoms-Free Survival Curves comparing PARKIN-PD and GU-PD for dopaminergic motor complications
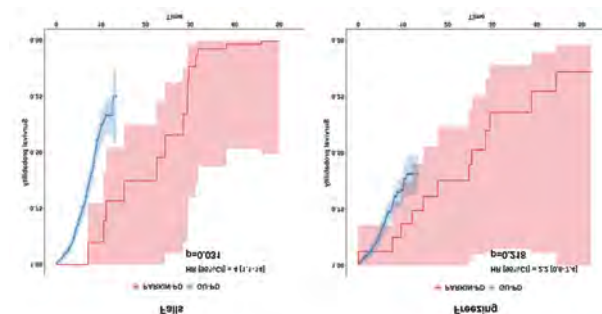
Figure 2: Symptoms-Free Survival Curves comparing PARKIN-PD and GU-PD for non-dopaminergic motor complications

Conclusion: The better characterization of disease progression in the Parkin-PD population is important to determine the best endpoints for potential clinical trials.

Disclosure: No specific funding was received for this work. None of the authors declare any conflict of interests with respect to current work.

EPO-615

The neurological assessment of driving fitness of patients with Parkinson's Disease(PD): A review of existing guidelines

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Background and aims: Motor deficits, non-motor symptomatology and antiparkinsonian drugs may deteriorate driving ability of PD patients. Treating neurologists are frequently asked to evaluate driving fitness of their patients and provide evidence-based consultation. Although several guidelines have been published, the exact procedure to evaluate fitness to drive of PD patients as well as the neurologist's role on this procedure remain obscure.

Methods: We systematically reviewed the existing guidelines, regarding the evaluation of driving fitness of PD patients. The search was applied to MEDLINE and GoogleScholar and we identified 152 articles. After applying specified inclusion criteria, 14 articles were included (9 National Guidelines, 4 Recommendation Papers, 1 Consensus Statement).

Results: The treating physician is proposed as the initial evaluator in 13/14 articles (Neurologist in 2 articles) and may refer patients to practical Driving Assessment (proposed in 12 articles), to Driver Licensing Authority or to a driving rehabilitation specialist (each proposed in 6 articles). The evaluation should include motor, cognitive and visual assessment (proposed in 14, 12 and 8 articles, respectively). Review of the patients' antiparkinsonian medication and identification of sleep disorders are proposed in 9 and 6 articles, respectively. Specific neuropsychological and visual tests are proposed in 7 articles each, while specific motor tests are proposed in 6 articles. However, relative cut-off values for those tests are proposed in only 2 articles.

Conclusion: Neurological aspects of driving fitness of PD patients are recognized in most of the guidelines. However, clear-cut instructions regarding motor, neuropsychological and visual tests along with cut-off values are still lacking.

Disclosure: * This review is part of P. Stamatelos' PhD project with title " Evaluation of driving behavior of patients with MCI, Dementia or Parkinson's Disease: Diagnostic and Prognostic Markers", funded and supported by Onassis Foundation.

EPO-616

Prolyl Endopeptidase modulation by ACT-02 prevents a-synuclein aggregation in a transgenic model of Parkinson disease

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Background and aims: ACT-02 modulates alpha-synuclein (a-syn) aggregation, and mitochondria dysfunction. associated with Prolyl Endopeptidase (PREP) activity. ACT-02 is a highly selective and potent PREP inhibitor. We assessed ACT-02 in vivo efficacy in the Line 61 transgenic (Tg) mouse model overexpressing human α-synuclein under the Thy1 promoter.

Methods: A total of 64 male Tg Line 61 mice 1.5 months old, and 16 non-transgenic age- and sex-matched littermates were randomly allocated to 5 groups of 16 animals per group. All animals received daily gavage administration of ACT-02 at three different doses (1, 5 and 10 mg/kg) or vehicle (n=16 animals/group) for a period of 13 weeks. At the end of treatment, protein was extracted from the cortex, hippocampus, and striatum from all groups (5 groups, 40 animals in total). Human a-syn aggregation and complex I activity were determined in the cortex, hippocampus, and striatum of all animals.

Results: We observed a significant decrease on a-syn aggregation in the cortex in Tg mice treated with ACT-02 10 mg/kg compared to placebo (p=0.0207). Regarding complex I activity in the cortex, treatment with 10 mg/kg restored complex I activity compared to vehicle-treatment. No statistical differences were detected in the hippocampus and striatum between all groups compared to Tg control animals.
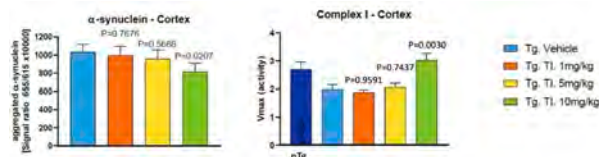
Efficacy of ACT-02 on a-syn aggregation and complex I activity in the Line 61. A) Quantification of aggregated human a-syn in the cortex of Line 61 animals. Data are displayed as means + SEM of all animals (n=8 per group); B) Quantification of Complex I a

Conclusion: PREP modulation by ACT-02 improves PD neurodegeneration via multiple mechanisms in the Line 61 a-syn transgenic model, and therefore has potential therapeutic value for disease modifying treatment of PD.

Disclosure: Pablo Villoslada is has recevied payments and hold stocks from Accure Therapeutics, CLight, NeuroPrex, Spiral Therapeutics, Attune Neurosciences and Adhera Health Roger Prades is an employee of Accure Therapeutics

EPO-617

Is prediction of the response to Deep Brain Stimulation a fiction?

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Background and aims: Deep Brain Stimulation of the subthalamic nucleus (STN-DBS) is an effective and evidence-based treatment for idiopathic Parkinson's disease (iPD). A minority of patients does not sufficiently benefit from STN-DBS. We evaluate the predictive validity of the L-Dopa challenge on a large multicenter dataset on STN-DBS in iPD applying state-of-the-art statistical methods.

Methods: Datasets from Berlin (n=78), Kiel (n=253) and Toronto (n=98) of follow-up examinations (9.15 months ± 3.39) were joined. Insufficient DBS outcome was defined as an overall UPDRS-III reduction <33% compared to UPDRS-III in med off at baseline or alternatively if the minimal clinically important improvement of 5 points was not reached. Single UPDRS-Items and sub-scores were dichotomized. Following exploratory analysis we trained supervised regression- and classification models for outcome prediction.

Results: Data-analysis confirmed a significant correlation between the absolute UPDRS-III reduction during L-dopa challenge and after stimulation (R=0.57, p≤0.001). However, individual improvement was inaccurately predicted with a range of up to 30 UPDRS III points. Multivariate and game-theory analysis identified the preoperative UPDRS-III/med-off-score and the preoperative Levodopa-improvement as most influential factors. The models for UPDRS-III and sub-scores improvement achieved low accuracy.
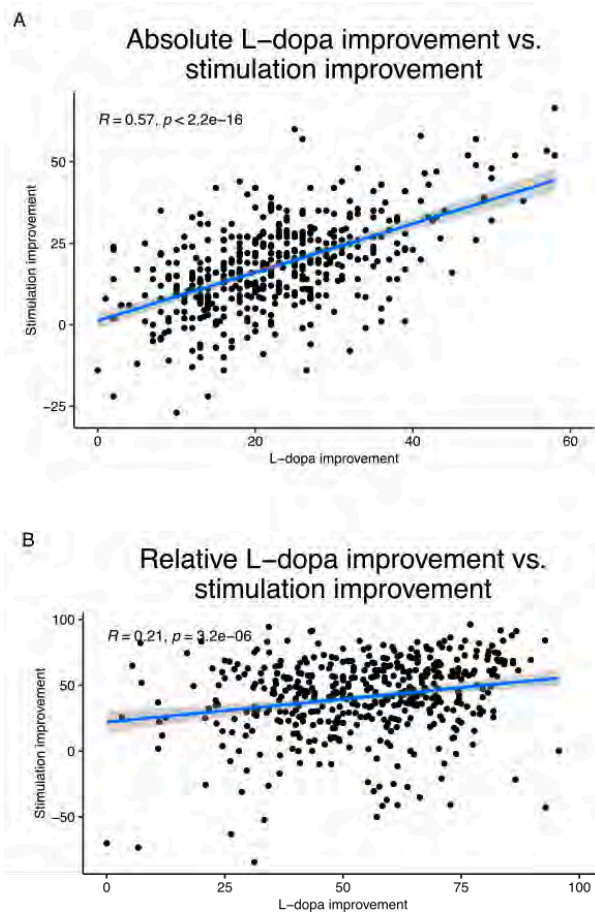
Figure: This plot illustrates the relations between the preoperative UPDRS-III during med off, L-dopa improvement and stimulation improvement. Plot A shows the L-dopa vs. stimulation improvement and the preoperative UPDRS-III med off as a color gradient

Conclusion: While the confidence limits for the mean are small and reproducible, the prediction intervals for individual patients of the models are clinically insufficient. The levodopa-test is important for excluding non-responders to Levodopa but must be thoughtfully used for individual patient counseling. Developing new clinical tests for prediction may be more promising than using advanced statistical methods.

Disclosure: No conflicts of interest related to this work.

Movement disorders 6

EPO-618
Abstract withdrawn

EPO-619
A PSP-like syndrome revealing a Neuro-SJögren

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Background and aims: Sjögren's syndrome (SS) is an autoimmune disorder involving glandular and extraglandular lymphocytic infiltration. The central neurological manifestations are commonly reported (31%) . Abnormal movements are rarely reported, with Parkinsonism being the most common presentation.

Methods: A 42-year-old patient, with no remarkable medical history, consulting for gait disturbances . The initial examination revealed a bilateral and symmetrical parkinsonian akineto-rigid syndrome, postural instability, cervical dystonia. Brain MRI showed demyelinating lesions in the subcortical and periventricular. The isoelectric focusing CSF analysis identified a type-2 profile oligoclonal bands. The ophthalmological examination revealed a severe xerophthalmia. The BASG confirmed the a sialadenitis grade 4 . The symptomatic management of the Parkinsonism syndrome included a combination of corticosteroid therapy, L-dopa and dopaminergic agonists.

A brain MRI axial T2 : Hypersignals in the subcortical

A brain MRI axial T2 : Hypersignals in the periventricular

A

brain MRI axial FLAIR : Hypersignals in the subcortical and periventricular white matter

Results: Our patient developed a rapidly progressing and unusual Parkinsonian syndrome with bilateral onset and important postural instability associated to a upper gaze palsy, a cervical dystonia realizing a PSP syndrome. His young age and the rapid aggravation of his symptoms in addition to the demyelinating lesions on cerebral MRI led to the consideration of an inflammatory pathology, particularly NS, The particular therapeutic feature of our patient is that he presented with a PSP-Like syndrome and responded to Levodopa with even motor fluctuations and dopa-induced dyskinesias

Conclusion: The Neurological manifestations are commonly seen and non-specific in SS but parkinsonian syndrome still remains rare. The case presentation thighlighted the importance of looking for a secondary etiology in case of an atypical parkinsonian syndrome, especially an inflammatory one,

Disclosure: The authors declare no conflicts of interest.

EPO-620

Not so elementary Mr. Holmes Case report

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Background and aims: Holmes' tremor is a low-frequency tremor with varying amplitude at different phases of motion. It's produced by lesions in the brainstem, diencephalon or thalamus involving the dentate-rubro-thalamic pathway. A brainstem or central-variant Posterior Reversible Encephalopathy Syndrome (PRES) has been previously described in some case-reports as a white matter vasogenic oedema involving posterior fossa. This case report relates these two clinical concepts.

Methods: A 59-year-old man presented an acute onset of gait disorder associated with an hypertensive crisis and acute kidney failure. Physical examination revealed dysmetria of the left upper extremity, significant gait ataxia and low frequency (<5Hz) tremor with moderate amplitude at rest that worsened with posture and movement in the left hand. A cranial CT scan showed diffuse hypodensity of the midbrain, pons, and cerebellar peduncles.
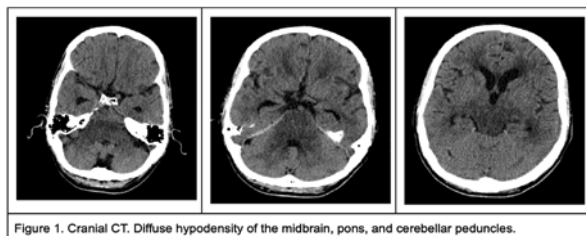
Figure 1. Cranial CT. Diffuse hypodensity of the midbrain, pons, and cerebellar peduncles.

Results: After blood pressure control, the patient improved progressively and the tremor disappeared 48 hours later. Brain MRI showed brainstem T2-FLAIR hyperintensity and slightly increased signal intensity on diffusion-weighted images and increased ADC values extending towards the midbrain and both middle cerebellar peduncles, associated with hemorrhagic lesions in the pons. The case was oriented as an atypical PRES with predominant involvement of the posterior fossa, complicated with hemorrhagic lesions in the context of hypertensive encephalopathy and acute kidney failure.
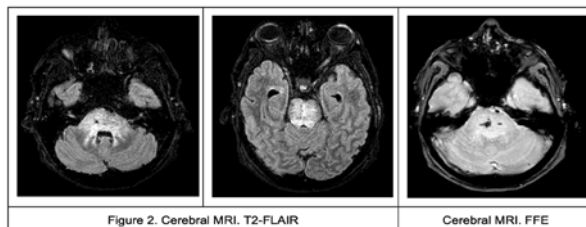
Figure 2. Cerebral MRI. T2-FLAIR   Cerebral MRI. FFE

Conclusion: Most of Holmes' tremor etiologies are irreversible, but reversible cases had been reported after the resolution of spontaneous intracranial hypotension or hyperglycemia; to our knowledge, this is the first case reported of reversible Holmes' tremor due to central or brainstem variant PRES.

Disclosure: No disclosures related to the manuscript.

EPO-621
Abstract withdrawn

EPO-622

Dystonic features with cerebellar syndrome: a rare case of spinocerebellar ataxia type 16

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Background and aims: Spinocerebellar ataxia (SCA) type 16 is a rare form of spinocerebellar ataxias caused by homozygous or compound heterozygous mutation in the STUB1 gene on chromosome 16p13. Since this rare entity has a clinical manifestation of progressive cerebellar symptoms including dysarthria, ataxia, instability, gait disturbance, we here presented a case of SCA16 with dystonia combined with progressive cerebellar symptoms.

Methods: A 24-year-old male presented to our movement disorders clinic with progressive deterioration in gait, slurred speech, and balance problems. His initial symptom was difficulty while walking that was noticed when he was 18 years old. His medical and family history was unremarkable. He was the son of consanguineous parents. Brain magnetic resonance imaging showed cerebellar atrophy. Routine laboratory investigations, ataxia screening was normal.

Results: Genetical analysis revealed homozygous mutation in STUB1 gene supporting the diagnosis of SCA16. Previous prescriptions included vitamin E, Coenzyme Q10, valproic acid, clozapine, baclofen without any sufficient symptomatic response. He was under physical therapy.

Conclusion: SCA 16 is a rare type of spinocerebellar ataxia characterized by cerebellar symptoms with cerebellar atrophy. Most common onset is in teenage years. Although the prominent clinical manifestation is cerebellar syndrome, mild peripheral sensory neuropathy, cognitive deficits are also reported. Dystonia is a common symptom in some spinocerebellar ataxias including SCA3, SCA2, SCA1, SCA6. Though it is not described as a frequent clinical symptom of SCA16 so far, we here reported this rare case of SCA16 with accompanying dystonic features to discuss in the light of literature knowledge.

Disclosure: Nothing to disclose.

EPO-623

Abstract withdrawn

EPO-624

Resting heart rate variability in Parkinson's disease with and without freezing of gait

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Background and aims: Freezing of gait (FOG) and autonomic dysfunction are common in patients with Parkinson's disease (PD). Heart rate variability (HRV) parasympathetic parameters are reduced in idiopathic PD and related to autonomic dysfunction. Information on the relationship between HRV and FOG are scarce. The aim of the study was to investigate HRV in PD patients with and without FOG.

Methods: Idiopathic PD patients with and without FOG, and age-matched healthy individuals were recruited. Participants were continuously monitored by Equivital physiological monitoring system, which recorded two lead electrocardiograms. Beat-to-beat ventricular interval (RR) series recorded in resting conditions were processed offline to compute heart rate and HRV parameters in the time, frequency, and information domains. HRV parameters were compared among the three groups by using analysis of variance and post-hoc multiple comparisons.

Results: A total of 50 individuals were recruited and 37 were included in the analysis: 15 healthy individuals, 11 patients with PD and FOG, and 11 patients with PD without FOG. Heart rate was increased ($p<0.05$) and time domain (standard deviation of normal-to-normal intervals) and frequency domain (low-frequency and high-frequency spectral power) parameters were reduced in idiopathic PD compared to healthy controls ($p<0.005$ and $p<0.0005$, respectively). PD patients with FOG did not display any difference from PD patients without FOG in any measured HRV parameter.

Conclusion: Our study showed that HRV at rest was reduced in PD patients compared to healthy controls; however, there were no differences in PD patients with and without FOG in this condition.

Disclosure: Nothing to disclose.

EPO-625

Gait and balance assessment after unilateral Gamma Knife thalamotomy for treatment of tremor'

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Background and aims: Parkinson's disease (PD) and essential tremor (ET) are among most common causes of tremor. Pharmacotherapy is the first line of treatment. It can sometimes be ineffective or have unacceptable side effects. In such cases, surgical treatment is an option. Deep brain stimulation or thalamotomy are among commonly used methods.

Methods: The aim of our study was to assess the impact of unilateral Gamma Knife thalamotomy on gait and balance of ET and PD patients. We included 20 conscutive patients with PD (n=10) or with ET (n=10) with pharmacoresistant tremor. The mean age was 63.5 (±9.5), 15 male and 5 female. They underwent assessments before (n=20); 12 months (n=20), and 24 months (n=15) after the thalamotomy. Timed "Up and go" test, tandem stance test, tandem pivot test, and walking tandem tests were performed. Stabilometry was performed using TecnoBody Prokin-M-line stabilometric platform with Prokin 3 software and gait was assessed on Zebris treadmill. Friedman's ANOVA and Wilcoxon's signed-rank test were used to compare the outcomes. Patients with PD were assessed in "ON" and "OFF" dopaminergic treatment state.

Results: Statistical analysis revealed no significant deterioration in gait and balance in performed tests in a 2-year follow-up.

Conclusion: We conclude that unilateral Gamma Knife thalamotomy does not affect gait and balance of ET and PD patients.

Disclosure: Authors report no conflict of interest regarding this manuscript.

EPO-626

WHODAS 2.0 to access functional disabilities of Wilson Disease's patients

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Background and aims: Wilson disease (WD) is a metabolic disorder that can be successfully treated. Nonetheless, patients still have a relentlessly progressive course of disease and disability, and a wide range of social limitations. Therapy that requires lifelong medication, and periodical medical controls, may also affect the way they see themselves and relate to others. We aim to analyze the disability status of WD patients by using the World Health Organization Disability Assessment Schedule 2.0 scale (WHODAS 2.0) and to observe the correlation between the severity of disease, depression, and cognitive status with functional abilities of these patients.

Methods: Cross-sectional study with 26 participants with WD. The severity of WD was assessed by the Global Assessment Scale for WD; survey measured disability level using WHODAS 2.0; the mental status using Mini Montreal Cognitive Assessment, and Patient Health Questionnaire (PH9) for depression symptoms.

Results: We found a strong association between disability and severity of symptoms (rs=0.773; p=0,001). The median score of WHODAS 2.0 was 17.00 [IQR12–51], and the most affected domain was Participation (median 4.5[IQR2–9]). Life Activities (rs=0.840;p=0.001) showed the strongest association with the severity of the disease (rs=0.840; p=0.001). Dysfunction in Participation in society was best related to musculoskeletal symptomatology (rs=0.625; p=0.003) and higher scores in PH9 (rs=0.628; p=0.011). We also found a stronger association between functional status and predominantly WD neurological dysfunction versus WD liver dysfunction.

Conclusion: The severity of disease, depression, and cognitive status are associated with functional activities. Looking beyond mortality and disease by describing how people live with their health conditions should not be neglected.

Disclosure: Nothing to disclose.

EPO-627

Spinocerebellar ataxia type 5 (SCA5): Undescribed variant of the SPTBN2 gene

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Background and aims: Spinocerebellar ataxia type 5 (SCA5) is a very rare autosomal dominant entity, caused by a mutation of the SPTBN2 gene (11q13.2) that encodes a beta spectrin subunit. It causes a clinical syndrome, which comprises cerebellar involvement and ophthalmoparesis, usually begins in middle age and has a latent course.

Methods: We present a clinical case compatible with SCA5.

Results: A 75-year-old man consulted for progressive gait instability and motor incoordination for the last 20 years. Family history show a similar clinical history in maternal grandmother, mother, maternal uncle, niece, sister and daughter. All made their clinical debut between 30–40 years of age. No toxic consumption was reported. The neurological examination revealed scanned dysarthria, horizontal-rotatory nystagmus in all gaze positions, horizontal gaze paralysis and severe cerebellar ataxia. Motor, sensory examination and stretch reflexes were normal. Blood tests, which included onconeuronals test, ruled out most frequent nosological entities. Cranial MRI (image 1) showed marked cerebellar atrophy especially of cerebellar vermix. The genetic study identified a variant of the SPTBN2 gene C.5399C>T p. (Ala1800Val) with a CADD bioinformatic predictor that estimates a pathogenic effect. Family segregation is pending.

Conclusion: This clinical case presents a chronic cerebellar syndrome and ophthalmoparesis with an undescribed variant of the SPTBN2 gene and a family history compatible with SCA-5. The descriptions of new variants are important as they provide information for research and genetic advice.

Disclosure: The descriptions of new variants are important as they provide information for research and genetic advice

EPO-628

Parkinson's disease induced by SARS-CoV2.

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Background and aims: COVID-19 infections are reported in numerous case-reports as a trigger for development of Parkinson's disease (PD). We report 4 patients with symptoms of PD developed or exagerated after SARS-CoV2 infection.

Methods: Patients were retrospectively recruited in an outpatient clinic of Department of Neurology, Faculty of Health Science, Medical University of Warsaw. Patients were independently assessed by 2 neurologists experienced in movement disorders.

Results: We identified 4 patients with rapid onset of PD symptoms following COVID-19. All patients were female. Symptoms of COVID-19 included headache in 4/4 cases and anosmia in 3/4 cases. PCR test confirmed SARS-CoV2 infection in all cases. The age of onset was between 28 and 62 years old. The rest tremor was present in all patients, ridgidity in 3/4 patients. Non-motor symptoms included RBD in 2/4 patients. Two patients were treated with levodopa with good response. MRI findings were non-significant. The SPECT-DatScan was performed in one patient and was typical for parkinsonian disorders. The positive family history was present in two patients.

Conclusion: We conclude that COVID-19 may trigger development of parkinsonian motor symptoms or exaggerate the slight disease progression. The cause is unknown. Involvement of olfactory bulb could trigger neuroinflammation in line with Braak's hypothesis. COVID-19 may also induce parkinsonism in patients with genetic predisposition.

Disclosure: Authors declare no conflict of interests.

EPO-629

Sex, pain and depression, all in PD

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Background and aims: Sexual dysfunction is a common non-motor feature of Parkinson's Disease (PD) -33%, which alters the quality of life of this patients, often under recognized (only 45.5% of our patients declare it on visit).

Methods: We conducted a retrospective study on 187 patients with PD admitted in Neurology Department of Elias University Emergency Hospital from 2016 to 2021. Patients were evaluated with: Hoehn& Yahr scale, UPDRS III, Parkinson's Well Being Map (items for sex, pain, disposition), Hamilton Depression Rating Scale (HDRS). We performed a statistical analysis of the data collected.

Results: The characteristics of patients in our study were: sex distribution – mostly men, with mean ages 63,7 years old, with mild disease duration (7,2 years), Hoehn&Yahr 2.5, UPDRS III 20 points. 68 % of patients had mild altered interest in sex. Mild sex difficulty: 70% of patients. Pain: mostly severe (52%). Depression: mostly severe (59%) on Parkinson's Well Being Map, moderate on HDRS .The correlations analyzing the degree of simultaneous alteration in both sexual desire and physical difficulties showed that 64% declared both items mildly affected.

Conclusion: In our study, both pain and depression were the most important element who modified the sexual life of patients with PD, although altered libido and sexual difficulties are mildly affected. The reasons might be the fear of communication with the doctor, considering this subject as a taboo or under auto analyzing this aspect of life that is covered by the severe spectrum of manifestations in PD.

Disclosure: Nothing to disclose.

EPO-630

Wilson disease – long term follow up. Report from national reference center in Poland

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Background and aims: WD is a rare genetic disorder causing copper accumulation and subsequent liver and brain damage. Since the end of the 1950s, life-long anti-copper therapies (mainly d-penicillamine - DP, trientine, zinc salts) have been available. We present seven decades of experience of a single reference centre covering most adult Wilson disease (WD) patients in Poland.

Methods: Electronic prospective data collection was started in the middle of the 1990s; WD patients diagnosed before were recorded retrospectively from medical records. Demographic, clinical characteristics, diagnostic methods, treatment were followed and analyzed over time decades.

Results: Up to 2019 929 patients were recorded; the number of WD patients increased over the decades from 20 to 237 before 1960 and in the 2010s, respectively. No substantial differences were noted for the mean age of diagnosis (~30 yrs), time from first signs to diagnosis (~35 months). Initially, the majority of WD patients presented with neurological signs, while last decades, half of the patients reported predominantly hepatic symptoms. The diagnosis was mostly based on ceruloplasmin in serum, copper in urine and Kayser-Fleischer ring; in the last two decades, DNA analysis and brain MR imaging were commonly used, which resulted in more mild WD patients identified. WD patients were treated mainly with DP before the 1970s and subsequently also zinc. Switch between DP and zinc was recorded for up to 6–7% of patients. Treatment compliance, survival and clinical prognosis over decades improved.

Conclusion: Early diagnosis and long-term monitoring are needed to better WD patients' outcomes.

Disclosure: Nothing to disclose.

EPO-631

Gait digital parameters and dopaminergic deficits in drug naïve and early Parkinson's disease patients

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Background and aims: The correlation between motor severity and dopaminergic depletion is an open issue in Parkinsons' disease (PD). We aimed to study the possible correlation between digital gait parameters assessed in normal and dual task conditions and striatal dopaminergic depletion in drug-naïve and early Parkinson Disease (PD) patients.

Methods: The prospective study included consecutive early PD patients with and without dopaminergic treatment and age-matched controls. Each subject underwent gait analyses in supervised normal and dual-task conditions using mobile health technology. PD patients underwent [123I] FP-CIT-SPECT imaging and the occipital-adjusted specific to nondisplaceable binding ratio (SBR) in striatal regions were extracted. The study evaluated gait parameters differentiating HC from PD and their specific correlations with dopaminergic imaging in drug-naïve and early PD patients.

Results: 53 early PD patients (including 31 drug-naïve) and 44 age-matched controls entered the study. Step, stride and stance time under supervised conditions differentiate PD patients from controls. These parameters exhibited strong correlation to putamen (r=-0.47, p=0.013) and caudate (r=-0.46, p=0.017) uptake in naïve patients; while no correlation was found between gait parameters and dopaminergic imaging in early PD patients under dopaminergic treatment.

Conclusion: Mobile health technology gait parameters correlate with dopaminergic basal ganglia deficits in drug-naïve patients. Larger ongoing longitudinal studies are needed in order to evaluate gait alterations within the prodromal phases of the disease and the impact of dopaminergic medication on gait performance over-time.

Disclosure: Nothing to disclose.

MS and related disorders 5

EPO-632

Previous treatments influence the lymphocyte kinetics of people with Multiple Sclerosis switching to ocrelizumab

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Absolute lymphocyte and lymphocyte subset counts at baseline and after six 6 months in naïve to treatment (NTT; blue dots), switching from fingolimod (SF; red dots) and switching from natalizumab (SN; green dots) patients.

Changes in absolute lymphocyte count and lymphocyte subset absolute counts (absolute value) from baseline to 6 months, in naïve to treatment (NTT; blue line), switching from fingolimod (SF; red line) and switching from natalizumab (SN; green line).

Background and aims: Recently, concern has been raised about previous disease-modifying treatments (DMTs) and the influence they might have on the clinical efficacy of ocrelizumab (OCR). During the first six-month period of treatment with OCR, patients switching from fingolimod (SF) were found to have a higher clinical activity than those switching from natalizumab (SN). We aimed to evaluate whether the previous DMT affects the lymphocyte subset kinetics of people with Multiple Sclerosis (MS) switching to OCR and whether the lymphocyte subset kinetics influence the clinical response to OCR.

Methods: This is a multicenter, retrospective, real-word study on consecutive MS patients who started or switched to OCR. We grouped them by prior DMT in naïve-to-treatment (NTT), SF and SN. Differences in lymphocyte subset changes over all the three groups were compared using analysis of covariance. A linear mixed model was applied to compare subset changes between patients with and without early inflammatory activity.

Results: After adjusting for age, sex, disease duration and clinical phenotypes, CD4+ and CD8+ cell count decrease was more pronounced in the SN group than in either NTT (p=0.004 and p<0.001) or SF (p<0.001 and p<0.001) groups. CD4+ cell count decrease was more pronounced in NTT than in SF patients (p=0.030). Patients with early inflammatory activity showed a less pronounced CD8+ decrease than stable patients (p=0,0332).

Conclusion: Previous DMTs influence the lymphocyte kinetics of people with MS switching to OCR. CD8+ cell decrease might account for early clinical response to OCR. Reassessment of these findings over a larger population may help optimize the switch.

Disclosure: The authors have stated explicitly that there are no conflicts of interest in connection with this article.

EPO-633

Neuroinflammation is associated with GFAP and sTREM2 levels in Multiple Sclerosis

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Background and aims: Astrocytes and microglia play an important role in the inflammatory process of multiple sclerosis (MS). We investigated the associations between the cerebrospinal fluid (CSF) levels of glial fibrillary acid protein (GFAP) and soluble triggering receptors expressed on myeloid cells-2 (sTREM-2), inflammatory molecules, and clinical characteristics in a group of patients with relapsing-remitting MS (RRMS).

Methods: 51 RRMS patients participated in the study. Clinical evaluation and CSF collection were performed at the time of diagnosis. The CSF levels of GFAP, sTREM-2, and of a large set of inflammatory and anti-inflammatory molecules were determined. MRI structural measures (cortical thickness, T2 lesion load, cerebellar volume) were examined.

Results: The CSF levels of GFAP and sTREM-2 showed significant correlations with inflammatory cytokines IL-8, G-CSF, and IL-5. Both GFAP and sTREM-2 CSF levels positively correlated with age at diagnosis. GFAP was also higher in male MS patients, and was associated with an increased risk of MS progression, as evidenced by higher BREMS at the onset. Finally, a negative association was found between GFAP CSF levels and cerebellar volume in RRMS at diagnosis.
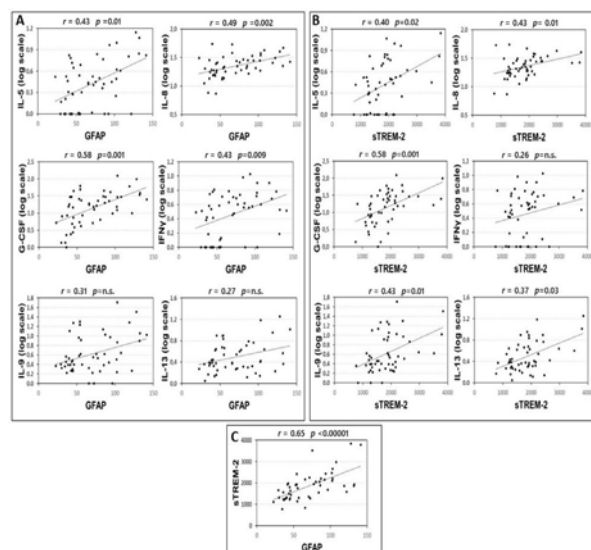
Fig. 1. Correlation between CSF levels of GFAP, TREM-2 and inflammatory cytokines. Spearman's correlations between levels of GFAP and cytokines(A), sTREM2 and cytokines(B) and GFAP and sTREM2(C). p-value is shown according to Benjamini-Hochberg correction
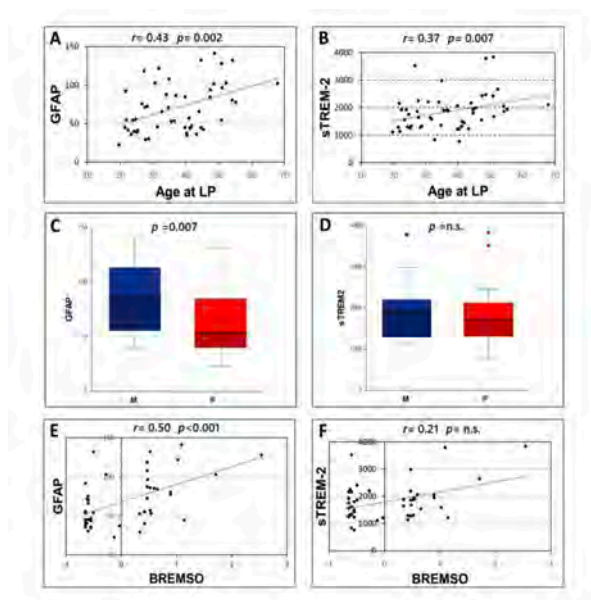
Fig.2.Correlation of CSF levels of GFAP and sTREM2 with clinical characteristics. Spearman's correlations between GFAP and sTREM2 and age at lumbar puncture(A,B) and BREMSO(E,F). Comparison between CSF GFAP/sTREM2 levels in male/female(C,D), Mann Withney
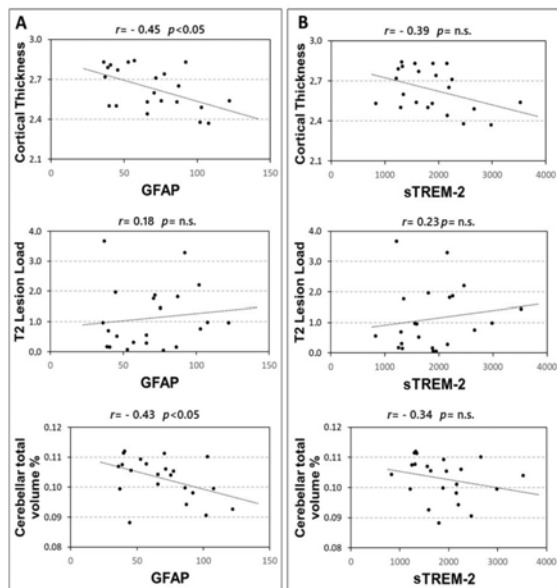
Fig.3 Correlations between CSF GFAP and sTREM2 and MRI structural measures. Spearman's correla-tions between CSF GFAP and MRI structural measures (A) and sTREM2 and MRI measures (B).

Conclusion: GFAP and sTREM-2 represent suitable biomarkers of central inflammation in MS. Our results suggest that enhanced CSF expression of GFAP may characterize patients with a higher risk of progression.

EPO-634

Pediatric-onset multiple sclerosis: difference in disease burden and activity in pediatric-onset vs adult-onset patients

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Background and aims: Approximately 2–10% of individuals with Multiple Sclerosis (MS) experience their first episode as a child. The aim of this study is to compare the clinical, paraclinical, and radiological features of pediatric-onset multiple sclerosis (POMS) with the adult-onset form (AOMS).

Methods: We used medical records to collect data from 173 POMS patients and 173, age- and sex-matched, AOMS patients (both group, age: 41.5±13.7, male/female ratio: 54/119). Demographic, clinical, radiological, and paraclinical data at onset, diagnosis, and follow-up were collected.

Results: The POMS group had a higher prevalence of family history for MS (8.09% vs 2.89%, p-value: 0.034). The time-gap between onset and diagnosis was longer in POMS subjects (months: 77.3±102.9 vs 27.9±43.0, p-value: <0.001) and, in the same group, the diagnosis was based on clinical criteria in a higher percentage of patients (80.92% vs 65.90%, p-value: 0.002). At follow-up, the prevalence of progression was higher in the AOMS group (2.00% vs 2.50%, p-value: 0.020) and the time-gap between onset and progression was longer in POMS patients (22.6±11.3 vs 12.1±9.6, p-value: 0.004). However, the POMS subjects had a higher number of T2w lesions (27.27±29.24 vs 12.83±11.63, p-value: 0.040).

	PO-MS (n=173)	AO-MS (n=173)	p-value (CI / Fisher's)
Age at onset, mean ± SD	14.6±2.7	27.5±8.3	<0.001 (11.5804 - 14.1999)
Age at diagnosis, mean ± SD	21.1±8.5	29.3±9.0	<0.001 (6.1009 - 10.1434)
Time-gap from onset to diagnosis (months), mean ± SD	77.3±102.9	27.9±43.0	<0.001 (-68.2129 - -30.6840)
Type of onset, prevalence (%):			
supratentorial	24/173 (13.87%)	17/173 (9.83%)	0.244 (Fisher's 0.318)
optic pathway	47/173 (27.17%)	49/173 (28.32%)	0.810 (Fisher's 0.904)
brainstem-cerebellum	67/173 (38.73%)	63/173 (36.42%)	0.657 (Fisher's 0.739)
spinal cord	63/173 (36.42%)	58/173 (33.53%)	0.573 (Fisher's 0.652)
Polysymptomatic onset, prevalence (%)	29/173 (16.76%)	23/173 (13.29%)	0.367 (Fisher's 0.452)
Progression at onset, prevalence (%)	1/173 (0.58%)	5/173 (2.89%)	0.099 (Fisher's 0.215)
EDSS at onset, median (range)	2.0 (0.0 - 6.5)	1.5 (0.0 - 6.0)	0.143 (-0.8528 - 0.1243)
FS score at onset, median (range):			
pyramidal FS	1.0 (0.0 - 4.0)	1.0 (0.0 - 4.0)	0.286 (-0.5239 - 0.1556)
visual FS	0.0 (0.0 - 3.0)	0.0 (0.0 - 3.0)	0.555 (-0.2669 - 0.1437)
sensory FS	0.0 (0.0 - 3.0)	0.0 (0.0 - 3.0)	0.138 (-0.0643 - 0.4589)
cerebellum FS	0.0 (0.0 - 5.0)	0.0 (0.0 - 3.0)	**0.009 (-0.6881 - -0.1029)**
brainstem FS	0.0 (0.0 - 4.0)	0.0 (0.0 - 3.0)	**0.019 (-0.6358 - -0.0566)**
sphincteric FS	0.0 (0.0 - 2.0)	0.0 (0.0 - 1.0)	0.470 (-0.0544 - 0.1175)
cortical FS	0.0 (0.0 - 2.0)	0.0 (0.0 - 1.0)	0.961 (-0.0750 - 0.0713)
ambulation	0.0 (0.0 - 6.0)	0.0 (0.0 - 5.0)	0.300 (-0.6139 - 0.1905)
Clinical criteria at diagnosis, prevalence (%)	140/173 (80.92%)	114/173 (65.90%)	**0.002 (Fisher's 0.002)**

Table 1: Clinical features of the population enrolled at onset

	PO-MS (n=173)	AO-MS (n=173)	p-value (CI / Fisher's)
Radiological criteria at diagnosis, prevalence (%)	126/173 (72.83%)	114/173 (65.90%)	0.162 (Fisher's 0.199)
Brain MRI: T1w lesions (number), mean ± SD	1.81 ± 2.02	3.61 ± 6.23	0.161 (-0.7357 – 4.3308)
Brain MRI: T1w Gd+ lesions (number), mean ± SD	1.42 ± 2.03	1.20 ± 3.33	0.719 (-1.4748 – 1.0207)
Brain MRI: T2w lesions, prevalence (%) normal abnormal MS-typical abnormal MS-atypical	5/39 (12.82%) 28/39 (71.79%) 6/39 (15.38%)	4/61 (6.56%) 52/61 (85.25%) 5/61 (8.20%)	0.260 (Fisher's 0.284)
Brain MRI: T2w lesions (number), mean ± SD	11.47 ± 14.13	14.62 ± 15.80	0.352 (-3.5488 – 9.8476)
Spine MRI: T1w lesions (number), mean ± SD	0.17 ± 0.41	0.00 ± 0.00	0.116 (-0.3784 – 0.0451)
Spine MRI: T1w Gd+ lesions (number), mean ± SD	0.19 ± 0.40	0.43 ± 1.01	0.441 (-0.3847 – 0.8722)
Spine MRI: T2w lesions, prevalence (%) normal abnormal MS-typical abnormal MS-atypical	6/12 (50.00%) 5/12 (41.67%) 1/12 (8.33%)	10/28 (35.71%) 18/28 (64.29%) 0/28 (0.00%)	0.173 (Fisher's 0.145)
Spine MRI: T2w lesions (number), mean ± SD	1.78 ± 1.73	1.49 ± 1.29	0.465 (-1.0705 – 0.4945)
Positive OCBs, prevalence (%)	68/87 (78.16%)	88/116 (75.86%)	0.701 (Fisher's 0.739)
Number of OCBs, mean ± SD	6.58 ± 4.48	5.74 ± 3.84	0.532 (-3.5617 – 1.8656)
Link Index, mean ± SD	0.69 ± 0.33	1.05 ± 0.59	0.020 (0.0624 – 0.6677)

Table 2: Radiological and paraclinical features of the population enrolled at onset

	PO-MS (n=173)	AO-MS (n=173)	p-value (CI / Fisher's)
Age at follow-up, mean ± SD	35.5 ± 13.9	38.1 ± 11.7	0.098 (-0.4760 – 5.6039)
Disease duration (years), mean ± SD	20.34 ± 14.14	10.25 ± 9.00	<0.001 [-12.9127 – -7.2549]
Type of disease, prevalence (%): RR-MS SP-MS PP-MS	127/160 (79.38%) 31/160 (19.38%) 2/160 (1.25%)	118/132 (89.39%) 13/132 (9.85%) 1/132 (0.76%)	0.067 (Fisher's 0.048)
Progression, prevalence (%)	33/160 (2.00%)	14/132 (2.50%)	0.020 (Fisher's 0.025)
Age at progression, mean ± SD	37.8 ± 11.6	43.6 ± 8.8	0.098 (-17.4321 – 12.8907)
Disease duration at progression, mean ± SD	22.6 ± 11.3	12.1 ± 9.6	0.004 (-17.4321 – -3.4944)
EDSS at onset, median (range)	2.5 (0.0 – 8.5)	1.5 (0.0 – 9.00)	0.046 (-1.2190 – -0.0120)
FS score at follow-up, median (range): pyramidal FS visual FS sensory FS cerebellum FS brainstem FS sphincteric FS cortical FS	2.0 (0.0 – 5.0) 0.0 (0.0 – 4.0) 0.0 (0.0 – 4.0) 0.0 (0.0 – 5.0) 0.0 (0.0 – 4.0) 0.0 (0.0 – 6.0) 0.0 (0.0 – 4.0)	1.0 (0.0 – 5.0) 0.0 (0.0 – 4.0) 0.0 (0.0 – 4.0) 0.0 (0.0 – 4.0) 0.0 (0.0 – 4.0) 0.0 (0.0 – 5.0) 0.0 (0.0 – 3.0)	0.033 (-0.7624 – -0.0326) 0.099 (-0.1979 – 0.1946) 0.809 (-0.3184 – 0.2488) 0.155 (-0.5146 – 0.0824) 0.002 (-0.7056 – -0.1609) 0.279 (-0.4786 – 0.1373) 0.187 (-0.3455 – 0.0678)
ambulation	0.0 (0.0 – 10.0)	0.0 (0.0 – 11.0)	0.262 (-1.1335 – 0.3096)
Total relapses (number), mean ± SD	7.60 ± 7.52	3.76 ± 3.92	<0.001 (-5.1888 – -2.4912)
Annual relapse rate, mean ± SD	0.52 ± 0.43	0.59 ± 0.63	0.225 (-0.0477 – 0.2016)
Brain MRI: T1w lesions (number), mean ± SD	8.55 ± 13.21	5.13 ± 5.28	0.500 (-13.8920 – 7.0511)
Brain MRI: T2w lesions, prevalence (%) normal abnormal MS-typical abnormal MS-atypical	0/18 (0.00%) 17/18 (94.44%) 1/18 (5.56%)	1/20 (5.00%) 19/20 (95.00%) 0/20 (0.00%)	0.366 (Fisher's 0.730)
Brain MRI: T2w lesions (number), mean ± SD	27.27 ± 29.24	12.83 ± 11.63	0.040 (-28.1562 – -0.7250)
Spine MRI: T1w lesions (number), mean ± SD	0.63 ± 1.06	0.00 ± 0.00	0.096 (-1.3754 – 0.1254)
Spine MRI: T2w lesions, prevalence (%) normal abnormal MS-typical abnormal MS-atypical	6/15 (40.00%) 9/15 (60.00%) 0/15 (0.00%)	8/20 (40.00%) 11/20 (55.00%) 1/20 (5.00%)	0.675 (Fisher's 1.000)
Spine MRI: T2w lesions (number), mean ± SD	2.07 ± 1.64	2.04 ± 2.31	0.952 (-1.1013 – 1.0375)

Table 3: Clinical features of the population enrolled at follow-up

Conclusion: Our results confirm that the POMS patients had a higher inflammatory activity, but a slower conversion to the progressive phase. These findings suggest that the inflammatory and neurodegenerative processes could affect differently the disease according to the age of onset.

Disclosure: The authors have not disclosure for the study.

EPO-635

Resting-state, structural and diffusion MRI metrics related to fatigue in MS, MOGAD AND NMOSD

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Background and aims: Fatigue is frequent in patients with Multiple Sclerosis (MS), Aquaporin-4 antibody Neuromyelitis Optica Spectrum Disorder (AQP4-NMOSD) and Myelin-Oligodendrocyte-Glycoprotein antibody disease (MOGAD). We aimed to assess the presence of a single resting-state functional MRI (RS-fMRI) network biomarker and of common diffusion, structural imaging measures related to fatigue across MS, AQP4-NMOSD, MOGAD.

Methods: 16 MS, 17 MOGAD and 17 AQP4-NMOSD underwent Modified Fatigue Impact Scale (MFIS) and a same-day 3T brain and spinal cord MRI. Structural, diffusion, RS-fMRI metrics were derived using Freesurfer, FSL, Spinal cord toolbox. The linear relationships between the MRI metrics and the total (t-), cognitive (c-) and physical (p-) MFIS scoring were assessed in the total cohort and then, compared between MS and antibody-mediated diseases.

Results: Figure 1 shows the cohorts baseline clinical characteristics. A positive relationship existed between the t-MFIS score and functional connectivity (FC) of the fronto-temporal network (p=0.033) and between the p-MFIS score and FC of the sensory-motor network (p=0.032). A negative relationship was found between the t-MFIS score and FC of the salience network (p=0.023) and of the left fronto-parietal network (p=0.026) (figure 2). FC of the spinal cord was not related to the MFIS scores. Structural and diffusion results are depicted in figure 3. MS patients did not differ in fatigue-related structural, diffusion and FC alterations compared to the other two antibody-mediated diseases.

DESCRIPTIVE CLINICAL RESULTS	MS N=16	MOGAD N=17	AQP4-NMOSD N=17	P-value
Female n%	10 (62.5)	8 (47)	13 (76.5)	Ns
Median disease duration, yrs (range)	11.5 (1-19)	2 (0-24)	9 (0-24)	Ns
Median number of prior attacks, (range)	4 (1-13)	2 (1-11)	2 (1-11)	Ns
Mean age ± SD	43.6 ± 6.8	42.1 ± 10.9	56.7 ± 13.4	0.0005
Total MFIS score ≥ 38, n (%)	6 (37.5)	5 (29)	10 (58.8)	Ns
Mean total MFIS score ± SD	37.7 ± 16.3	29.5 ± 21	38.4 ± 18.4	Ns
Mean cognitive MFIS score ± SD	16.4 ± 8.2	13.3 ± 9.7	14.8 ± 8.6	Ns
Mean physical MFIS score ± SD	17.9 ± 8.4	13.5 ± 9.9	19.3 ± 8.6	Ns
EDSS median (range)	2 (0-6)	1.5 (0-7)	3 (0-7)	Ns
HADS depression score, median (range)	2 (1-14)	3 (0-11)	4 (0-12)	Ns
HADS anxiety score, median (range)	5 (2-14)	7.5 (0-19)	7 (0-18)	Ns
Clinical depression, n (%)	2 (12.5)	1 (6)	1 (6)	Ns

Baseline clinical and questionnaires data in MS, MOGAD and AQP4-NMOSD
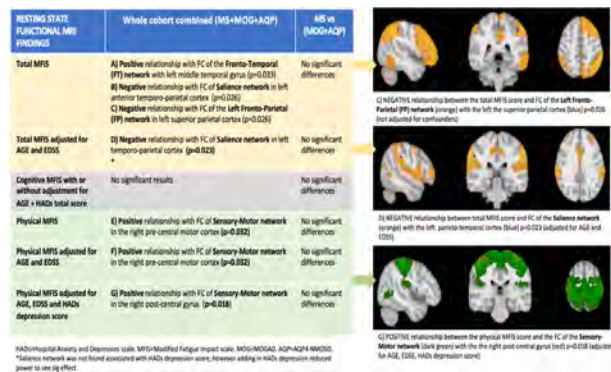
Resting-state functional networks alterations in relation to total, cognitive and physical fatigue
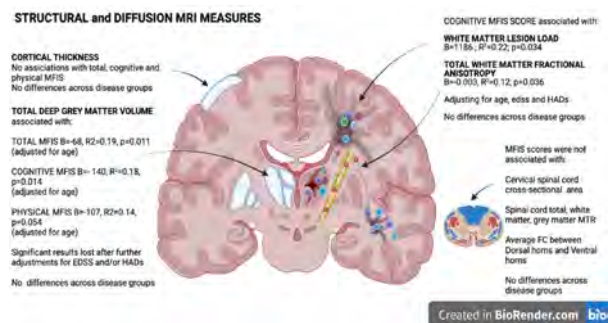
Brain and spinal cord structural and diffusion measures related to fatigue scores

Conclusion: Fatigue-related imaging metrics do not differ across MS, MOGAD and AQP4-NMOSD. Fatigue may be a disconnection between perception of activity and the actual performance. Future research should focus on rehabilitative strategies.

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EPO-636

Clinical characteristics of secondary progressive multiple sclerosis – a 10 years follow-up study

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Background and aims: Secondary progressive multiple sclerosis (SPMS) occurs in the majority of MS patients after a relapsing phase with variable course of disease. Here we describe the characteristics of a SPMS population followed over 10 years.

Methods: Of 265 SPMS patients 99 fulfilled the inclusion criteria of fully documented clinical data over 10 years after SPMS onset. We used the multiple sclerosis severity score (MSSS) stratifying patients into 10 deciles according to the progression rate over time, with the first decile representing the slowest progression. We defined progressive disease when patients shifted at least one decile up at the end of the 10 years period. Otherwise, patients had stable disease. We compared various parameters between progressive and stable patients as shown below.

Results: Of 99 patients 63 had progressive and 36 had stable MSSS. Of 62 female patients 66% and of 37 male patients 59% were progressive. At SPMS onset age in progressing patients was 42 (38–48) years, disease duration was 12 (9–20) years, and EDSS was 3.0 (2.5–4.0) whereas stable patients were 42 (33.3–47.8) years, disease duration was 7 (4–12.5) years, and EDSS was 5.25 (4.0–6.0); median values (interquartile ranges). During the SPMS period mean annualised relapse rates were 0.14 (±0.37) in progressive patients and 0.18 (±0.39) in stable patients. Of progressing patients 24% never had DMD during the SPMS period whereas all stable patients received DMD at least for one year.

Conclusion: Lower disease burden at SPMS onset has a higher risk of progression requiring special attention for appropriate treatment.

Disclosure: Nothing to disclose.

EPO-637

When to screen for osteoporosis in MS patients? A new risk score

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Background and aims: Due to the demographic development and improved treatment options, the role of comorbidities is of increasing importance in the medical care of patients with MS (pwMS). A higher risk of osteoporosis is well known in chronic autoimmune diseases, and is also described in MS. While there are several screening indications in the elderly or in patients with rheumatoid arthritis, there are no generally accepted recommendations when to perform bone mineral testing in pwMS under the age of 65 years.

Methods: Densitometry (hip and lumbar spine) was performed in 159 pwMS and 81 age- and sex-matched healthy controls (HC) with age ≤65 years. Osteoporosis was defined according to WHO criteria as a bone density of 2.5 SD or more below the mean of young adults. Risk factors were identified by multivariate regression analysis.

Results: Osteoporosis occurred more frequently in postmenopausal pwMS and male pwMS as compared to HC. Besides age, sex, menopausal status in females, body-mass-index (BMI) and smoking, a higher degree of disability - as assessed by the EDSS – was identified as MS specific risk factor, whereas the cumulative steroid dose was not associated with osteoporosis risk. Based on these risk factors, we developed an MS-specific risk score which allows to determine the individual probability of osteoporosis.

Conclusion: This risk score allows individual screening recommendation for pwMS and, subsequently, early prevention of osteoporosis, probably reduction of fractures and morbidity.

Disclosure: Study was supported by a research grant of Roche.

EPO-638

Serum glutamate as a diagnostic biomarker for differentiating between Neuromyelitis Optica and Multiple Sclerosis

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Background and aims: Neuromyelitis Optica (NMO) is an autoimmune disease that predominantly affects the optic nerves and the spinal cord, it was previously regarded as a variant of multiple sclerosis (MS) and still the distinction between both can be sometimes challenging, our study objective was to evaluate of the potential usefulness of serum glutamate as a biomarker in distinguishing NMO from MS patients.

Methods: This cross sectional study included 20 NMO patients, 30 MS patients and 20 matched healthy controls.

	Group 1a (n = 12)		Group 1b (n = 8)		Group 2a (n = 15)		Group 2b (n = 15)	
	Range	Mean ± SD	Range	Mean ± SD	Range	Mean ± SD	Range	Mean ± SD
Age	25 - 57	37.6 ± 8.4	26 - 48	38.7 ± 7.5	24 - 43	35 ± 6.4	26 - 45	33.2 ± 5.8
Age at onset (years)	21-48	31.66 ± 8.03	21-48	34.37 ± 10.41	18-36	26 ± 7.06	18-37	26.53 ± 6.38
Duration of illness	5 m - 15 y	5.4 ± 4.36	5 m – 16 y	4.34 ± 5.31	10 m -16 y	7.03 ± 4.76	6 m - 11 y	5.36 ± 4.36
Period from last relapse to sampling	4 m: 36 m	26.7 ± 21.3 m	1day: 3 m	1.25± 1.03 m	3.47m: 87 m	16.6 ± 21.35 m	1:31 days	13.3 ± 11.6 days
	Range	Median	Range	Median	Range	Median	Range	Median
Total number of relapses	2 - 6	3.5	1 -11	3	1 - 10	3	1 - 11	6
Number of relapses in the last year	0 – 3	1	1 - 3	2	0 – 4	1	1 – 5	3
Total EDSS	1.5 - 7	4	2 - 7	5	1 - 5	2.5	1.5 – 5.5	2.5

m, month, y, year

Table 1 Characteristics of the patients' sample.

Results: Serum glutamate was significantly higher in NMO patients without relapse (16.78±7.38 μg/mL) and NMO patients with relapse (18.40±11.17 μg/ml) compared to controls (3.37±1.28 μg/ml, p<0.01 for both); the serum glutamate was also significantly higher in NMO patients without relapses (16.78±7.38 μg/mL) compared to MS patients without relapses (10.84±3.26 μg/ml, p=0.005). Cut off value of >10.3 μg/ml was found to predict diagnosis of NMO rather than MS in patients without relapses (sensitivity 83.3 % and specificity 60%, p=0.008).

Item	Glutamate μg/mL	Range	P value
Group 1a (n=12)	16.78 ± 7.38	8.2 - 33.6	< 0.0001*
Group 1b (n=8)	18.40 ± 11.17	5.09 - 34.2	0.69**
Group 2a (n=15)	10.84 ± 3.26	5.3 -17.5	< 0.0001***
Group 2b (n=15)	23.69 ± 8.64	10.8- 38.4	0.005*****
Controls (n=20)	3.37 ± 1.28	1.9 - 5.7	0.1*****

P value < 0.05 considered statistically significant.

*comparison between group 1a and controls; group 1b and controls ** comparison between group 1a and 1b*** comparison between group 2a and controls; 2b and controls; 2b and 2a ****comparison between group 1a and 2a *****comparison between group 1b and 2b.

Table 2 Serum Glutamate (μg/mL) in study groups

Glutamate	1a		1b		2a		2b	
	P	R	P	R	P	R	P	R
Age	0.9	0.003	0.9	0.02	0.01	0.63	0.9	-0.03
Age at onset	0.4	0.22	0.7	0.14	0.01	0.61	0.8	-0.07
Period from last relapse	0.6	-0.13	<0.01	-0.84	0.7	0.09	0.7	0.08
Total number of relapses	0.6	0.16	0.8	-0.07	0.3	-0.28	0.5	0.18
No of relapses in the last	0.6	0.16	0.7	0.15	0.8	-0.05	0.15	0.39
EDSS	0.5	0.21	0.8	-0.06	0.3	0.27	0.6	0.13
Total duration of disease	0.4	-0.26	0.8	-0.18	0.02	0.57	0.4	0.21

Table 3 Correlation between glutamate level and different demographic and clinical features among study groups

Conclusion: our study demonstrated the potential value of serum glutamate as a diagnostic biomarker to distinguish NMO patients from MS patients in between relapses.
Disclosure: This study was funded by Cairo University.

EPO-639

Olfactory Function Assessment in Neuromyelitis Optica and Comparison with Multiple Sclerosis

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Background and aims: Olfactory dysfunction may be an occasional presymptomatic sign of demyelinating diseases such as multiple sclerosis (MS), and neuromyelitis optica (NMO). In our study, we aim to investigate and compare the olfactory functions in NMO and MS patients using a validated olfactory test tool and to evaluate the association of olfaction with the disease duration, disease severity and according to the presence of antibodies.
Methods: This study was comprised of 16 NMO patients [9 women (56.2%), 7 men (43.8%)], 26 MS patients [17 women (65.4%), 9 men (34.6%)]; and 35 healthy volunteers [25 women (71.4%), 10 men (28.6%)] were included in the study as the control group. The Connecticut Chemosensory Clinical Research Center olfactory test, developed for assessing orthonasal olfaction, was used.
Results: The odour identification score, smell threshold, and mean olfactory combined scores of the NMO patients were significantly lower than the healthy controls and MS patients. All the odour scores in the control group and the MS group did not differ significantly (p>0.05). There was no difference in the olfaction scores of NMO population with regard to the AQP4-IgG positivity/negativity status.
Conclusion: Our study suggests that olfactory dysfunction might be a part of clinical spectrum of NMO, so physicians treating patients with central nervous system demyelinating diseases should be aware of the potential for olfactory deficit and should counsel their patients accordingly.
Disclosure: None of the authors has any conflict of interest to disclose any sources of fundi. We confirm that we have read the Journal's position on issues involved in ethical publication and affirm that this report is consistent with those guidelines.

EPO-640

Microstructural damage in the cerebellum is related to cognitive impairment in Relapsing-Remitting Multiple Sclerosis.

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Background and aims: Cerebellar pathology has been linked to cognitive impairment (CI) in multiple sclerosis (MS), although it's unclear whether cerebellar pathology is an early or late event in CI development.
Methods: Patients underwent 3T brain MRI (Siemens, Prisma) and neuropsychological evaluation with assessment of the Symbol Digit Modalities Test, the California Verbal Learning Test and the Brief Visuospatial Memory Test. MRI protocol included 1mm isotropic 3D-T1-weighted images for cerebral and cerebellar segmentation, 3D-FLAIR for lesion segmentation and Diffusion-Weighted-Imaging for microstructure assessment, including Diffusion Tensor Imaging and Neurite Orientation Dispersion and Density Imaging.
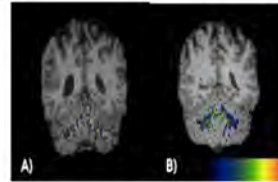
Fig.1 Cerebral MRI: A) MS patient ISO VF scale 0.03. B) Healthy Control ISO VF scale 0.03.
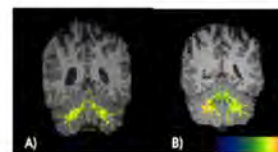
Fig.2. Cerebral MRI: A) MS patient NDI scale 0.1. B) Healthy Control NDI scale 0.1.

Lobule I-IV   Lobule VI   Crus II   Lobule VIIIa   Lobule IX   White matter
Lobule V   Crus I   Lobule VIIb   Lobule VIIIb   Lobule X   Brainstem

Fig.3. Cerebellar segmentation with SUITer.

Results: 54 pts with RR MS [41 females (76%), mean disease duration 11 (8) years, median baseline EDSS 2(1–

3.5)] were prospectively enrolled. Eight patients (15%) were classified as cognitively impaired. Impaired patients had lower brain grey matter volume (GMV) and higher cerebellar lesion volume (LV) than cognitively preserved patients. CI patients had higher isotropic volume fraction (IsoVF) and slightly lower neurite density index in the cerebellar normal-appearing white matter (NAWM) than preserved patients, while no differences were noted in the cerebral NAWM. Using a binary regression model including brain GMV, cerebellar LV and cerebellar IsoVF (Nagelkerge R2 0.44), cerebellar IsoVF was the only independent variable predicting the presence of cognitive impairment (p=0.028).

Conclusion: In RRMS patients, cognitive impairment seems to be related to cerebellar lesional load and microstructural white matter damage leading to cerebellar and cerebral atrophy due to diaschisis phenomena.

Disclosure: Matilde Inglese received grants from the National Institutes of Health, National Multiple Sclerosis Society, FISM and received fees for consultation from Roche, Genzyme, Merck, Biogen and Novartis.

EPO-641

ANALYSIS OF VISUAL ACUITY, CONTRAST SENSITIVITY AND COLOR PERCEPTION IN MULTIPLE SCLEROSIS PATIENTS

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Background and aims: Optic neuritis is a frequent manifestation of MS , which worsens the quality of life of MS patients. Objective: Analyze low contrast visual acuity (VA), contrast sensitivity (CS) and color perception in multiple sclerosis patients with and without optic neuritis (ON).

Methods: MS patients with more than six months of follow-up and clinically stable in the last six months were analyzed. We performed a complete ophtalmologic study comparing patients with ON and without ON.

Results: Of the 50 eyes that were evaluated, 16 had previous optic neuritis and 34 not. Patients who had past ON showed a slight decrease in low contrast VA (greater reduction in the 1.25% test) and in the contrast sensitivity test both monocularly and binocularly comparing with patients without ON. By the Farnsworth Munsell D28 test only 12 patients were normal trichromats in both eyes, 2 patients clearly showed color defects in the blue-yellow axis (tritan) in both eyes, 2 patients showed an undefined pattern in both eyes and the rest of the patients presented different patterns in each eye, however the results obtained in the Ishihara test were normal

Conclusion: Patients with ON have worse low-contrast VA and worse contrast sensitivity than without ON. Chromatic perception was altered in more than 50% of the MS patients independent of previous ON. Farnsworth Munsell D28 test is much more sensitive than the Ishihara test to discriminate chromatic alterations. These visual alterations can affect the quality of life of MS patients.

Disclosure: Nothing to disclose.

EPO-642

Predictors of cladribine effectiveness in multiple sclerosis: a real-world, multicenter, two-year follow-up study

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Background and aims: cladribine is an efficacious immune reconstitution therapy for relapsing Multiple Sclerosis (MS). Nonetheless, according to real-world data from national registries, about one-third of patients experiences relapses or disability progression after 2 or 3 years from cladribine therapy. Here, we explored the impact of baseline features on disease activity and progression in cladribine treated MS patients, in order to identify potential treatment response predictors.

Methods: 243 subjects were enrolled from eight tertiary MS centers in a retrospective observational setting (Table 1, Figure 1). The association between baseline characteristics and non-evidence of disease activity (NEDA-3) at median follow-up was tested via logistic regression models. Each model included the following covariates: sex, age at cladribine start, disease duration, number of treatments before cladribine, relapses in the year before the start of treatment, presence of basal active lesions, basal EDSS, basal lymphocytes, switch or naïve status.

	n=243
Age at cladribine start, mean (SD), range	34.2 (10.0), 15-63
Females, n (%)	163 (66.5)
Years from symptom onset, mean (SD)	6.6 (9.6)
Years from diagnosis, mean (SD)	5.5 (9.5)
Baseline EDSS, mean (SD), range	1.94 (1.3), 0-6.0
ARR previous year, mean (SD)	0.69 (0.78)
Active lesions at baseline, n (%)	138/243 (56.7)
N. of previous DMTs, mean (range)	1.5 (0-7)
naïve, n (%)	71 (29.3)
Switch, n (%)	172 (70.7)
Inefficacy	124 (72)
Safety	31 (18.1)
Other	16 (9.3)
Wash-out, months mean (SD)	3.7 (0.8)
Follow-up, years mean (SD)	1.7 (0.86)
N. of cycles, n (%)	
1	243 (100)
2	204 (83.9)

Table 1: Demographic and clinical characteristics of the patients enrolled in the study.
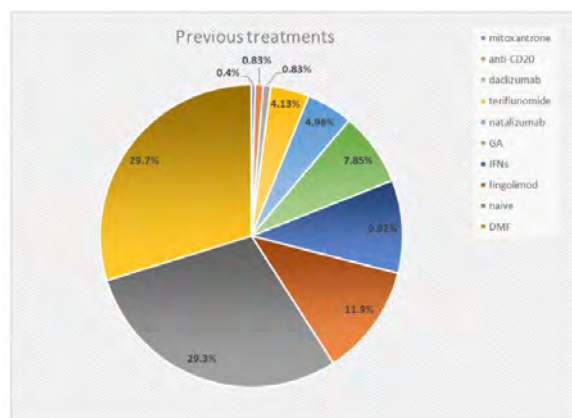
Figure 1: Treatment frequencies before cladribine start

Results: Patients with a higher number of previous therapies had lower odds to retain NEDA-3 after 22 months of follow-up (OR 0.64, 95% CI 0.41- 0.98, p 0.04).

Conclusion: our results point to higher cladribine effectiveness in patients with lower number of therapeutic switches along the disease course.

Disclosure: The Authors report no disclosures related to the presented work.

EPO-643

Vaccinations in patients with multiple sclerosis: a real-world, single-center, experience

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Background and aims: Practical indications to orient proper vaccinations' timing in multiple sclerosis (MS) patients are missing.

Methods: Vaccination schedules were costumed according to national recommendations, clinical-/serological data, ongoing disease modifying drugs (DMDs) or therapy-start urgency. Clinical-relapses and magnetic resonance imaging (MRI) activity within 3 months stated the need of an accelerated cycle. Two different vaccines could be administered together and between the different administrations a 15-days-interval was recommended. Moreover, minimum 2 weeks from last inactivated-vaccine-administration to new therapy-start were required, 4–6 if live-attenuated. Adverse events (AEs) were monitored during the vaccination-cycle.

Results: 195 patients across 2017–2021 were enrolled. 124 patients (63.6%) were addressed to vaccination before a therapy-start/-switch and 108 of them (87.1%) effectively started the protocol before the beginning of the DMDs without any significant deferral. The remaining 71 (36.4%) underwent vaccination during an ongoing-therapy. Regarding AEs during the cycle, 2 (1.0%) patients presented clinical-relapses and 4 (2.0%) MRI-activity. Along the 3 months after the completion of the vaccination-cycle, no relapses were reported and just 1 (0,5%) patient had MRI-activity. The median (95% confidence interval) time for therapy-switch was 65 (32) days. The core vaccination-cycles had a duration of 40 (42) days. Thanks to the growing expertise, we observed a progressive reduction in the time to vaccination-completion, reaching a median of 27 (22) in 2021.

Conclusion: Our study confirmed the optimal tolerance-safety profile of vaccination in MS-patients. A vaccination-cycle of 27 days might be considerate adequate in order to vaccinate MS-patients without interfering with therapy-start.

Disclosure: The authors have no conflicts of interest to declare that are relevant to the content of this article.

EPO-644

Cognitive improvements accompanied with WPAI improvements in OCR-treated patients with RRMS: 96-week CASTING data

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Background and aims: Symbol Digit Modalities Test (SDMT) measures cognitive processing speed, and the Work Productivity Activity Impairment (WPAI) questionnaire is a patient-reported outcome assessing percentage work time missed (absenteeism), impairment while working (presenteeism), overall work impairment (work productivity) and activity impairment, 7 days prior. We report changes in SDMT and WPAI over 96 weeks in patients with relapsing-remitting multiple sclerosis in the Phase IIIb CASTING trial (NCT02861014).

Methods: Patients (Expanded Disability Status Scale score ≤4.0) with a suboptimal response to one or two prior disease-modifying therapies received intravenous ocrelizumab 600mg every 24 weeks for 96 weeks. SDMT was measured at baseline, Weeks 48 and 96. Scores were translated to z-scores with a cut-off of –1 to define cognitive impairment; baseline z-score ≤–1 defined the cognitively impaired subgroup and baseline z-score >–1 the minimally impaired subgroup. WPAI was completed at baseline, Weeks 24, 48 and 96.

Results: Overall baseline mean z-score was –1.36. Mean SDMT score improved from baseline to Week 96 in the overall population; this change was mainly observed in the impaired subgroup (Table 1). Change in SDMT score between subgroups was significantly different (p=0.018). WPAI scores improved from baseline to Week 96 across all WPAI parameters, in both subgroups (Table 2). No correlations were observed between improvement in SDMT and WPAI.

	Overall population			Impaired subgroup (Baseline z-score <=−1)			Minimally impaired subgroup (Baseline z-score >−1)		
	Baseline	Week 96	p value	Baseline	Week 96	p value	Baseline	Week 96	p value
SDMT score, mean (SD)	53.8 (13.0)	55.2 (13.2)	0.005	46.5 (10.3)	49.5 (11.4)	<0.001	65.6 (6.9)	64.1 (10.1)	0.007

SD, standard deviation; SDMT, Symbol Digit Modalities Test.

Table 1: SDMT score at baseline and Week 96 for the overall population, impaired patients and the minimally impaired patients.

	Impaired subgroup (Baseline z-score <=−1)			Minimally impaired subgroup (Baseline z-score >−1)		
	Baseline	Week 96	p value	Baseline	Week 96	p value
Absenteeism, mean (SD)	11.1 (27.1)	5.6 (16.7)	<0.001	10.3 (26.3)	5.7 (18.8)	<0.001
Presenteeism, mean (SD)	24.6 (25.3)	20.5 (24.7)	0.009	16.3 (21.0)	14.1 (18.5)	0.008
Work productivity, mean (SD)	28.9 (29.1)	22.7 (25.7)	<0.001	20.3 (25.1)	17.5 (23.5)	0.004
Activity impairment, mean (SD)	33.9 (28.4)	27.5 (28.1)	<0.001	26.6 (26.6)	20.9 (23.2)	<0.001

SD. standard deviation: WPAI. Work Productivity Activity Impairment.

Table 2: WPAI score per parameter (absenteeism, presenteeism, work productivity, activity impairment) at baseline and Week 96 in impaired and minimally impaired patients.

Conclusion: There was significant improvement in SDMT score over 96 weeks of ocrelizumab treatment mainly observed in the cognitively impaired subgroup. WPAI scores improved in all four domains over 96 weeks of ocrelizumab treatment, with greatest improvement in absenteeism.

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MS and related disorders 6

EPO-645

The effect of highly active immunotherapy on inflammation and tissue repair in aggressive multiple sclerosis

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Background and aims: The effect of highly active immunotherapies, including autologous-hematopoietic-stem-cell-transplantation (AHSCT), on the resolution of CNS inflammation and on tissue repair in aggressive multiple sclerosis (MS) is unknown. The aim of this study was to compare the time-of-onset and the extent of the immunosuppressive effect of different immunotherapies on white-matter microstructure and brain volumes in aggressive MS.

Methods: In this ongoing study, aggressive MS patients underwent 3T-MRI at the time of disease breakthrough, at 6 and 12 months after treatment initiation. Changes in lesion volume(LV), percentage-brain-volume-change(PBVC) and multi-compartment spherical-mean-technique(SMT) diffusion metrics of the normal-appearing-white-matter were evaluated.

Results: Nineteen patients were included in the analysis (8 AHSCT,5 ocrelizumab,3 natalizumab,3 cladribine). Median number of baseline gadolinium-enhancing lesions was 4(IQR=2-6). At 6 months, LV decreased by 1.8mL(SD=4.6) in AHSCT-treated patients and by 0.73mL(4.7) in the other treatment group, with PBVC of -2.25%(1.79) and -0.63%(0.90) respectively (p=0.04), with the most pronounced volume reduction in the grey-matter (-3.4%vs-0.33%). At 6 months, 0/8 AHSCT-patients had new/gadolinium-enhancing lesions vs 4/11 in the other treatment group. Average extra- mean and transversal diffusivities decrease, which reflects reduction in extracellular water and increased myelin integrity, was more pronounced in the NAWM of AHSCT patients (-0.03vs-+0.03 and -0.03vs-0.002 respectively,p<0.01). Between 6 and 12 months, no differences were noted in PBVC between the two groups (-0.88%AHSCT vs1.27%other treatments) and SMT metrics continued to ameliorate in the AHSCT group. Mean EDSS reduction was -1.1(1.5) in AHSCT vs-0.3(1.3).

Conclusion: AHSCT allows faster and more pronounced resolution of CNS inflammation than other highly active immunotherapies and facilitates myelin repair.

Disclosure: Boffa G was supported by a research fellowship FISM - Fondazione Italiana Sclerosi Multipla 2019/BR/016 and financed or co-financed with the '5 per mille' public funding. Inglese M received grants NIH, NMSS, FISM; received fees for consultation from Roche, Genzyme, Merck, Biogen and Novartis.

EPO-646

Prevalence of Myelin Oligodendrocyte Glycoprotein antibodies in patients with Optic Neuritis: a single-center experience

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Background and aims: The prevalence of optic neuritis (ON) related to myelin-oligodendrocyte-glycoprotein-abs (ON-MOG) and Aquaporin-4-abs (ON-AQP4) is still debated in the literature. We investigated the presence of these autoantibodies among all patients with a diagnosis of ON and we compared their characteristics to ON related to Multiple Sclerosis (ON-MS).

Methods: 36 patients diagnosed with ON were recruited in our three-years single-centre prospective study. MOG-Abs and AQP4-Abs were assessed with a Live Cell-Based assay. Demographic and clinical characteristics of patients diagnosed with ON-MOG were compared to those diagnosed with ON-MS, using Chi-squared or Mann-Whitney-U test as appropriate. Kaplan-Mayer survival curves were performed to compare the occurrence of relapses between the two groups. (Fig.1)

Figure 1. Demographic and clinical features of patients.

Results: The prevalence of ON-MOG, ON-AQP4 and ON-MS was 27.8% (10/36), 5.5% (2/36) and 66.7% (24/36) respectively. (fig.2). Female sex was prevalent both in the ON-MOG and ON-MS patients (70% and 62.5% respectively). ON-MOG were characterized by older age (p=0.02), severe visual loss(p=0.02), bilateral presentation (p=0.007) and optic disc swelling (p<0.001), compared to ON-MS. At onset, ON-MS patients exhibited more encephalic/spinal cord MRI lesions (p=0.002). (fig.2) The relapse risk was lower in the ON-MOG group than ON-MS patients. (p=0.02). (fig.3)
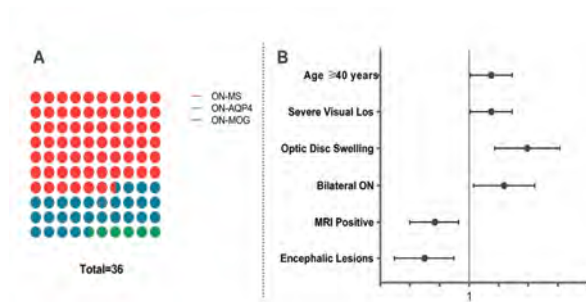
Figure 2. A, Study cohort of ON. 66.7% where CIS or MS patients (MS-ON), 27.8% presented MOG-Abs (MOG-ON) and 5.5% AQP4-Abs (AQP4-ON). B, binary logistic regression was performed to test clinical and demographical characteristics between MOG-ON and MS-ON
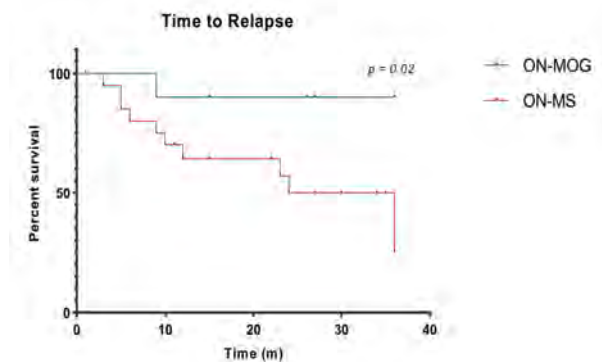
Figure 3. Time-to-event analysis using Kaplan-meier survival plot. Log-rank test was performed to test differences in the occurrence of relapse from onset between ON-MOG and ON-MS.

Conclusion: The occurrence of ON-MOG for about one-third of all patients diagnosed with ON suggested the need to test MOG-abs routinely. Moreover, the ON-MOG group exhibited a lower relapse risk compared to the ON-MS group. The data needed to be confirmed in a larger population study with longer follow-up.

Disclosure: MT has served on Scientific Advisory Boards for Biogen, Novartis, Roche, Merck, and Genzyme; has received speaker honoraria from Biogen Idec, Merck, Roche, Teva, Sanofi-Genzyme, and Novartis; and has received research grants for her Institution from Biogen Idec, Merck, Roche, and Novartis. PI has served on scientific advisory boards for Biogen Idec and has received funding for travel and/or speaker honoraria from Sanofi-Aventis, Biogen Idec, Teva, and Novartis. DP received advisory board membership, speaker's honoraria, travel support, research grants, consulting fees, or clinical trial support from Almirall, Bayer Schering, Biogen, Celgene, Excemed, Genzyme, Merck, Mylan, Novartis, Sanofi, Roche, and Teva.

EPO-647

Cut-off Values of Timed Up and Go Test and 5-Repetition Sit-To-Stand Test for Predicting Fall Risk in MS

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Background and aims: Falling is an important problem that causes injuries, reduces quality of life and limits daily living activities in multiple sclerosis (MS). Therefore, it is important to identify patients at higher risk for falling. Subjective measures such as The Falls Efficacy Scale International may provide insights on fall risk, however patients' statements in the questionnaires may not always reflect their true condition. We aimed to provide cut-off values for two practical and objective measures for predicting fall risk in MS patients.

Methods: 84 MS patients (40.98±9.33 years) were evaluated with timed up-and-go test (TUG) and the five-repetition sit-to-stand test (5STST). Patients were classified as "fallers" or "non-fallers" according to their falling history in the last 3 months. Cut-off values of TUG and 5STS for discriminating between fallers and non-fallers were calculated.

Results: Twenty-five patients (30%) were identified as fallers and 59 (70%) as non-fallers. Both TUG and 5STST tests provided significant discrimination between groups, having an area under ROC curve of 0.738 and 0.730, respectively (p<0.001). The optimal cut-off value was "7.2 s" for TUG (sensitivity: 0.68; specificity:0.64) and "11.2 s" for 5STST (sensitivity 0.68; specificity: 0.64).

Conclusion: Performing worse than 7.2 s in TUG or 11.2 s in 5STST may indicate higher fall risk in MS patients. Both tests can be performed rather quickly in the clinical practice, and these cut-off values may help detecting patients who need to be more careful in their routine lives or who may highly benefit from balance training or such rehabilitative approaches.

Disclosure: No conflict of interest.

EPO-648

Myelin oligodendrocyte glycoprotein (MOG) antibody-associated disease, induced by pembrolizumab, both or neither?

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Background and aims: Immune checkpoint inhibitors (ICI) are increasingly used in Oncology due to their high efficacy. Neurologic immune-related adverse events are rare, including recent reports of central nervous system (CNS) demyelinating disease.

Methods: N/A

Results: A 50-year-old female, with a history of lung cancer treated by chemotherapy, presented with progressive left facial hemi-hypoesthesia. The brain magnetic resonance imaging (MRI) showed a left pontine enhancing lesion, interpreted as a metastasis. Treatment with pembrolizumab was initiated. After five months, she developed progressive right homonymous hemianopia. The brain and spinal cord MRI revealed demyelinating lesions involving the supratentorial (juxtacortical, subcortical, periventricular, corpus callosum), infratentorial (pons) and spinal cord compartments. The cerebrospinal fluid (CSF) showed a lymphocytic pleocytosis and CSF-restricted oligoclonal bands. Serum MOG antibodies were positive (title 1:40). Infectious and paraneoplastic investigations were negative. Pembrolizumab was interrupted and the patient received high dose intravenous corticosteroids. There was clinical remission as well as radiological improvement, with reduction in lesion size and count, resolution of the Gad-enhancement and no new lesions. MOG-antibody title remained stable at reassessment four months later.

Conclusion: This case highlights the clear temporal association between initiation of pembrolizumab and multifocal CNS demyelination. To our knowledge, this is the first report of demyelinating disease and positive MOG antibodies in a patient treated with ICI. It also raises key discussion points, most notably: i) the role of pembrolizumab either as a causative agent or as a revealing factor of a pre-existing auto-immune disease; ii) MOG antibodies as an epiphenomenon or a marker of a chronic demyelinating disease.

Disclosure: Nothing to disclose.

EPO-649

Real-world experience of ocrelizumab in MS in the Turkish population: A single-center study

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Background and aims: Ocrelizumab is a humanized monoclonal antibody effective against CD20 positive B cells, approved by the FDA in 2017 to treat RRMS and PPMS. Despite these clinical studies, real-life data on ocrelizumab are limited.

Methods: We conducted a retrospective single-center study in Turkey. We obtained medical record data of patients who received at least one infusion of ocrelizumab and were followed for one year before and after treatment initiation.

Results: 240 MS patients were included in our study (58.75%) RRMS, (21.25%) SPMS, and (20%) PPMS). Median follow-up was14 months (range, 4–42). 92% of all patients received another DMT or immunosuppressant (98.58% of RRMS, 100% of SPMS, 64.58% of PPMS) prior to treatment with ocrelizumab. ARR before and after initiation of ocrelizumab for both the RRMS and SPMS groups (RRMS, 0.8 vs. 0.1; SPMS, 0.44 vs. 0.04). The most common reason for switching to ocrelizumab was clinical and/or radiological activity. NEDA status at year one was achieved in 88.54% of the RRMS population, and disability progression was found at 12.77% in the same MS subtype. Despite premedication (97.91%), infusion-related reactions were reported in (15.41%). The most common infection in our study was COVID-19 infection (18.33%), followed by urinary and upper respiratory tract infections.

Conclusion: According to the first real-world preliminary study in the Turkish MS population using ocrelizumab, it is a well-tolerated, safe, and effective treatment agent in suppressing disease activity in both RRMS and progressive MS forms.

Disclosure: There is no conflict of interest.

EPO-650

Humoral immune response to SARS-CoV-2 booster vaccination in patients with multiple sclerosis and healthy controls

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Background and aims: Booster vaccination against SARS-CoV-2 is recommended for everyone approximately six months after the last vaccination, including for patients with multiple sclerosis (pwMS).

Methods: In this prospective single-center study on 171 pwMS and 38 healthy controls (HC), who had all received two vaccinations, SARS-CoV-2 IgG response was measured in the month before and 2–4 months after booster vaccination. PwMS were categorized as follows: untreated (N-DMT, n=17), receiving DMT with expected humoral response (er-DMT: all but S1PM and CD20mAB; n=65) or no expected humoral response (nr-DMT: S1PM, CD20mAb; n=89).

Results: Absolute antibody levels (median 253.5 U/ml [range 0.4–2500]) before booster vaccination were similar between HC (516 [49.5–2500]), N-DMT (648 [0.4–2345]) and er-DMT (858.5 [25.6–2500]), while nr-DMT had significantly lower antibody levels (32.8 [0.4–2500]; p<0.001). After booster vaccination, the absolute antibody levels were as follows: HC (2500 [2190–2500]), N-DMT (2500 [32.2–2500]), er-DMT (2500 [1951–2500]), and nr-DMT (548 [0.4–2500]; p<0.001). We did not find differences in antibody levels after homologous (n=96; 2500 [0.4–2500]) and heterologous (n=53; 2500 [0.4–2500]) booster vaccination. Time to revaccination (6 months [1–10] was not associated with antibody level. Four of 13 (30.8%, all CD20mAB) seronegative pwMS remained seronegative after booster vaccination. Seven patients reported a SARS-CoV-2 infection (1 N-DMT, 6 nr-DMT). Efficacy rate for preventing hospitalization or death was 100% in all groups.

Conclusion: Humoral response to SARS-CoV-2 booster vaccination in pwMS is excellent. While reduced by immunosuppressive DMT, protective humoral response is still expected in the majority of patients.

Disclosure: Nothing to disclose.

EPO-651

Impaired antisaccades are more strongly associated with fatigue score than cognitive impairment in multiple sclerosis

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Background and aims: Antisaccade error rate may be an easily accessible biomarker for multiple sclerosis (MS) cognitive impairment. This study aimed to investigate its correlation with cognitive dysfunction, fatigue, and mood disorders.

Methods: Patients with familial forms of MS underwent video-oculography (Eyelink camera) and a battery of neuropsychological tests (Paced Auditory Serial Addition Test (PASAT), Stroop test, Symbol Digit Modalities Test (SDMT), Digit Span, Modified Fatigue Impact Scale (MFIS), Hospital Anxiety and Depression scale (HAD)). Univariate and multivariate linear regression models with a random effect on siblings were used to estimate the influence of neuropsychological scores and other confounding variables on antisaccade error rate.

Results: 49 patients (40 female, median age: 36, median EDSS: 2) were included. Error rate on antisaccades was 22% (16) (mean (SD)). Univariate analyses showed: i) negative correlations with attention, working memory and processing speed (SDMT (−0.6, p=0.002) and PASAT (−0.43, p=0.03)) but not with executive functions (Stroop interference score); ii) positive correlations with fatigue (MFIS score (0.37, p=0.001)), depression (HAD depression subscale (1.74, p=0.011)) and age (0.66, p=0.012). At multivariate analysis, MFIS score was the only variable significantly associated with antisaccade error rate (p=0.026, aR2=0.21).

Variables	Univariate analysis			Multivariate analysis (Forward selection)		
	Estimates	CI [CI95%]	p	Estimates	CI [CI95%]	p
Demographic						
Age	0.66	[0.15, 1.18]	0.012 *	-	-	-
Gender	2.46	[-9.77, 14.70]	0.693	-	-	-
MS clinical score						
EDSS	2.15	[-0.61, 4.91]	0.127	-	-	-
Cognitive scores						
PASAT	-0.43	[-0.82, -0.04]	0.03 *	-0.21	[-0.52, 0.09]	0.16
SDMT	-0.6	[-0.99, -0.21]	0.002 **	-	-	-
Digit Span forward	-1.85	[-4.21, 0.50]	0.123	-	-	-
Digit Span backward	-2.46	[-5.00, 0.08]	0.057	-	-	-
Stroop Word	0.37	[-0.6, -0.15]	0.001 ***	-	-	-
Stroop Color	-0.53	[-0.84, -0.22]	0.001 ***	-	-	-
Stroop Interference	-0.29	[-0.90, 0.33]	0.363	-	-	-
Psychological scores						
MFIS	0.37	[0.16, 0.57]	0.001 ***	0.33	[0.04, 0.63]	0.026 *
HAD depression score	1.74	[0.40, 3.07]	0.011 *	-	-	-
HAD anxiety score	0.91	[-0.21, 2.03]	0.112	-	-	-

Conclusion: Although antisaccade testing is considered a measure of inhibitory control, it does not correlate with the Stroop interference score in our cohort. Fatigue should be taken into account if we aim to use antisaccade error rate as a surrogate of cognitive impairment.

EPO-652

Physical Activity in Young Relapsing Remitting Multiple Sclerosis Patients – A case-control study

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Background and aims: Physical activity (PA) is beneficial in Multiple Sclerosis (MS); nevertheless, previous studies report lower PA rates among these patients. This study aims to assess PA in relapsing-remitting MS (RR-MS) patients. Fatigue and sleep were also evaluated.

Methods: Objective PA was measured during a 7-day period in which 23 MS patients (EDSS<4.0) and 15 healthy controls (HC), with mean ages of 27.87 ($\pm$4.7) and 27.2 ($\pm$3.9) years-old, respectively, used a Xiaomi Mi Band 5® armband (MiBand) that reported daily step count, kilometer (km) count, active time, and hours of sleep. Subjective assessment was derived from the International Physical Activity Questionnaire (IPAQ) long version. Quality of sleep and fatigue in MS patients were assessed using the SATED score and the Modified Fatigue Impact Scale (MFIS), respectively.

Results: Neither IPAQ nor MiBand found differences in PA between MS patients and HC: MS patients had an active time of 84.81 minutes/day, 6,712 steps/day, and 4.28 km/day, while HC had 79.29 min/day, 5,538 steps/day and 3.65 km/day. People who self-reported higher PA levels had higher measured active time (r 0.502; p=0.005). MS patients with higher scores in MFIS showed lower PA levels (r $-$ 0.477 and p=0.021) and SATED scores (r $-$ 0.700; p<0.001). Most participants reported a decrease in PA due to the pandemic.

Conclusion: Self-reported physical activity correlated with objective measurements while more fatigability and less sleep correlated with lesser PA in RR-MS patients. Adequate evaluation is important to promote healthy physical activity habits. A bigger sample may reveal differences regarding PA levels.

Disclosure: The authors have no conflict of interest to disclose.

EPO-653

Ocrelizumab treatment in multiple sclerosis patients with anti-HBc (+)

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Background and aims: In clinical practice, we are increasingly faced with the risk of reactivation of latent pathogens associated with disease-modifying (DMD) treatment in patients with MS. The risk of HBV (hepatitis B virus) reactivation is high in patients treated with B-cell lowering drugs. The use of nucleoside or nucleotide (AN) analogues is recommended for the prophylaxis of HBV reactivation.

Methods: At the Department of Neurology in Zabrze, we treat 6 patients with multiple sclerosis and latent HBV infection with ocrelizumab. Patients concomitantly treated with an anti-CD20 antibody and a nucleoside analogue (entecavir). Two patients with primary progressive multiple sclerosis (PPMS) and 4 patients with relapsing-remitting multiple sclerosis (RRMS). Mean age 56.8 years and average EDSS disability 4.8 points. in the PPMS group and the mean age of 39.8 years and the average EDSS disability level of 3.5 pt. in the RRMS group. Entecavir administered orally at a dose of 0.5 mg once daily.

Results: All anti-HBc (+) patients treated with ocrelizumab and entecavir showed no elevated levels of transaminases or evidence of liver dysfunction. In patients with MS and latent HBV infection, no progression of disability on the EDSS scale was observed during ocrelizumab and entecavir treatment, and no relapse was seen in patients with RRSM.

Conclusion: Latent HBV infection did not reactivate during treatment with ocrelizumab and entecavir.

Disclosure: Nothing to disclose.

EPO-654

4-year follow-up of multiple sclerosis patients treated with cladribine: Clinical outcomes and third-year course

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Background and aims: Cladribine is the first oral immune reconstitution therapy for relapsing multiple sclerosis (RRMS) and is only administered in 2 treatment courses approximately 1 year apart. A third-year course is still controversial.

Objective: To analyse demographics, clinical outcomes, discontinuations and additional treatment courses in MS patients treated with cladribine tablets during 4 years of follow-up.

Methods: Observational prospective study in patients with RRMS starting treatment with cladribine since June 2018. Demographics, clinical characteristics and safety were collected.

Results: Among the 90 patients currently using oral cladribine 67% were females with a mean age of 44 years old, a disease duration of 7,9 years and a basal EDSS of 2.01. 25% of patients were naïve, 51% switched from first line therapies and 24% from second line. From the four patients having a relapse in year 1, two discontinued the treatment and switched to antiCD20 therapy. One patient has two relapses in the first two years and switched to ocrelizumab. 92% patients were free of clinical activity in years 1/2 and 82% in years 3/4. Four of seven patients suffering from a relapse in years 3/4 have received a third treatment course with very mild adverse events. Adverse events during the 4 years follow-up were mild, with the most frequent being headache, fatigue and hair thinning. There was no case of serious infection, no opportunistic infections

Conclusion: Cladribine is effective and safe in the real-world setting. A third treatment course were efficacious and very well tolerated. No new safety signals were observed.

Disclosure: C. Oreja-Guevara has received honoraria for speaking and/or consultancy from Biogen, Celgene, Sanofi Genzyme, Merck, Roche, Teva and Novartis.

EPO-655

Multiple sclerosis: Analyses of intrathecally produced antimicrobial antibodies suggest unique role of EBV

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Background and aims: Epstein-Barr virus (EBV) is the leading cause of multiple sclerosis (MS), but the underlying mechanisms currently remain unclear. Patients with MS typically show a polyspecific intrathecal immunoglobulin (Ig)G synthesis, part of which targets microbial antigens. Intrathecal antimicrobial antibody production can be detected by elevated antibody indices (AIs). To explore a possible link between EBV and intrathecal antibody production, we systematically analyzed seroprevalences and frequencies of elevated AIs for EBV as compared to other microbes in patients with MS.

Methods: IgG against Epstein-Barr nuclear antigen-1, the EBV viral capsid antigen (VCA) and 10 further microbes was measured by enzyme-linked immunosorbent assays in paired serum and cerebrospinal fluid samples of 50 patients with MS. AIs were calculated according to standard formula.

Results: While all patients with MS were EBV-seropositive, none of the other 10 microbes showed a similarly high seroprevalence. In marked contrast, the frequency of intrathecally produced EBV antibodies was lower than that of the other investigated microbes, especially with regard to the respective seroprevalences (Table).

Microbe	Seroprevalence Antibody positive/total number of patients tested (%)	Intrathecal AI >1.5 AI >1.5/number of seropositive patients (%)	Frequency AI >1.5/ Seroprevalence
Epstein-Barr nuclear antigen-1	50/50 (100%)	5/50 (10%)	0.10
EBV viral capsid antigen	50/50 (100%)	5/50 (10%)	0.10
Varicella zoster virus	47/50 (94%)	19/47 (40%)	0.43
Rubella virus	44/50 (88%)	18/44 (41%)	0.47
Measles virus	41/50 (82%)	15/41 (37%)	0.45
Mumps virus	35/50 (70%)	13/35 (37%)	0.53
Herpes simplex virus	33/50 (66%)	3/33 (9%)	0.14
Parvovirus B19	26/50 (52%)	19/26 (73%)	1.40
Cytomegalovirus	21/50 (42%)	2/21 (10%)	0.23
Toxoplasma gondii	12/50 (24%)	2/12 (16%)	0.67
Tick-borne encephalitis	8/50 (16%)	0/8 (0%)	not applicable
Borrelia burgdorferi	3/50 (6%)	1/3 (33%)	not calculated due to low numbers

AIs>1.5 are considered elevated

Table

Conclusion: Given the universal seroprevalence of EBV in MS, the frequency of intrathecally produced antibodies against EBV in patients with MS is paradoxically low. These findings point towards a unique role of EBV in MS and may be explained by the hypothesis that B lineage cells responsible for intrathecal antibody production are primed during acute EBV infection, that is, at a time point when anti-EBV antibody producing cells have not yet been generated, to subsequently enter the central nervous system of patients with MS.

EPO-656

Macular thickness and volume in multiple sclerosis patients using optical coherence tomography angiography

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Background and aims: Optical Coherence Tomography Angiography (OCTA) is a new imaging method to detect changes and alterations in retinal vascular density in neurodegenerative and inflammatory diseases. The aim is to investigate vascular changes detected by optical coherence tomography angiography (OCT-A) in multiple sclerosis (MS) subjects with and without optical neuritis We aimed to investigate vessel density in macular and papillary regions over two years after an initial demyelinating event (IDE).

Methods: 28 MS patients clinically stable within the last six months and with a follow-up of more than six months were examined. A complete ophthalmological study was carried out, assessing both visual function and retinal microvasculature using the OCTA Heidelberg Spectralis device. We compared patients with and without optic neuritis.

Results: Of the 56 eyes tested, 18 had optic neuritis in the past and 38 had no previous optic neuritis. The mean vessel thickness in macula in patients with previous optic neuritis was clearly lower ($230.33\mu \pm 22.29\mu$) than in patients without previous optic neuritis ($250.47\mu \pm 25.18\mu$) (p-value=0.007) (Fig.1 y 2). All sectors except the temporal quadrant and the nasal and lower outer sectors are significantly reduced.
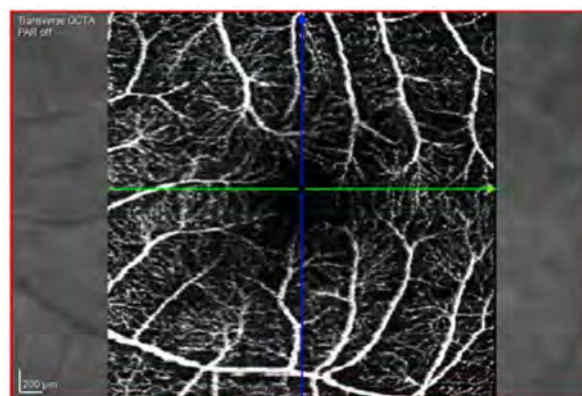
Superficial Vascular Complex (SVC)
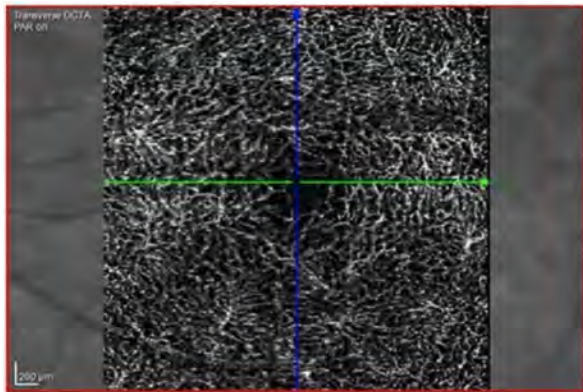
Deep Vascular Complex (DVC)

Conclusion: MS patients with ON have a significant retinal vascular loss compared without previous neuritis. Retinal vessel density could represent a novel early biomarker to monitor the MS pathological burden.

Disclosure: Johnny Quezada Sánchez, Elda Alba Suarez, Judit Díaz Díaz, Irene Gómez Estévez and Enrrique Santos Bueso have nothing disclosure. Celia Oreja Guevara has received speaker and consultation fees from Biogen Idec, BMS, Celegene, Sanofi, Novartis, Roche, Merck and Teva.

EPO-657

Intrathecal IgM synthesis as a risk factor of a second relapse of multiple sclerosis - a prospective observational study

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Background and aims: The objective of the study was to evaluate the importance of intrathecal IgM synthesis as a risk factor for second relapse of multiple sclerosis (MS).

Methods: We conducted a single-center prospective observational cohort study at the Department of Neurology, University Hospital Ostrava, Ostrava, Czech Republic. Intrathecal IgM synthesis was demonstrated as cerebrospinal fluid-restricted oligoclonal IgM bands and calculated using the Reiber, Auer and Öhman formula and IgM index.

Results: A total of 61 patients after the first demyelinating event were enrolled into the analysis, 37 women (61%). The median age at the disease onset was 32 years (interquartile range [IQR] 25–42), median disease duration was 2.8 years (IQR 2.4–3.5) and median follow-up was 2.6 years (IQR 2.1–3.3). 38 (62%) patients experienced a second relapse of the MS with median 312 days (IQR 208–412). The Kaplan–Meier analysis did not demonstrate any significant difference in the time to second relapse in patients with positive vs. negative intrathecal IgM synthesis expressed by any method. Similarly, the Cox regression analysis was not significant.

Conclusion: Our analysis did not confirm the presence of intrathecal IgM synthesis to be an independent risk factor for a second MS attack in our prospective cohort.

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Neurogenetics 2

EPO-658

A detailed phenotypic description of a series of patients with genetically confirmed CANVAS

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Background and aims: Cerebellar ataxia, neuropathy and vestibular areflexia syndrome (CANVAS) presents in middle life as a slowly progressive ataxia, a sensory neuropathy and a bilaterally impaired vestibulo-ocular reflex. Patients report imbalance, sensory disturbance and/or dizziness. Many patients associate chronic cough. Diagnosis is based on clinical findings, recently supported by a biallelic AAGGG expansion in the replication factor complex subunit 1 (RFC1). We present a series of 9 genetically confirmed carriers of biallelic repeat expansions in RFC1.
Methods: We have retrospectively collected data to describe symptoms, physical examination, family history, complementary tests and prognosis.
Results: All patients are Caucasian, predominantly male. The median age of symptom onset, excluding cough, is 55. Imbalance is the main complaint in 5 patients, followed closely by sensory disturbance in 4 patients. All patients present biallelic repeat expansions in RFC1, 3 patients deny family history. All patients present ataxia with instability and broad-based gait, some also present dysmetria, dysphagia or altered proprioception. 7 patients refer hypoesthesia and hypopalesthesia, 6 describe paresthesia. Vestibular symptoms are less frequent. Associated symptoms include chronic cough, altered reflexes, pruritus and syncope. The main radiologic finding is mild cerebellar atrophy in 7 patients. All patients who underwent ENG present sensory axonal polyneuropathy. Patients require walking aids after a median of 8 years from debut.
Conclusion: CANVAS is very likely to be underdiagnosed. We must include CANVAS in our differential diagnosis for late onset ataxia and sensory neuropathy, taking into account that genetic diagnosis is now available.
Disclosure: No conflicts of interest.

EPO-659

A puzzling case of treatable adult-onset leukodystrophy

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Background and aims: A 44-year-old male with a mild intellectual delay presented with a subacute onset of spastic paraparesis, rapidly progressing in a few months, along with episodes of urinary incontinence and erectile dysfunction. Current neurological examination showed a bilateral lower limbs weakness associated with marked spasticity. Tone and strength were normal at upper limbs. Deep tendon reflexes were brisk at both upper and lower limbs, and Hoffman and Babinski sign were present bilaterally. Cranial nerves and sensory examination were normal. The patient underwent spinal cord MRI, which was normal, and brain MRI, that showed an extensive T2 hyperintensity, involving bilaterally and symmetrically the white matter of the centrum semiovale and corona radiata, mainly of the posterior lobes, with corresponding T1 isointense signal. LMNB1 duplication and a targeted resequencing gene panel for leukodystrophies resulted negative.
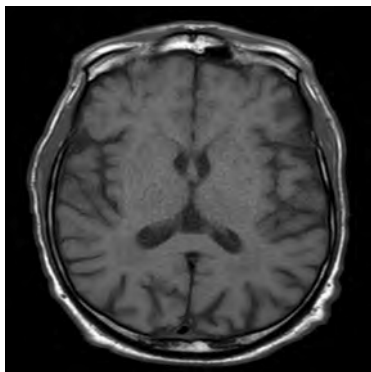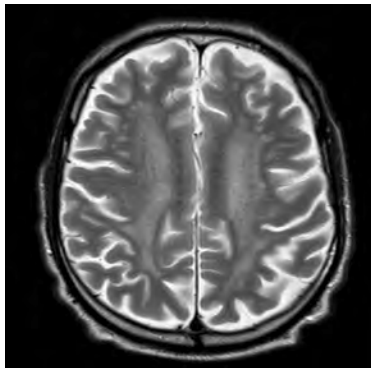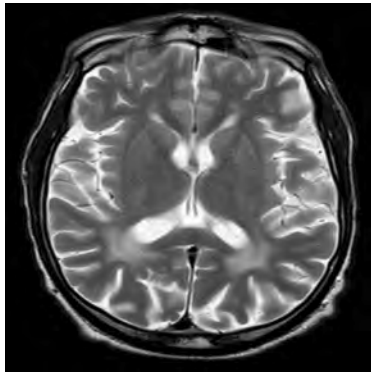
Methods: DNA of the patient was then sent for Next-generation clinical exome sequencing.

Results: Genetic testing showed compound heterozygosity for c.842 C>T and c.143 T>C of PAH gene mutations, prompting dosage of plasma phenylalanine (Phe), which was 10 times above the upper reference limit.

Conclusion: Phenylketonuria (PKU) is an autosomal recessive inborn error of Phe metabolism, causing excessive Phe levels interfering with brain growth, myelination, and neurotransmitter synthesis. The Italian National newborn screening programme, including PKU, was commenced only in 1992, after the birth of our patient.

Disclosure: As this is one the rare treatable causes of intellectual and motor disability, PKU should always be excluded in patients presenting with leukodystrophy and cognitive and motor impairment.

EPO-660

Cognitive function and quality of life in a cohort of HSPs patients

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Background and aims: HSPs are a group of neurogenetic disorders characterized by spasticity and weakness of the lower limbs. Although motor features are well described, there are few studies about non-motor symptoms. Our aim is to assess cognitive abilities and the impact of the disease on quality of life in a cohort of HSP patients.

Methods: 25 patients with genetically confirmed HSP diagnosis (60% SPG4, 15% SPG7, 10% SPG5, 15% others) and 20 matched healthy controls were evaluated. All patients underwent clinical evaluation through SPRS-scale and a battery of cognitive tests (MMSE, MOCA, Stroop Test, Trail Marking Test, Weigl Sorting Test, FAB, FAS Test, RAVLT). To evaluate quality of life Short-Form Health Survey 36, Hospital Anxiety and Depression Scale, Beck Inventory Scale were administered. To evaluate pain we used VAS and BPI. FACIT was used to assess fatigue.

Results: The HSP patients studied did not have intellectual disability but they had worse performances in memory, fluency and attention. Interestingly the visuospatial abilities were the most affected executive functions. FAB seems to be insufficiently sensitive to screen for diminished executive functions whereas WEIGL was useful to evaluate diminished problem solving and visuospatial abilities deficits. Cognitive changes did not correlate with disease severity. Depression, anxiety and fatigue were significantly increased in our patients and correlated with quality of life.

Conclusion: Cognitive impairment in our patients was subtle, with predominant involvement of executive functions. Pain, fatigue and depression severely contribute to the overall disease burden suggesting that non-motor symptoms should be regularly evaluated and treated.

Disclosure: Nothing to disclose.

EPO-661

Expanding the genetics of ALKUS´s syndrome: compound heterozygosity for two deleterious variants in SMG8 gene.

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Background and aims: SMG8 pathogenic homozygous variants have been described to cause a novel neurodevelopment disorder characterized by microcephaly, facial dysmorphism, and variable congenital and eye malformations. This is now defined as Alzahrani-Kuwahara syndrome (ALKUS). The ALKUS´s phenotype greatly resembles that associated with SMG9, which comprises severe global developmental delay, microcephaly, facial dysmorphism, and congenital heart and eye malformations. Only nine subjects from five families with ALKUS have been described to date.

Methods: We present a patient with two pathogenic variants in compound heterozygosity in the SMG8 gene and the literature revision about previously published reports of this entity.

Results: We describe a 27 year old male, of a non-consanguineous family, with no family history of developmental delay or dysmorphism, whose genetic analysis showed two variants, c.1,159C>T (p.Arg387*) and c.2,407del (p.Arg803Glyfs*10), in the SMG8 gene, classified as pathogenic and probably pathogenic, respectively. As described by Fatema Alzahrani et al in a series of 8 patients, our patient had global developmental delay, facial dysmorphism and limb disproportion. Additionally, our patient had lower limb spastic paraparesis, marked osteotendinous hyperreflexia with extensor plantar response bilaterally and paretic gait.

Conclusion: This is the first case of ALKUS described in the European population and only the tenth worldwide. Our patient resembles the phenotype described by Fatema Alzahrani et al, however he is the first patient with two SMG8 in compound heterozygosity. Moreover, it is the first patient to exhibit markedly pyramidal signs and gait disorder as part of the phenotype

Disclosure: Nothing to disclose.

EPO-662

Horizontal Gaze Palsy with Progressive Scoliosis: Neuroimaging findings and the presence of a novel missense variant.

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Background and aims: We present a novel homozygous missense variant in the ROBO3 gene, causing horizontal gaze palsy with progressive scoliosis (HGPPS). HGPPS is a rare congenital disorder, caused by loss of ROBO3 protein function. ROBO3 plays an important role in decussation during the development of the hindbrain. We aimed to delineate extensively the genotypic and phenotypic characteristics associated with this novel mutation.

Methods: A young Afghan male with severe scoliosis and horizontal gaze palsy displayed neuroimaging findings pathognomonic for HGPPS. In order to uncover a genetic cause for the disorder, his DNA was sampled and whole exome sequencing took place. Video material of the clinical syndrome was obtained for in-depth description.

Results: A novel missense variant, p.Leu446Phe, was detected. It was deemed pathogenic given consanguinity in the patient's parents, absence in databases of normal variation and the unmistakable phenotype. Neuroimaging in this patient showed characteristic tenting of the fourth ventricle, split pons sign and butterfly medulla.
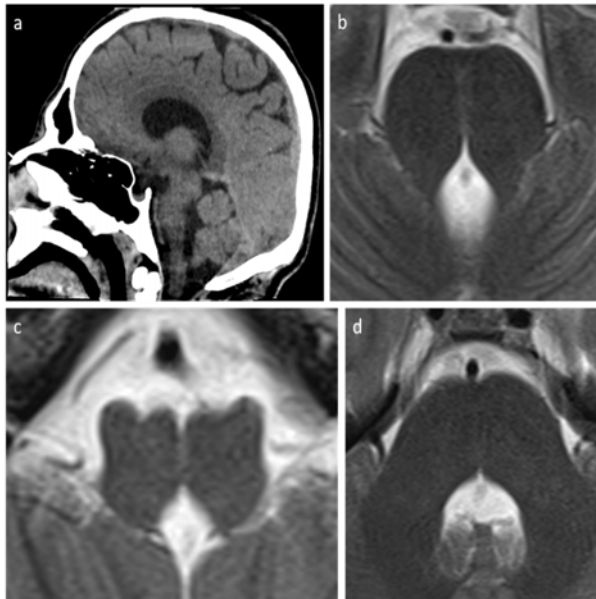
Neuroimaging findings showing midline hypoplasia of the pons and medulla. We see a split pons sign, butterfly medulla sign, tenting of 4th ventricle.

Full spine radiograph showing severe sinistroconvex scoliosis.

Conclusion: We describe a patient with absent conjugate horizontal eye movements and severe scoliosis, born to consanguineous parents. A split pons sign and a butterfly-shaped medulla prompted the suspicion of HGPPS. Subsequent genetic analysis revealed the presence of a novel homozygous missense variant in the ROBO3 gene. Our case illustrates the importance of familiarity with the typical imaging findings of HGPPS, as well as the value of genetic investigations in patients with early-onset eye movement disorder and progressive scoliosis, and sheds new light on the allelic and phenotypic variability of the disease.

Disclosure: Nothing to disclose.

EPO-663

Prophylactic allogeneic hematopoietic stem cell therapy for CSF1R-related leukoencephalopathy

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Background and aims: Introduction Allogeneic hematopoietic stem cell therapy (allo-HSCT) has appeared to arrest progression of leukoencephalopathy in patients with pathogenic variants in CSF1R (1–4). We report the results of prophylactic HSCT aimed at preventing the development of leukoencephalopathy in a healthy carrier.

Methods: A 31 year old healthy woman was heterozygous for the pathogenic CSF1R variant NM_005211.3(CSF1R): het c.1754-2A>G previously detected in her family. At her request and following extensive deliberations, HSCT was performed August 2020, using the Mayo Clinic reduced intensity conditioning regimen (1) with a 9/10 HLA-matched unrelated male donor.
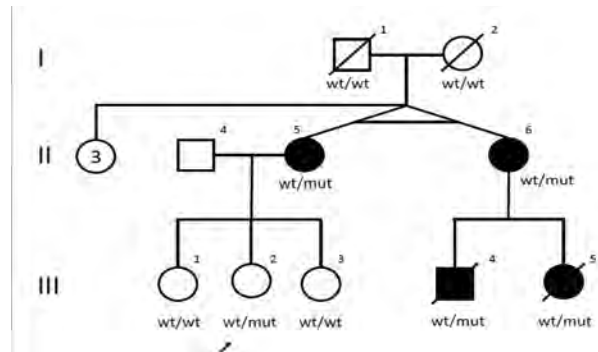
Figure 1. Pedigree of family with patogenic CSF1R variant

Results: Complete donor chimerism was reached at day +27. Lumbar puncture at +12 months showed 99 % donor chimerism in the cerebrospinal fluid. No manifestations of graft versus host disease were seen during the first year. Neurologic testing was unremarkable prior to and at +12 months after HSCT. Serial cerebral MRIs before and at +12 months after HSCT were normal. Neuropsychological testing at -5 and +12 months was unremarkable. One year after transplantation, she developed a self-limiting course of inflammation in the brain and medulla. An allogeneic immunological reaction was suspected.

Conclusion: To our knowledge, this is the first report of prophylactic allo-HSCT in a patient with a pathogenic variant in CSF1R. At +17 months, evidence of leukoencephalopathy is absent. This might be due to variable expressivity and does not prove that the intervention was efficacious. It remains unresolved whether asymptomatic individuals with pathogenic CSF1R variants should be offered such treatment.

Disclosure: The autors declare no conflicts of interest.

EPO-664

Monoallelic carriers of WWOX mutations show mild intellectual disability and attention deficit hyperactivity disorder

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Background and aims: Mutations in the WWOX (WW domain-containing oxidoreductase) gene have been associated with different autosomal recessively inherited disorders including SCAR 12 (spinocerebellar ataxia type 12) and WOREE (WWOX-related epileptic encephalopathy). We show for the first time, that monoallelic carriers of WWOX mutations may present a phenotype characterized by mild intellectual disability, attention deficit hyperactivity disorder and increased CSF tau levels.

Methods: We collected clinical data from three monoallelic carriers. In one of them, studies were completed with neuropsychological evaluation, brain MRI and lumbar puncture. Moreover, we isolated skin-derived fibroblasts to measure WWOX levels through Western blotting.

Results: The proband is a 3-years old child with WOREE and two pathogenic mutations in WWOX (c.689A>C and c.136C>T). His older brother, his mother and his grandfather are all carriers of the variant c.689A>C (Figure 1). These carriers showed mild learning difficulties and attention problems. The grandfather consulted to our Neurology Department because of memory complaints. Neuro-psychological evaluation showed a low limit IQ as a consequence of impaired working memory and sustained attention. Complementary studies showed a normal brain MRI and EEG and an increased tau (1558pg/ml; normal range<360pg/mL) and phospho-tau (105pg/ml; normal range: <61pg/mL) levels in CSF. Furthermore, we performed protein expression analyses from skin-derived fibroblasts showing WWOX haploinsufficiency (Figure 2)
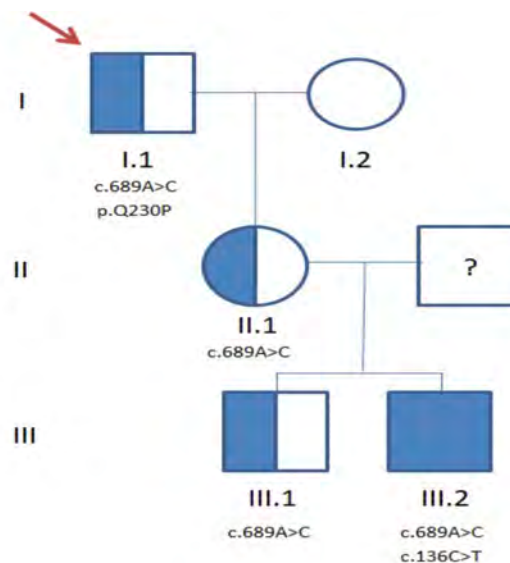
Pedigree of the family. III.2 has a WWOX-related epileptic encephalopathy. His older brother (III.1), his mother (II.1) and his grandfather (I.1) all show the variant c.689A>C and mild learning difficulties with attention deficit.
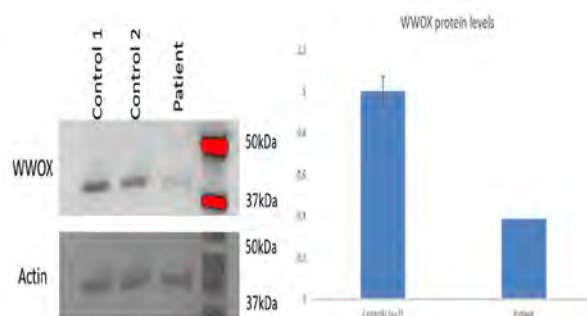
Western blot of skin-derived fibroblasts from patient I.1 showed an haploinsufficiency of WWOX protein.

Conclusion: Here, we expand the neurological phenotype associated to the c.689A>C WWOX mutation, showing a milder phenotype in monoallelic carriers.

Disclosure: No conflicts of interest.

EPO-665

DNAJC30-Leber's Hereditary Optic Neuropathy: further expanding the clinical phenotype

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Background and aims: DNAJC30 recessive mutations have been associated with Leber's Hereditary Optic Neuropathy (LHON) and Leigh syndrome. The majority of patients carry the c.152A>G mutation and from Eastern Europe pointing to a founder effect. Incomplete penetrance, male prevalence and high percentage of clinical relevant recovery (CRR) are described (Stenton et al., 2021)

Methods: We here report the ophthalmological phenotype of 5 male Italian patients, all from East Europe ancestry, carrying the same homozygous c.152A>G mutation. The peculiar phenotype of one case who also developed an autoimmune/demyelinating disease is discussed.

Results: Age at onset was 19.2±6.3 and the interval between eyes 3.25±0.96 weeks. Visual acuity at nadir was 0.02±0.02-OD and 0.05±0.05-OS, at last follow-up 0.32±0.39-OD and 0.45±0.43-OS. All patients were treated with idebenone and showed CRR. Average RNFL thickness at last visit was 49.4±12.5-OD and 49.2±13.8-OS. One patient presented, 4 year after LHON onset, vertigo and ataxia. Brain MRI disclosed area postrema hyperintensity with gadolinium enhancement and cerebrospinal fluid evaluation oligoclonal bands. Iv steroids were administered with complete recovery of the neurological symptoms, regression of the brain lesion and improvement of visual function. Another similar episode occurred after one year with evidence of right area postrema enhancing hyperintensity. A therapy with rituximab was added.

Conclusion: We here report the ophthalmological and neurological features of a case series of 5 DNAJC30-LHON patients further expanding the clinical phenotype to the possible co-occurrence of an autoimmune disease, as already reported for classical mtDNA-related LHON co-occurring with Multiple Sclerosis

Disclosure: Consultancies for Chiesi Farmaceutici, Regulatory Pharma Net and Thenewway srl; speaker honoraria from Santhera Pharmaceuticals, Chiesi Farmaceutici, Regulatory Pharma Net, Thenewway srl, First Class srl and Biologix. The study is supported by the research grant RF-2018-12366703 to LC

EPO-666

Tremor and frontal epilepsy secondary to gain-of-function mutation in SCN8A: a case report

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Background and aims: SCN8A mutations are quite rare and produce different clinical manifestations. The most frequent is epilepsy but also developmental delay and movement disorders

Methods: We introduce the case of a 14 year-old patient who has tremor and seizures. Genetic test indicated a gain-of-function mutation in SCN8A.

Results: A Chinese adolescent, who was adopted at the age of 16 months (familiar history unknown) came to our center for the first time at the age of 12 due to tremor and nocturnal generalized tonic-clonic seizures beginning at 3 years of age. It is predominantly resting and postural tremor, also kinetic. It mainly affects the eyelids, tongue and upper limbs. It is associated with trunk ataxia and mild intellectual disability. Blood tests (metabolic and thyroid test), cerebrospinal fluid (neurotransmitters), urine (including SAICAR and biotinidase tests), cranial magnetic resonance imaging (MRI) and electroencephalogram were performed in other centers without pathological findings. In our center, we repeated a blood test and an extended neurophysiological study (electroencephalogram, somatosensorial evoked potentials, electromyogram) which were normal. The first genetic test, array- CGH 60 k, was normal. Lastly, epileptic encephalopathies gene panel revealed a gain-of-function mutation in SCN8A. She was admitted to the intensive care unit twice because of increased disabling tremor. Currently, 3 years later, she is clinically stable from both epilepsy and tremor. Her treatment consists on carbamazepine, zonisamide, and propranolol.

Conclusion: The clinical variability produced by SCN8A mutations should make us include it in the differential diagnosis of epileptic-dyskinetic disorders. Thus, genetic testing is essential for an accurate diagnosis.

Disclosure: Nothing to disclose.

EPO-667

Niemann Pick disease type C: two variants of unknown significance in a patient with atypical presentation

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Background and aims: Niemann Pick disease type C (NPC) is a rare autosomal recessive disease affecting lysosomal storage, caused by mutations in NPC1 and NPC2 genes. We present a case carrying two variants of unknown significance (VUS) of NPC1.

Methods: Review of the patient's clinical history

Results: A 52 year-old man developed progressive change in his voice, difficulty in swallowing and in looking downward. He reported bilateral progressive sensorineural hearing loss from his young age. Neurological examination showed: dysphonia, dysphagia, supranuclear vertical gaze paralysis, upper limb asymmetric dysmetria, diffuse hyporeflexia. Abdominal ultrasonography showed splenomegaly while neuropsychological testing highlighted disexecutive deficits. His sister had bilateral progressive sensorineural hearing loss from a young age; the rest of his family history was negative. We investigated genetic causes of deafness and NPC disease. The blood levels of oxysterols were increased while two heterozygous VUS, c.481C>T (p.Arg161Trp) and c.1070C>T (p.Ser357Leu), were found in the NPC1 gene. The Filipin test showed the typical biochemical alteration. Each parent carried one of the two VUS found in the proband; both exhibited normal blood oxysterol levels and did not complain any neurological symptoms.

Conclusion: We confirmed the pathogenic role of p. Ser357Leu substitution in NPC disease pathogenesis. We also suggest that p.Arg161Trp variant, which was not previously reported, could be considered pathogenic for NPC. In our patient, these mutations lead to an atypical NPC presentation.

Disclosure: The authors declare no rilevant disclosures for the present work.

EPO-668

Multi-infarct encephalopathy as the debut of CADASIL during COVID infection

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Background and aims: CADASIL (brain autosomal dominant arteriopathy with subcortical infarcts and leukoencephalopathy) is the most frequent genetic cause of stroke and vascular dementia in adults. Cerebral ischemic pathology usually starts in the 4th decade as a single subcortical stroke, although some cases of subcortical multi-infarcts have been described, especially in patients with a concomitant inflammatory state (systemic infection, surgery, severe trauma, etc.)

Methods: Case-report of a CADASIL patient with a multi-infarct presentation in the context of SARS CoV 2 infection and review of the literature.

Results: A 56-years-old-man, without cardiovascular risk factors, who consulted to emergencies due to more than 24 hours' duration of dysarthria and one week of myalgia and fever. An initial progression with mild right hemiparesis, worsening of dysarthria and dysphagia, and a marked bradipsychia stood out. Laboratory and X-ray studies showed pneumonia due to SARS-CoV-2 infection. Neuroimaging (CT and MRI) showed signs of severe microangiopathy and multiple bilateral acute infarcts in the internal border zone. Mutation of the NOTCH3 gene was demonstrated.

Figure 1: Craneal Magnetic Resonance at second day from his admission. In the upper row, diffusion sequences (DWI) with images of bilateral acute infarcts in the internal border area. In the lower row, T2 FLAIR sequence with typical CADASIL findings, hyperintense lesions in white matter, predominantly frontal, with involvement of both temporal poles and external capsule
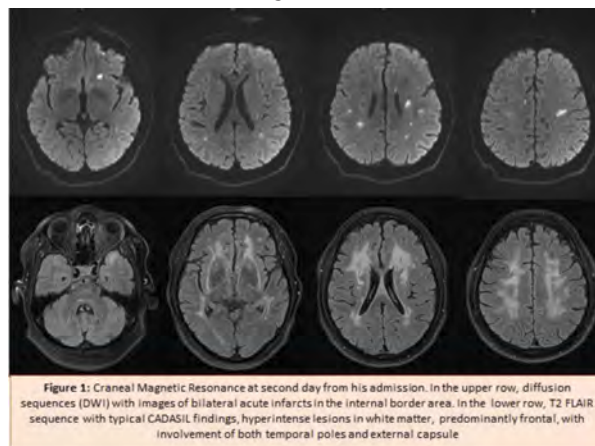
Figure 1: Craneal Magnetic Resonance at second day from his admission.

Conclusion: NOCH3 receptors are found on smooth muscle cells of the microvasculature cerebral. In CADASIL, degeneration occurs with stenosis and impaired flow autoregulation, a tendency to hypoperfusion, and microthrombotic complications. In a severe infection because of cytokines, hypoxemia, and hypotension, as in this case COVID-19, sensitivity to ischemia is increased. Last year, several similar cases of CADASIL diagnosis during covid infection have been published. They had similar clinical presentations and a neuroimaging with border zone multi-infarcts.

Disclosure: The authors have nothing to disclose.

Neuroimaging 2

EPO-669

Cerebral fat embolism syndrome as a consequence of acute pancreatitis

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Background and aims: Fat embolism syndrome (FES) is an uncommon syndrome caused by embolization of fat particles into multiple organs including the brain. Most common etiology is trauma, such as orthopedic and aesthetic surgeries, although it is also associated with non-traumatic causes like acute necrotizing pancreatitis. Multiple embolisms result in global cerebral hypoperfusion and sometimes, the death of the patient.

Methods: We present a clinical case compatible with FES.

Results: We describe the case of a 70-year-old woman with a prolonged hospital stay. The patient is admitted to have an endoscopic retrograde cholangiopancreatography (ERCP) which ends in an acute pancreatitis with multiple infectious complications. After a few hours, she presents a progressive decrease in the level of consciousness. The main findings in the brain scan were the presence of fatty density material in several vascular territories, suggestive of massive cerebral fat embolism. This caused a decrease in the cortical density of the right hemisphere, evidence of hypoperfusion/ischemia and edema. Clinically, it led to a deep coma of the patient, causing her death within a few hours.
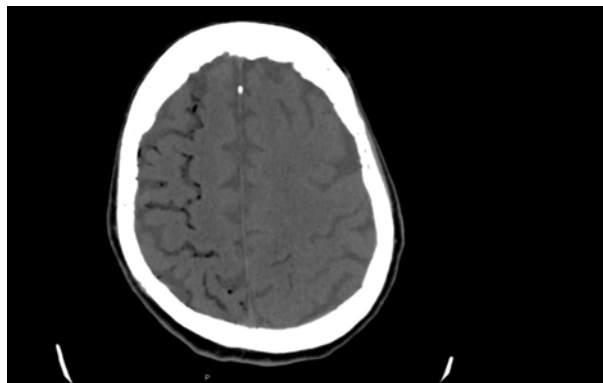
Fatty density material (around 40 Hounsfield units (HU)) in several vascular territories

Conclusion: Although there is no specific aethiological treatment, an urgent brain scan should be done in this kind of patients when there is a neurological worsening event in order to establish a diagnosis and adequate support treatment.

Disclosure: The incidence of FES is very low in patients without a previous traumatic history, although it can occur as a complication from other pathologies such as pancreatitis or osteomyelitis, and also as a side effect of some drugs (corticosteroids, propofol).

EPO-670

Information Processing Differences in Deep Sedation May Indicate Subjective Differences in Anaesthetic States

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Background and aims: Through identifying similarities in the characteristics of low conscious states induced via anaesthetics with dissimilar mechanisms of action, it may be possible to elucidate unitary characteristics of deep sedation and unique characteristics of respective anaesthesia.

Methods: Here, we analyse the information flow from the resting state functional MRI data obtained in healthy volunteers during sedation induced by three distinct anaesthetic agents: propofol (n=16), ketamine (n=9) and dexmedetomidine (n=10), reanalysing data presented in Bonhomme et al., 2016. Leveraging a framework based on principles from information theory, we calculated the global and local active information storage (AIS) and transfer entropy (TE). The whole brain and regional group differences for baseline and sedation were assessed using pair-wise two sample t-test. Results were considered significant at $p < 0.025$ at the whole brain level, and at $p < 0.05$ (FDR corrected for 214 ROIs) at the regional level.

Results: Our results show a decreased capacity of information storage across frontal, thalamic and sensory areas and common and distinct alterations in information flow between each of the three sedation conditions when compared to wakefulness.
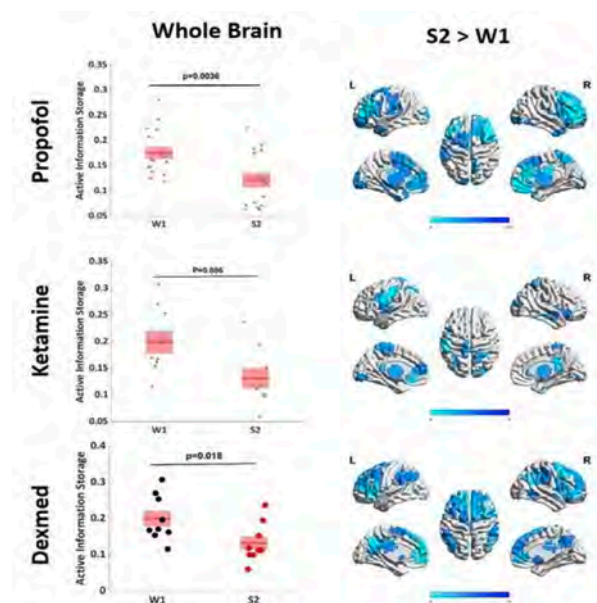
Figure 1: (A) Global Active Information Storage (AIS) for propofol (n=16), ketamine (n=9) and dexmedetomidine (n=10) during wakefulness and sedation. (B) Local changes in AIS for propofol, ketamine and dexmedetomidine comparing sedation to normal wakefuln
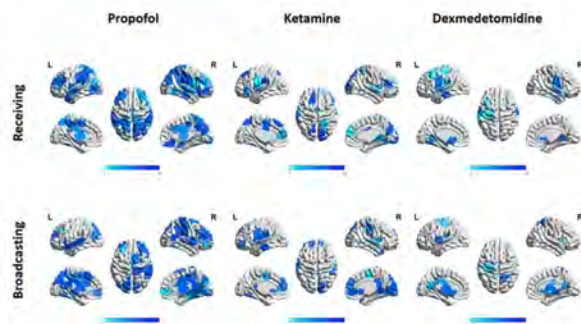
Figure 2: Differences in Transfer Entropy (TE) between normal wakefulness and sedation induced by propofol (n=16), ketamine (n=9) and dexmedetomidine (n=10).

Conclusion: The widespread disruption of TE during propofol sedation likely underlies the absence of conscious content. The relative maintenance of AIS in the dorsolateral frontal cortex during ketamine sedation may indicate conscious processing unrelated to the environment in a dream-like state. The preservation of AIS in the thalamus during dexmedetomidine sedation could be associated with the capacity of subjects to rapidly recover responsiveness to external stimulation.

Disclosure: Nothing to disclose.

EPO-671

COMBINING MORPHOLOGICAL AND TOPOGRAPHIC CHARACTERISTICS OF WHITE MATTER LESIONS TO DIFFERENTIATE MS FROM VASCULAR MIMICS

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Background and aims: Focal vascular white matter lesions (WMLs) are more prevalent than demyelinating lesions in adults. We aimed to identify MRI WMLs characteristics to help the differentiation between multiple sclerosis (MS), migraine and patent foramen ovale (PFO).

Methods: Patients with MS (n=20, 15F, mean age: 47 years), migraine (n=18, 14F, age: 47 years) and PFO (n=18, 13F, age: 44 years) with WMLs on a previous scan, underwent a 3T brain MRI. WMLs were first identified on FLAIR and classified considering location, size (punctate/>3mm/>10mm) and shape (round/oval); subsequently, hypointensity on T1-w and the central vein sign (CVS) on SWI were assessed. Linear regression was used to compare lesion characteristics, logistic regression to assess the association between lesion characteristics and diseases.

Results: A total of 497, 224 and 340 WMLs were found in MS, migraine and PFO, respectively. Characteristics of WMLs in MS were: periventricular location, size >10mm, oval shape, T1-hypointensity and CVS, while in the other two diseases were punctate and with round shape, mostly located in the frontal and deep white matter regions. The combination of periventricular location, oval shape, larger size, T1-hypointensity and CVS best discriminated MS from migraine (accuracy/specificity/sensitivity: 83%/79%/86%, p<0.001), while a frontal location, oval shape, T1-hypointensity and CVS best discriminated MS from PFO (accuracy/specificity/sensitivity: 89%/86%/91%, p<0.001).

Conclusion: The combination of morphological and topographic WMLs characteristics can accurately differentiate MS from vascular MRI-patterns. This might be helpful in case of association of demyelinating and vascular lesions, frequent with aging.

Disclosure: R. Cortese was awarded a MAGNIMS-ECTRIMS fellowship in 2019. N. De Stefano has received honoraria from Biogen-Idec, Bristol Myers Squibb, Celgene, Genzyme, Immunic, Merck Serono, Novartis, Roche and Teva for consulting services, speaking, and travel support. He serves on advisory boards for Merck, Novartis, Biogen-Idec, Roche, and Genzyme, Immunic and he has received research grant support from the Italian MS Society. F. Aprile, G. Severa, A. Covelli, M. Battaglini, J. Zhang, L. Luchetti, G. Gentile, M.L. Stromillo, M. Ulivelli, D. Plantone, A. Giorgio have nothing to disclose

EPO-672

Multimodality brain imaging used to increase the accuracy of invasive epilepsy treatment

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Background and aims: Despite extensive presurgical work up of epilepsy surgery candidates not all treatment procedures are successful. In case of treatment failure re-analysis can help to identify reasons why procedures failed. Use of multimodality brain imaging tools allows to combine initial and re-analysis results, thus providing a clearer image of the underlying networks aiding the decision-making process towards a more accurate invasive treatment.

Methods: Multimodality imaging software was developed bringing brain imaging and functional neurophysiological datasets acquired during presurgical work up of a patient in the same co-ordinate system. Integration with 3D-mapping of stereo-EEG (SEEG) recordings translates invasive neurophysiology recordings into the same 3D-space. By combining pre- and post-resection brain images and the results of both SEEG recordings clinicians were able to evaluate the initial treatment strategy against the re-analysis imaging results what improved the decision making towards reoperation.

Results: Illustrations how the integration of non-invasive imaging with 3D-mapping of depth electrode EEG recordings may guide the re-evaluation of candidates for surgical treatment are shown. Combination of pre- and post-resection datasets showed that following a first SEEG implantation and subsequent resection 1) in case of reoperation the original resection has to be enlarged 2) part of the original network now has to be treated as an independent epileptogenic focus.

Conclusion: The CE-marked software applications made it possible to combine data of all intracranial and non-invasive brain imaging of two different presurgical work ups in the same patient and appears to be a valuable tool in the re-analysis of surgical candidates aimed at reoperation.

Disclosure: A. Colon is member of the advisory board of CNSprojects. P. Ossenblok is founder of CNS projects.

EPO-673

Resting state fMRI correlates of pseudobulbar syndrome in Amyotrophic Lateral Sclerosis (ALS)

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Background and aims: Emerging evidence reveals that pseudobulbar syndrome (PBS), consisting in inappropriate emotional responses, is mainly related to bilateral degeneration of corticobulbar tracts. We aimed at investigating brain functional connectivity (FC) correlates of PBS in a cohort of patients with amyotrophic lateral sclerosis (ALS).

Methods: 27 ALS patients (13 with PBS; 14 without PBS) and 26 healthy controls underwent a multimodal MRI approach, including resting state functional MRI (RS-fMRI) and voxel-based morphometry (VBM) analyses, to investigate functional and structural abnormalities underlying PBS.

Results: In patients with PBS compared to those without PBS, seed-based analysis revealed increased FC between cerebellar peduncle and posterior cingulate cortex (PCC); FC between cerebellar peduncle and left medial frontal gyrus was decreased. Moreover, patients with PBS showed reduced FC between left precentral gyrus and anterior cingulate cortex, between right precentral gyrus and left inferior frontal gyrus, and between pons and right insula. Independent component analysis revealed: decreased FC in the right middle temporal gyrus (MTG), right precuneus and PCC and an increased FC in the left MTG (default mode network); increased FC in bilateral precuneus (frontoparietal network), right precentral gyrus (sensory-motor network), right insula (salience network) in patients with PBS compared to patients without PBS. VBM analysis showed no significant differences.

Conclusion: Our findings suggest that alterations of extra-motor networks may be related to PBS in ALS. In particular, the alterations of FC showed in fronto-cerebellar circuits of PBS patients confirmed that alterations of fronto-temporo-ponto-cerebellar circuits underlay PBS in ALS.

Disclosure: Nothing to disclose.

EPO-674

Screening for early clinical changes in premanifest Huntington's disease

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Background and aims: There is increasing evidence that olfactory dysfunction is a common symptom in Huntington's disease (HD). The aim of this study was to assess if a quick and easy olfactory and cognitive test battery might be able to detect early changes in premanifest HD mutation carriers.

Methods: We consecutively recruited HD patients, HD mutation carriers and their healthy caregivers (as controls) during their routine control in a specialized outpatient clinic at the Medical University of Innsbruck, Department of Neurology, Austria. All participants had to score more than 25/30 points on the Mini Mental State Examination, without other neurological or non-neurological diseases compromising olfaction or cognition. Participants were tested on the Sniffin' sticks 16-items identification test and performed a cognitive battery including the trail making task part A and B and the symbol digit modality task.

Results: We included 36 manifest HD patients, 14 premanifest HD mutation carriers, and 19 controls. As expected, HD patients performed significantly worse on olfactory and cognitive tasks compared to both other groups (all p-values<0.01). Furthermore, in our small study cohort, carriers showed significant impaired odor identification compared to controls (p=0.002), while there were no differences in cognitive tasks between carriers and controls (all p-values>0.1).

Conclusion: This study suggests that olfactory dysfunction might be an early non-motor symptom possibly preceding cognitive changes in HD carriers.

Disclosure: Nothing to declare. The authors have no conflicts of interest.

EPO-675

Radiomic Signatures on Magnetic Resonance Imaging in Glioblastoma to Identify distinct Survival Classes

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Background and aims: The goal of the study is to assess radiomics in glioblastoma multiforme (GBM) patients and use them to stratify patients into groups based on overall survival.

Methods: 102 patients with GBM were selected from The Cancer Genome Atlas (TCGA)-GBM dataset and a total of 704 radiomic features from three subregions i.e., tumor enhancement area, tumor non-enhancement area, peritumoral edema area were obtained from multiparametric MRI using MATLAB 2019b. These radiomic features were subjected to 3 feature reduction methods: LASSO, Elastic Net, and Ridge with LASSO outperforming the other two. Further, a 10-fold cross validated LASSO model was built to predict overall survival (OS).
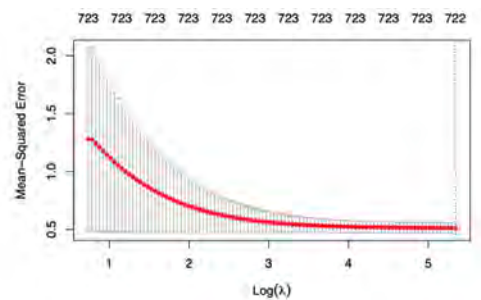
LASSO regression showing the lambda plot

Results: There were 38 female (mean age 54.7; SD±17.3) and 63 male patients (mean age 59.5; SD ± 11). Patients had a median OS of 559 days (range: 5–2, 126 days). The Kaplan Meier plot shows the survival probability divided into three categories, i.e., low (survival <12 months), medium (SURVIVAL between 12–36 months), high (SURVIVAL >36 months). Patients who lived for >36 months were stratified in low-risk of death group, while those who died before 12 months were stratified in high-risk group. There is a 50% probability that patients in low-risk group will survive for ~50 months while in high-risk group the probability of survival is <12 months (p<0.0001).
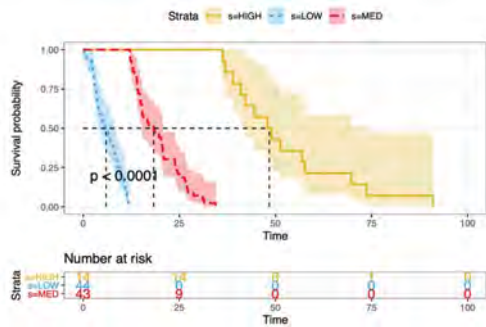
Kaplan Meir plot showing the stratification of three survival classes

	RMSE.Min.	RMSE.1st.Qu.	RMSE.Median	RMSE.Mean	RMSE.3rd.Qu.	RMSE.Max.	RMSE.NA.s
ridge	8.055390	10.334367	13.30225	14.88318	17.43958	27.87897	0
lasso	8.377530	9.913153	11.51076	14.15678	15.59330	34.10225	0
elastic	8.107193	10.962809	14.02682	14.79481	15.83443	27.45424	0

We can see that lasso has lowest median RMSE (root mean square error).

Comparison of the performance of three different regularization methods

Conclusion: LASSO feature reduction of radiomic parameters enhances survival prediction and hence has potential as a practical imaging biomarker.

Disclosure: I or the other co authors do not have any potential conflict of interest and the study is self funded.

EPO-676

Endolymphatic space is age-dependent

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Background and aims: Knowledge of the physiological endolymphatic space (ELS) is necessary to estimate the pathological endolymphatic hydrops (ELH) in vestibulocochlear syndromes such as Meniere's disease. The current study focused on age-dependent changes of the ELS.

Methods: 64 ears of 32 healthy vestibular controls with an age range between 21 and 75 years (HC, 20 females, 45.8 ± 17.2 years) were examined. Diagnostics included neuro-otological assessment, video-oculography during caloric and head-impulse test, as well as intravenous delayed gadolinium-enhanced MRI of the inner ear (iMRI). Analyses provided semi-quantitative (SQ) visual grading and automatic quantitative segmentation of ELS volume [3D, mm3] using a deep learning-based segmentation of the inner ear's total fluid space (TFS) and volumetric local thresholding (VOLT).

Results: Following a 4-point ordinal scale [3, 5], a mild ELH (grade 1) was found in 21/64 (32.8%) ears. Age and ELS were found to be significantly positively correlated for the inner ear ($r(64)= .33$, $p< 0.01$), and vestibulum ($r(64)= 0.25$, $p<0.05$). For the cochlea, the values correlated positively without reaching significance. HC group correlation results are visualized in Figure 1.
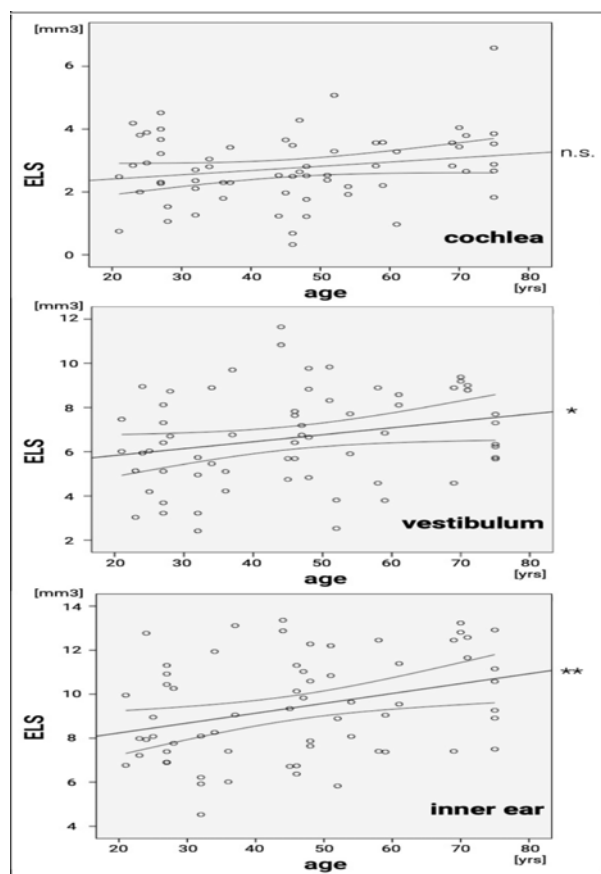
Figure 1: Scatter plot for age and 3D-quantification of the endolymphatic space correlation results for cochlea (top), vestibulum (middle) and inner ear (bottom). Significant linear agreements are marked (*) for p<0.01.

Conclusion: Following a 4-point ordinal scale, a mild ELH (grade 1) was found in 21/64 (32.8%) ears. Age and ELS were found to be significantly positively correlated for the inner ear (r(64)=033, p<0.01), and vestibulum (r(64)=0.25, p<0.05). For the cochlea, the values correlated positively without reaching significance.

Disclosure: There are no relationships, activities, or interests to disclose.

EPO-677

Diagnostic accuracy of Cerebral [18F]FDG PET in Atypical Parkinson Diseases

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Background and aims: Atypical parkinsonian disease (APD) often presents with Parkinson symptoms but have a much worse long-term prognosis. The diagnosis is presently based on clinical features but a cerebral positron emission tomography (PET) scan with [18F]fluoro-2-deoxy-2-D-glucose ([18F]FDG) may assist in the diagnosis of APD such as multiple system atrophy (MSA), progressive supranuclear palsy (PSP), corticobasal syndrome (CBS) and Lewy body dementia (DLB). Only few studies have evaluated the sensitivity and specificity of [18F]FDG PET for separating the illnesses in a mixed patient population, which we aim to assess in a retrospective material.

Methods: We identified 156 patients referred for a cerebral [18F]FDG PET for suspicion of APD during 2017–2019. The [18F]FDG PET was analyzed by a nuclear medicine specialist blinded to clinical information. The reference standard was the follow-up clinical diagnosis (follow-up: 6–72 months).

Results: The overall accuracy for correct classification was 74%. Classification sensitivity (95% CI), specificity (95% CI), positive and negative predictive values (95% CI), for MSA (n=20), DLB/PDD (n=19), and CBS/PSP (n=69) respectively, were 1.00 (0.83–1.00), 0.91 (0.85–0.95), 0.62 (0.49–0.74), 1.00 (0.97–1.00) for MSA; 0.81 (0.61–0.93), 0.96 (0.91–0.99), 0.81 (0.64–0.91), 0.96 (0.92–0.98) for DLB/Parkinson's disease with dementia (PDD); and 0.62 (0.49–0.73), 0.97 (0.90–0.99), 0.93 (0.82–0.99), 0.77 (0.71–0.82) for CBS/PSP.

Conclusion: Our results support the use of [18F]FDG PET for the clinical diagnosis of APD with moderate to high sensitivity and specificity. Use of [18F]FDG PET may be beneficial for prognosis and supportive treatment of the patients and useful for future clinical treatment trials.

Disclosure: None of the authors report any financial disclosures or conflicts of interest.

EPO-678

Hyper-perfusion mapping with computerized tomography in non-convulsive status epilepticus: a case-control study.

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Background and aims: People with NCSE may have acute-onset focal neurological symptoms, which prompt brain imaging, including Computerized Tomography Perfusion (CTP). CTP may offer insights in the hyperacute diagnosis of NCSE. However, lack of standardization and thresholds of perfusion parameters, operator-dependency and inaccurate co-localization with EEG limit the diagnostic value of CTP. This prospective case-control study aims at identifying the diagnostic value of Tmax inverted maps compared to standard perfusion mapping in cases of NCSE.

Methods: We enrolled patients with NCSE (Salzburg Consensus Criteria), with CTP and EEG at a maximum latency of 30', and stroke in a 1:1 fashion. CTP standard maps (MTT-CBV-CBF-Tmax) and hyper-Tmax maps were rated by two experts blinded to the final diagnosis. Hyper-Tmax maps were developed at 3, 2, and 1" thresholds.

Results: Overall, 16 NCSE and 16 stroke were included. Table 1 reports demographic data. In NCSE, 11/16 patients had positive Hyper-Tmax maps (68.8%) (Figure1) vs 0/16 in stroke (Figure2), and co-localized with the EEG abnormalities. For NCSE the reliability was higher for Hyper-Tmax maps than for standard CTP parameters (Chronbach's alpha 0.98 vs 0.81 respectively). For NCSE the concordance between MTT, CBF and CBV was poor (χ^2=0.21), while Hyper-Tmax 3, 2, and 1" were highly concordant (χ^2<0.001). Overall, Hyper-Tmax mapping had 84% accuracy in identifying NCSE, with 76% sensitivity and 100% specificity.
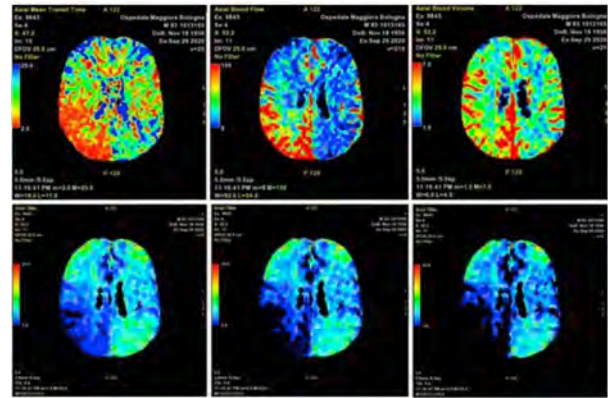
Figure1: An example of NCSE. Right temporal NCSE, with epileptiform abnormalities on T4 electrode. In the upper panels MTT (left), CBF (median) and CBF (right) maps. In the lower panel Tmax 1" (left), Tmax 2" (median) and Tmax 3" (right) reconstructions.
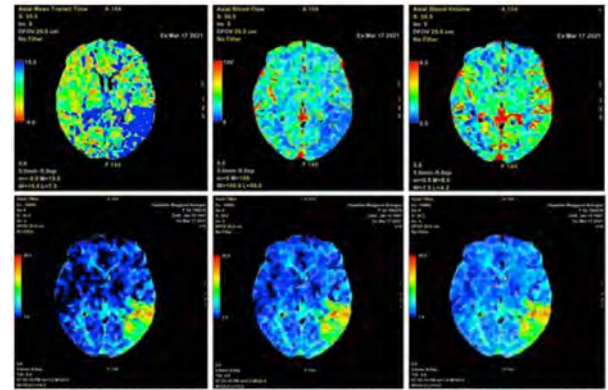
Figure2: An example of stroke. Left fronto-parietal ischemic stroke. No hyperperfusion is shown.

Conclusion: Hyper-Tmax mapping might represent a reliable tool to identify NCSE and its epileptic focus, shortening the path towards early treatment of NCSE.

Disclosure: Nothing to disclose.

		NCSE (n=16)	Stroke (n=16)	p-value
Age		80.2±6.8	71.5±15.6	0.05
Risk factors				
Hypertension		13 (81.25%)	8 (50%)	ns
Dyslipidemia		8 (50%)	6 (40%)	ns
AF		6 (37.5%)	7 (43.75%)	ns
Diabetes		6 (37.5%)	0 (0%)	0.007
Previous stroke		7 (43.75%)	1 (6.25%)	0.014
History of seizures		4 (25%)	0 (0%)	0.033
Epilepsy diagnosis		4 (25%)	0 (0%)	0.033
Clinical features				
Speech disturbances		15 (93.75%)	15 (93.75%)	ns
Motor deficit		7 (43.75%)	7 (43.75%)	ns
Sensory deficit		1 (6.25%)	1 (6.25%)	ns
Impaired consciousness		5 (31.25%)	0 (0%)	0.027
Hemianopia		6 (37.5%)	1 (7.6%)	ns
Time from symptom onset to CTP		2.3±0.8	2.4±1.5	
Standard perfusion				
MTT asymmetry		11 (73.3%)	16 (100%)	0.027
	volume	2.1±5.9	31.7±42.3	
CBF asymmetry		12 (80%)	15 (93.8%)	ns
	volume	0.8±3.2	20.3±23.1	
CBV asymmetry		8 (53.3%)	1 (6.3%)	0.004
	volume	0±0	0.3±0.7	
Hyper-Tmax maps				
Hyper-Tmax 3" positive		12 (75%)	4 (25%)	0.005
	volume	55.2±54.4	57.5±31	
Hyper-Tmax 2" positive		11 (73.3%)	2 (12.5%)	0.005
	volume	43.8±45.5	25±7.1	
Hyper-Tmax 1" positive		11 (68.8%)	0 (0%)	<0.001
	volume	20.9±27.8	0	

Table 1: Demographics of patients included.

EPO-679

Discriminating progression from radionecrosis through Amide Proton Transfer weighted imaging in brain metastases

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Background and aims: Distinguishing tumor recurrence from brain radionecrosis is often challenging. Amide Proton Transfer weighted (APTw) imaging is a molecular technique that can measure the chemical exchange saturation transfer between mobile amide protons and bulk water. We aimed to evaluate APTw imaging in predicting the differentiation between radiation-induced tissue changes from progression in 20 pre-irradiated brain metastases.

Methods: 20 contrast enhancing evolving lesions (22 ±19months from stereotactic radiosurgery) were prospectively examined at 3T Siemens system. APTw sequences (WIP816B, 3:07 minutes) and WASAB1 sequence (WIP816B, 2:03 minutes) were performed after a 3D FLAIR and before a standard multi-modal protocol that included dynamic susceptibility perfusion (DSC) imaging. Olea Sphere 3.0 software was used to post-process APTw data, to delineate regions of interest (ROIs) in APTw maps co-registered with structural FLAIR image and to calculate APTw metrics.

Results: Patients' clinical features and final diagnosis are reported in Figure 1. Among twenty patient's lesions, ten were consistent with radionecrosis and ten with tumor progression. APTw significantly separated these two entities (p<0.0001 before and after fluid suppression). After fluid suppression, APTw showed a higher discriminating value, reflected by a lower variance in both the populations (Figure 2). In some cases, tumor recurrence and radio-necrosis were not detected by DSC perfusion imaging (Figure 3).

Patient	Sex	Age	Primary tumor	SBRT to APTw (month)	Final diagnosis	Diagnosis evaluation
P_1	M	46.74	Lung	11.97	Necrosis	6 months' imaging follow-up
P_2	F	43.78	Germinal Tumor	37.77	Progression	6 months' imaging follow-up
P_3	F	55.26	Breast	3.10	Progression	histological examination
P_4	F	44.14	Breast	39.47	Progression	tumor response after a subsequent SRT
P_5	M	68.69	NSCLC	6.60	Necrosis	6 months' imaging follow-up
P_6	M	62.92	Melanoma	6.97	Progression	tumor response after a subsequent SRT
P_7	F	48.64	Lung	8.43	Progression	histological examination
P_8	F	63.80	Lung	34.37	Progression	6 months' imaging follow-up
P_9	F	59.01	Breast	33.80	Necrosis	PET-CT confirmation
P_10	M	54.12	Lung	21.77	Necrosis	6 months' imaging follow-up
P_11	F	85.63	NSCLC	6.60	Necrosis	6 months' imaging follow-up
P_12	F	71.48	NSCLC	27.63	Progression	histological examination
P_13	M	80.37	Melanoma	22.47	Necrosis	6 months' imaging follow-up
P_14	F	50.91	Melanoma	5.67	Progression	tumor response after a subsequent SRT
P_15	M	68.70	Melanoma	0.97	Progression	PET-CT confirmation
P_16	F	60.06	Lung	85.77	Necrosis	6 months' imaging follow-up
P_17	F	35.71	Lung	8.43	Necrosis	6 months' imaging follow-up
P_18	F	77.29	Breast	25.13	Necrosis	PET-CT confirmation
P_19	F	54.52	Breast	25.17	Necrosis	tumor response after a subsequent SRT
P_19_bis	F	54.52	Breast	25.17	Progression	tumor response after a subsequent SRT

Figure 1. This table summarizes clinical details of the subjects, their lesions, final diagnosis and diagnostic evaluation method. Abbreviation: Female (F), Male(M), Non Small Cell Lung Cancer (NSCLC), Stereotactic body Radiation Therapy (SRT).
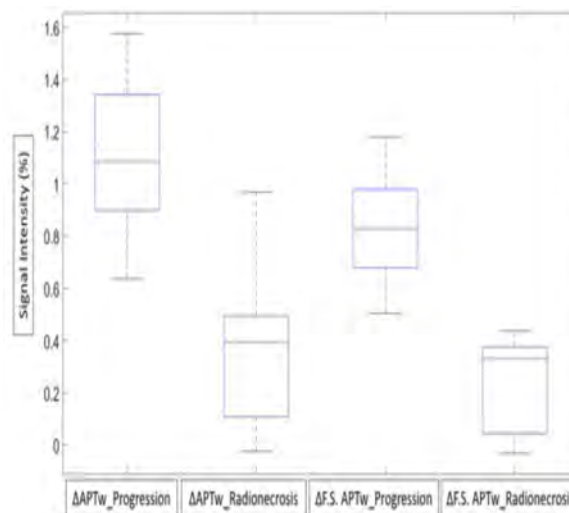
Figure 2. Boxplots of ΔAPTw= APTw_lesion - APTw_cNAWM and ΔF.S.APTw= F.S APTw_lesion -F.S. APTw_cNAWM (for both tumor progression and radionecrosis groups). Abbreviation: contralateral normal appearing white matter (cNAWM) and fluid suppression (F.S.).
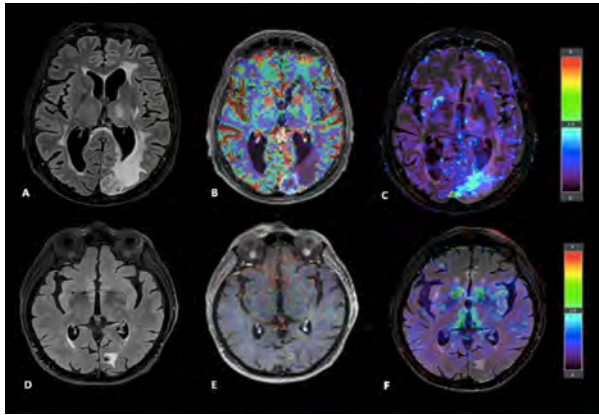
Figure 3. Clinical example of histological-proved tumor progression (A-C, P_12 on Figure1) predicted by APTw map (C) and not by DSC perfusion (B). Clinical example of radionecrosis (D-F, P_13 on Figure 1) predicted by APTw map (F) but not by DSC perfusion

Conclusion: Our results, in line with previous preclinical and clinical works, suggest that APTw metriscs can distinguish between progression and radio-necrosis, and for the first time emphasize the importance of suppressing fluid signal in APTw maps.

Disclosure: S.C. is currently an employee at Olea Medical (Research & Innovation Team Leader – Molecular Imaging Project Manager). The others author have nothing to disclose.

EPO-680

Differences in dynamic functional connectivity across the Alzheimer's disease spectrum

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Background and aims: To examine differences in dynamic functional connectivity (DFC) in cognitively normal subjects (CN), and patients with mild cognitive impairment (MCI) or Alzheimer's disease (AD).

Methods: Resting-state functional magnetic resonance imaging (rsfMRI data of 76 participants (41 CN, 24 MCI, 11 AD) from the ADNI database (http://adni.loni.usc.edu/) was used for analysis. Groups were matched according to age, sex and education. rsfMRI data were pre-processed using the CONN toolbox. For data reduction purposes, spatial independent and principal component analyses were performed on the normalized rsfMRI using GIFT. Resulting meaningful independent components were clustered into 13 functional resting-state networks. Using GIFT, a sliding window approach was employed to determine dynamic functional connectivity states across the scan period of 9 minutes. Afterwards, non-parametric t-tests were performed comparing the groups in measures of DFC such as dwell time (i.e. staying in a state), number of transitions (i.e. switching between states) and fraction time (i.e. total time spent in a state).

Results: The DFC analysis resulted in 4 distinct functional connectivity states, which were characterized by either global connectivity patterns or distinct connectivity patterns between certain rs-networks. Group comparisons yielded that one state was particularly more occupied by the AD group compared to the CN group (p=0.02) and the MCI group (p=0.001).

Conclusion: Network reorganization may influence dynamic functional connectivity patterns in pre- and clinical AD.

Disclosure: Nothing to disclose.

EPO-681

Ischaemic stroke imaging: CT or CT angiogram – which one is a better predictor of the infarct extension?

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Clínica Universitária de Imagiologia, Faculdade de Medicina de Lisboa, Lisboa, Portugal

Background and aims: ASPECTS score is calculated based on Computed Tomography (CT) studies and it allows to select patients with ischaemic stroke to mechanical thrombectomy. This study aims to compare the value of ASPECTS score in predicting the final infarct zone when applied to CT versus angiogram studies. Furthermore, it aims to evaluate the relation between the score and the recanalization level and to determine the inter-rater reliability of these measurements.

Methods: Retrospective cohort study. Patients included had a history of anterior territory ischaemic stroke, treated with mechanical thrombectomy in the Neurologic Radiology service from CHLN-EPE, from 2019 to 2020. ASPECTS score was calculated in the admission CT and angiogram and in the 24-hour CT. This score was also compared among different recanalization level subgroups. The inter-rater reliability was determined.

Results: 99 patients were included. ASPECTS score in angiogram was, in average, closer to the ASPECTS in the 24-hour CT. In TICI≥2B subgroup, ASPECTS score was, in average, closer to the 24-hour CT in both CT and angiogram when compared to the group with TICI<2B. A good inter-rater reliability was obtained.

Conclusion: ASPECTS score determined in CT angiogram studies was a better predictor of the final infarct zone when compared to CT studies. Both CT and angiogram had a better predictive value in TICI≥2B subgroup when compared to TICI<2B subgroup. Our study suggests that ASPECTS score calculated in CT angiogram can be used in the future for a better patient selection.

Disclosure: There are no conflicts of interest.

EPO-682

Abstract withdrawn

Neuroimmunology 2

EPO-683

Fatal paroxysmal sympathetic hyperactivity in patients with autoimmune encephalitis

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Background and aims: Paroxysmal sympathetic hyperactivity (PSH) is a potentially life-threatening neurological emergency due to dysregulation of autonomic function. PSH is usually secondary to acute acquired brain injuries but some cases have also shown an association to autoimmune encephalitis (AE). It is clinically characterized by the cyclic and simultaneous appearance of signs and symptoms secondary to exacerbated sympathetic discharge.
Methods: 3 patients diagnosed with AE from our center who died because of fatal PSH.
Results: Patient 1: A 38 year-old man diagnosed with encephalitis anti-Caspr2 who suddenly developed tachycardia, hypertension, tachypnea, fever, sweating, and painful cramps. He was transferred to ICU where he died because of multi-organic failure derived from the sympathetic storm. Patient 2: A 64 year-old man diagnosed with anti-amphiphysin encephalitis who was hospitalized due to pneumonia and presented unexplainable sweating, hypertension and episodes of ventricular tachycardia unresponsive to cardiopulmonary resuscitation maneuvers causing the death. Patient 3: A 61 year-old man diagnosed with anti-Hu encephalitis who suddenly developed cycling episodes of hyperthermia, tachypnea, dystonic posturing and ventricular tachycardia. One episode was refractory to treatment for PSH and the patient died because of cardiac arrest. All patients were men and had showed limbic encephalitis in the Brain MRI. Patient 1 presented the "sympathetic storm" as one of first clinical manifestations of the AE.
Conclusion: According to our case series fatal PSH is an unpredictable condition which is more frequent in men and is associated to limbic encephalitis caused by antibodies directed to neuronal surface receptors and onconeural antigens.
Disclosure: Nothing to disclose.

EPO-684

Six-month humoral response to mRNA SARS-CoV-2 vaccine in People with Multiple Sclerosis under Ocrelizumab and Fingolimod

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Background and aims: Real-world clinical data suggest an attenuated short-term immune response to SARS-CoV-2 vaccines in patients with Multiple Sclerosis (pwMS) receiving Ocrelizumab (OCR) and Fingolimod (FNG). The aim of our study was to explore: i) the humoral response up to six months after a full cycle of the BNT162b2 mRNA COVID-19 vaccine in pwMS treated with OCR and FNG compared to healthy controls (HC), and ii) the relationship between humoral response and clinical and immunological characteristics in the studied population.
Methods: IgG antibodies to SARS-CoV-2 spike protein (Anti-TSP IgG) from/of HCs and pwMS sera on OCR and FNG were detected before the first dose of the COVID-19 vaccine and 4, 8, 16 and 24 weeks after the first dose.
Results: 47 HCs and 50 pwMS (28 on OCR and 22 on FNG) were included in the study. All HCs mounted a positive humoral response at 4w and preserved it up to six months. Only 16 out 28 (57.1%) pwMS on OCR (p<0.001 compared with HCs) and 9 out of 22 (40.9%) on FNG (p<0.001) had a positive humoral response at 4w, and only 11 (39.3%) and 6 (27.3%) maintained it at the sixth month, respectively. In the OCR group, anti-TSP IgG titres was positively associated with time-window since last infusion while, in the FNG group humoral response was influenced by treatment duration, disease duration, and total lymphocyte count.
Conclusion: Our data show a weakened and transient humoral response to mRNA vaccine against COVID-19 in pwMS treated with OCR and FNG when compared with HCs.
Disclosure: Riccardo Maria Borgo, Rocco Capuano, Miriana Conte, Giovanna Donnarumma, Manuela Altieri, Elena Grimaldi, Gianluigi Franci, Annalisa Chianese, Nicola Coppola, Massimiliano Galdiero have no disclosures; Alvino Bisecco, Gioacchino Tedeschi and Antonio Gallo received speaker's honoraria and/or compensation for consulting service and/or speaking activities from Biogen, Roche, Merck, Novartis, Celgene and Genzyme.

EPO-685

Added value of 18F-FDG-PET scan in the diagnosis of MOG-antibody associated transverse myelitis

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Background and aims: Myelin oligodendrocyte glycoprotein antibody-associated disease (MOGAD) is a potentially serious condition, carrying a risk of permanent disability. A prompt diagnosis and treatment are therefore essential. Despite obvious clinical signs, however, the clinician can be confronted with normal or inconclusive MRI results. 18F-FDG-PET scan can show increased 18F-FDG uptake in the spinal cord, thereby supporting the diagnosis of an inflammatory myelopathy.

Methods: We report the imaging features of a patient admitted to a tertiary care center with the clinical picture of a rapidly progressive transverse myelitis.

Results: A 75-year old male patient presented to the emergency department with a subacute progressive gait disorder with clinical findings indicating a spinal cord lesion. Cerebrospinal fluid (CSF) examination showed a lymphocytic pleocytosis. A causative micro-organism could not be detected in the CSF. Brain MRI was normal and MRI of the spinal cord was inconclusive at the level of the cervical spine (Fig. 1). A whole body PET scan however demonstrated a mildly increased 18F-FDG uptake at the level of the cervical spinal cord (Fig. 2). MOG-antibodies were found to be positive in the serum, as confirmed by two tests using different techniques (fixed cell-based assay and live cell-based assay).
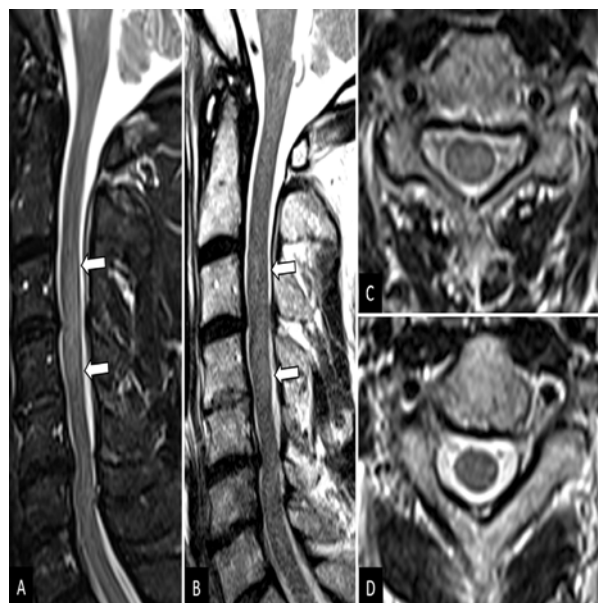
Cervical spinal cord MRI shows a slightly hyperintense signal on the sagittal STIR (A) and T2-weighted (B) images at level C3-C4 (arrows). Axial T2-WI (C) showing only discrete abnormalities. Normal axial spinal cord T2-WI at level C2 for comparison (D).
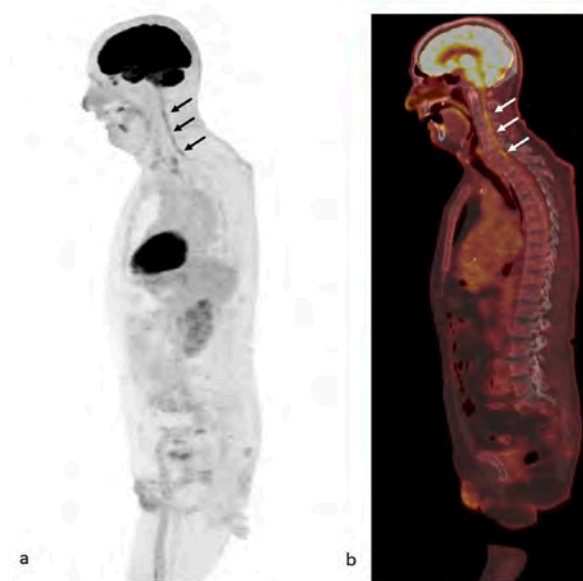
Whole body 18F-FDG-PET scan with Maximum Intensity Projection (MIP, a) and sagittal image (b) showing a diffuse increased 18F-FDG uptake in the cervical spinal cord.

Conclusion: In this patient, 18F-FDG-PET scan supported the diagnosis of a clinically suspected transverse myelitis. This case shows the potential added value of 18F-FDG-PET scan in diagnosing MOG-antibody associated transverse myelitis in patients with normal or inconclusive MRI examination.

Disclosure: The authors declare no conflicts of interest.

EPO-686

HU ANTIBODIES AUTOIMMUNITY AND IMMUNE CHECKPOINT INHIBITORS

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Background and aims: Paraneoplastic neurological syndromes (PNS) have been reported in patients treated with immune checkpoint inhibitors (ICI). Hu antibodies (Hu-Abs) are the most frequently found in PNS. We aimed to clinically describe a cohort of ICI-treated patients with Hu-Abs and neurological symptoms.

Methods: Retrospective nationwide study and comprehensive review of the literature. High-risk phenotypes were defined according the updated PNS criteria.

Results: We included in our series 7 patients (5/7 men, median age 66 years) (table 1). Most (6/7) cases had metastatic small cell lung cancer. ICI treatment comprised atezolizumab (4/7), pembrolizumab (2/7), and durvalumab (1/7). Median cycles before clinical onset were 4. Clinical phenotypes included limbic encephalitis (4/7), sensory neuronopathy (2/7), polyradiculoneuropathy (2/7), cerebellitis (1/7), brainstem encephalitis (1/7); overlapping in 4/7 and isolated in 3/7. MRI abnormalities included: FLAIR hypersignal involving limbic (3/7) or non-limbic (2/7) areas, pachymeningeal (1/7) and cauda roots enhancement (1/7) (figure 1). CSF was inflammatory in all cases. No patient improved despite immunotherapy (0/5). Final outcome (median follow-up 2 months, range 0.5-18) included severe neurological disability (mRS>3) in 2/7 cases and death in 5/7 cases. Additional 10 cases were retrieved from literature, with clinical features comparable to our series. However, 2/10 had atypical clinical phenotypes and completely improved after corticosteroids (table 2). Overall, 15/17 cases had syndromes consistent with high-risk phenotypes of PNS. Notably, in 4/10 cases retrieved from literature Hu-Abs were present before ICI initiation.

Present series: clinical and paraclinical findings, treatment, and outcome.

Brain magnetic resonance imaging findings in our series.

Cases from literature: clinical and paraclinical findings, treatment, and outcome.

Conclusion: ICI-related neurological disorders associated with Hu-Abs are mainly PNS triggered or worsened by ICI. Outcome is poor in most cases despite immunotherapy.

EPO-687

Brainstem lesions: clinical features, imaging and histological diagnosis

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Background and aims: Brainstem lesions have a wide diversity of possible diagnosis with magnetic resonance imaging (MRI) representing the primary diagnostic tool of these lesions. However, considering the growing need for molecular diagnostics of brainstem tumors and the inconsistency between MRI-based diagnosis and the pathological findings in 15–20% of the cases, invasive diagnostic procedures are frequently needed. In this study we report a series of cases of brainstem lesions comparing the imaging- based diagnostic with the histopathological findings.

Methods: This retrospective study analyzed all cases of intrinsic brainstem lesions submitted to stereotactic biopsies or open biopsies, between 2002 and 2021, in both adult and pediatric population. The demographic, imaging, pathological, clinical features and surgical characteristics were analyzed.

Results: We included 22 patients, with a median age at presentation of 39.2 years (range 4–68 years), 12 female (55.5%). 21 cases (95.5%) had a positive histopathological with a definitive diagnosis: 18 tumors (81.9%) (6 astrocytomas, 4 primary brain lymphomas, 3 diffuse gliomas, 1 oligodendroglioma, 1 glioblastoma, 1 medulloblastoma, 1 hemangioblastoma and 1 metastatic lesion) and 3 cerebral vascular malformations (13.6%) (2 cavernous hemangiomas and 1 arteriovenous malformation). The most common signs and symptoms at onset were ophthalmoplegia (13 [59.1%] of 22 patients) and motor deficit (13 [59.1%]). The imaging-based diagnosis was inconsistent with the pathological findings in 4 (18,2%) cases.

Conclusion: The consistency between imaging-based diagnosis and pathological findings is in line with other series in the literature, meaning that the histopathological diagnosis retains an important role in the workup and treatment selection of these lesions.

Disclosure: Nothing to disclose.

EPO-688

Visual system involvement in GFAP astrocytopathy: a case report and review of the literature

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Background and aims: Glial fibrillary acidic protein (GFAP) astrocytopathy is an inflammatory disorder of the Central Nervous System (CNS), associated with IgG autoantibodies against GFAP. It mostly presents as meningoencephalitis or meningoencephalomyelitis. Involvement of the optic system is frequent, generally manifesting as optic nerve papillitis with blurred vision, while optic neuritis (ON) and overt vision loss are rare. We report a patient with GFAP positive bilateral optic neuritis and present a literature review to evaluate available evidence of visual system involvement in GFAP astrocytopathy.

Methods: We report a case of GFAP positive severe bilateral optic neuritis. We then present a literature search of all published GFAP-astrocytopathy cases, assessing visual system involvement.

Results: A 33-year-old woman presented with a severe, rapidly progressing bilateral optic neuritis which led to bilateral blindness. Cerebrospinal fluid analysis revealed 100 cells/mm^3. GFAP-antibodies were positive in serum and CSF. Treatment with intravenous steroids and plasma exchange was only partially effective. Our literature search identified 506 patients. Visual symptoms, mainly blurred vision, were reported in 88/506 (17%), while bilateral optic disc edema in the absence of visual symptoms presented in 55/506 (11%). ON was reported in 36/506 (7%), in one patient leading to blindness and only in 14 patients as an isolated manifestation.

Conclusion: Visual impairment in GFAP astrocytopathy is relatively common, although many patients show asymptomatic optic disc involvement. Optic neuritis is often mild and monolateral and occurs concomitantly with other neurological manifestations, while isolated sudden blindness is a rare manifestation, with possibly poor response to immunotherapy.

Disclosure: Nothing to disclose.

EPO-689

Plasma Exchange in Neuroimmunologic Disorders

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Background and aims: Neuro-immunological diseases, neurologists have number of different drugs to choose from ranging from corticosteroids- IVIg-more specific cell based therapies. In some diseases, therapeutic plasma exchange is used. The most obvious advantage of therapeutic plasma exchange (TPE) is the usually rapid onset of action presumably due to removal of pathogenic auto-antibodies.

Methods: We followed up year between 2015–2022; 22 patients with multiple sclerosis attacks resistant to corticosteroid therapy, 8 neuromyelitis optica patients who were resistant to steroid- intravenous immunoglobulin therapy, 2 MOGAD spectrum diagnoses resistant to steroid-intravenous immunoglobulin therapy, 15 patients we followed up for myasthenic crisis who did not respond significantly to intravenous immunoglobulin therapy, The clinical findings of our 8 patients diagnosed with Guillan Barre syndrome who did not respond to immunoglobulin treatment and their responses to plasma exchange treatments will be discussed in detail in our oral presentation.

Results: It has been observed that our patients with multiple sclerosis-neuromyelitis optica-MOGAD spectrum disease-myasthenic crisis-Guillain Barre Syndrome resistant to corticosteroid and intravenous immunoglobulin treatments recovered almost completely after plasma exchange therapy.

Conclusion: In treatment-resistant neuroimmunological diseases, plasma exchange therapy is a very effective treatment method that provides almost complete clinical recovery, where complications are observed at an insignificant level in experienced centers.

Disclosure: Nothing to disclose.

EPO-690

Differentiating CNS demyelination: clinical, laboratory, imaging features and peripheral blood type I IFN activity

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Background and aims: While multiple sclerosis (MS) is considered the cornerstone of autoimmune demyelinating CNS disorders, systemic autoimmune diseases (SADs) are important MS mimickers. We sought to explore whether distinct clinical/laboratory characteristics and quantitation of peripheral blood type I interferon (IFN) activity could aid at differential diagnosis between the two entities.

Methods: 193 consecutive patients with clinical and/or radiological features suggestive of CNS demyelination were tested for specific antibodies against 15 cellular antigens by immunoblot. After joint neurological and rheumatological evaluation and follow up, patients were classified into MS spectrum and CNS autoimmune disorders, based on clinical and laboratory findings. Type I IFN score was calculated in peripheral blood by real time PCR.

Results: Compared to MS, patients with demyelinating disease in the context of systemic autoimmunity were older, predominantly females, with increased rates of hypertension/hyperlipidemia, family history of autoimmunity and higher ANA titers. Cortical dysfunction and atypical for MS MRI lesions, less frequent infratentorial and corpus callosum lesions, as well as CSF T2 oligoclonal bands and IgG index positivity were observed. Patients fulfilling criteria for SADs had significantly higher type I IFN activity at baseline compared to MS spectrum disorders (60.2 ± 90.9 vs 5.1 ± 17.1, p-value: 0.0008).

Conclusion: Distinct clinical, imaging and laboratory characteristics along with type I IFN peripheral blood activity can aid in the differential diagnosis between MS and systemic autoimmune disorders with CNS involvement. Early distinction between these entities will allow the institution of optimal therapeutic strategies.

Disclosure: Nothing to disclose.

EPO-691

Ageing with multiple sclerosis: a characterization of an elderly population.

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Background and aims: There is an increased prevalence of MS in the elderly. Nevertheless, the phenotype of MS at age 60 and above is still poorly understood. Safety and efficacy of disease modifying drugs (DMD) are unknown.

Methods: We performed a single-center cross-sectional study on demography, disease and treatment history of a population aged 60 years and older. We designed a questionnaire to acquire information about comorbidities and quality of life in this population and administered it to enrolled patients.

Results: 266 subjects matched age inclusion criteria. Mean disease duration was 29.4 (SD 11.7); 207 patients had a disease onset before the age of 50 (adult-onset-MS, AOMS), and 59 patients at 50 or older (late-onset-MS, LOMS) including 14 at the age of 60 or older (very-late-onset, VLOMS). Disease form at onset for AOMS was relapsing-remitting (RR) in 180/207, primary progressive (PP) in 26/207, unknown in 2/207; for LOMS: RR (37/59), PP (20/59) and unknown (1/59); for VLOMS: RR(8/14), PP (5/14), unknown (1/14) (χ^2 AOMS-LOMS, p< 0.0001; χ^2 AOMS-VLOMS, p=0.009). 27% had EDSS lower than 6.0. 29.2% were taking a DMD: interferon-beta (24.4%), glatiramer acetate (21.8%), and azathioprine (15.4%). 124/143 patients reported at least one comorbidity (increased BMI 42%; cardiovascular 39.9%; orthopedic 29.4%; metabolic/endocrine 25.9%.

Conclusion: MS patients above age of 60 have high prevalence of comorbidities. About 1/3 of patients is still able to walk without aid and is taking a DMD, suggesting a RR phenotype. Further studies are needed to ascertain safety and efficacy of DMD in this subpopulation.

Disclosure: There aren't competing relationships/activities/interests related with this manuscript.

EPO-692

Video-assisted thoracic surgery thymectomy in Sardinian double seronegative myastenic patients: a case series.

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Background and aims: Therapeutic thymectomy is mostly performed in Myasthenia Gravis (MG) patients with acetylcholine receptor antibodies (AChRAb). Over the last decade, video-assisted thoracic surgery (VATS) and robotic assisted thymectomy have replaced open surgery for the treatment of non-thymomatous MG. In this study, MG patients with negative serological testing for AChRAb, that is standard radioimmunoassay (RIA), are defined as seronegative MG (SNMG). Thymus pathology is rare in SNMG and in these patients there is no evidence for a pathogenic role of the thymus.

Methods: We retrospectively collected clinical data of 9 consecutive Sardinian SNMG patients (7 females, 2 males) undergone VATS thymectomy from 2014 to 2019 (Table 1). These patients were also seronegative for muscle-specific tyrosine kinase receptor (MuSK) with the standard RIA. Left sided approach was used in all cases.

Table 1. Follow up of 9 SNMG patients after VATS thymectomy.							
Patients	Sex	Age MG onset	Age thymectomy	MGFA stable	MGFA post-thymectomy	Follow up	Complications of surgery
1	F	35 y	37	3b	2b	19 m	0
2	M	44 y	45	2 a	No symptoms	24 m	0
3	F	45 y	46 y	3 a	2 a	27 m	0
4	F	31 y	32 y	4b	3b	31 m	0
5	F	35 y	39 y	3b	3b	35 m	0
6	F	26 y	28 y	3b	2 a	35 m	0
7	M	43 y	46 y	3 a	2 a	46 m	0
8	F	37 y	39 y	3 a	3b	53 m	0
9	F	49 y	50 y	2b	2b	70 m	0
Media		38 y	40 y			38 m	

Red = aggravation of symptoms; yellow = no modifications of clinical picture; green = clinical improvement; y= years; m= months

Results: Six patients (66,6%) showed an important clinical improvement, two patients remained stable and one patient showed a clinical worsening. The median follow up time after VATS thymectomy was 37,8 months (range 19–70) and the median time from MG diagnosis to VATS thymectomy was two years (range 1–4). Patients' immunosuppressive therapy was reduced or remained

unchanged after thymectomy. Histological evaluations revealed thymic hyperplasia in all patients, in accordance with a possible role of the thymus in SNMG pathogenesis.
Conclusion: The last International Consensus Guidance for Management of MG recommended thymectomy in generalized MG without AChR-Ab if immunosuppressive therapy fails or to minimize its adverse effects. According our findings VATS thymectomy may improve symptoms and reduce MGFA staging in SNMG patients.
Disclosure: Nothing to disclose.

EPO-693

Autoimmune neurological syndromes associated with melanoma.

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Background and aims: The clinical spectrum of autoimmune neurological syndromes associated with melanoma has expanded with the use of immune checkpoint inhibitors (ICI). We aimed to characterize melanoma-associated neurological syndromes in the ICI era.
Methods: Medical records from a nationwide cohort of patients with melanoma and neurological syndromes were retrospectively analyzed. All patients with previous exposure to ICI or suspicion of paraneoplastic neurological syndrome were included.
Results: 38 patients were included; 29/38 (76%) patients were treated with ICI. Central nervous system (CNS) disorders were more frequent in non-ICI patients (8/9, 88.89%; p=0.126), while peripheral nervous system (P NS) involvement was more frequent in ICI patients (16/29, 55.17%; p=0.026), including 13/16 (81.25%) patients affected with polyradiculoneuropathy. Neural antibodies were more frequently detected in non-ICI patients (6/7, 85.71%; p=0024). Paraneoplastic neurological syndromes in patients not treated with ICIs included Stiff-person syndrome (n=1), limbic encephalitis (n=2), retinopathy (n=2), brainstem encephalitis (n=1) polyradiculoneuropathy (n=1) and non-limbic encephalitis (n=2). The median follow-up was 16.38 months. Among those non-ICI patients who received treatment, 5 out of 7 improved.
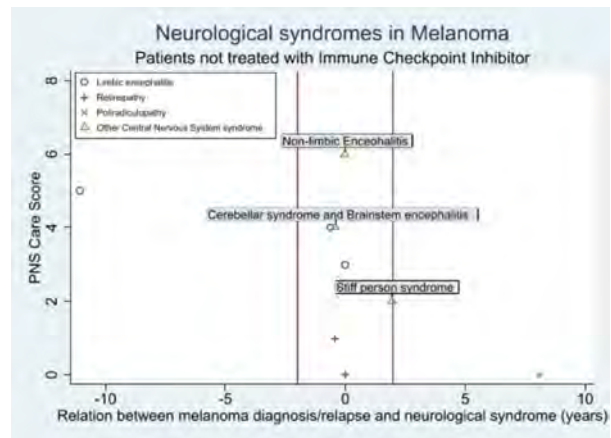
Schematic representation of neurological syndromes in patients with Melanoma not treated with Immune Checkpoint Inhibitor

Conclusion: Most melanoma-related neurological syndromes are ICI-induced and affect the PNS. More studies are needed to better characterize a possible immune-mediated neurological syndrome in patients affected with Melanoma not treated with ICI.
Disclosure: Nothing to disclose.

Peripheral nerve disorders

EPO-694
Abstract withdrawn

EPO-695

Switch from IVIg to SCIg in patients with CIDP: 6 months follow up study of quality of life

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Background and aims: Studies investigating the quality of life (QoL) in patients with chronic inflammatory demyelinating polyneuropathy (CIDP) after the switch from intravenous immunoglobulin (IVIg) to subcutaneous immunoglobulin (SCIg) therapy are scarce. We sought to investigate the QoL in patients with CIDP six months after switch to SCIg.

Methods: In this prospective, open-label, observational study sixty-nine patients with CIDP treated with IVIg were switched to an equivalent (1:1) dose of SCIg one week after last IVIg treatment. Patients' QoL was evaluated with SF-36 questionnaire. Medical Research Council Sum Score (MRC-SS), INCAT disability score, 100m walk test (100mwT), timed 25-Foot Walk Test (T25-FW), RODS Score and modified Rankin Scale (mRS) were also used.

Results: No change in total SF-36 score was observed six months after switch from IVIg to SCIg (p>0.05), while patients' social functioning was better (p<0.05). Following parameters at the time of switch showed correlation with SF-36 total score six months after the switch: age at the time of switch (p<0.05), MRC-SS (p<0.01), INCAT (p<0.01), 100mwT (p<0.01), T25-FW (p<0.01), RODS (p<0.01) and mRS (p<0.01). Lower mRS score (β = - 0.38, p < 0.05) at the time of switch was a significant predictor of better QoL six months after the switch.

Conclusion: No change in QoL six months after the switch from IVIg to SCIg was observed, while patients' social functioning was better. Patients with worse mRS scores at the time of switch to SCIg need special attention of clinicians since they could be at higher risk to have worse QoL.

Disclosure: Nothing to disclose.

EPO-696

Acute piriformis syndrome mimicking cauda equina syndrome: a case report

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Background and aims: We present a case of acute secondary piriformis plus syndrome due to piriformis muscle hematoma. The clinical presentation was similar due that of cauda equina compression, for which it was primarily mistaken.

Methods: A 55-year male with a history of low back pain and chronic limb ischemia, chronically administered warfarin, was admitted by his general practitioner with left-sided gluteal pain and administered analgesics via an intramuscular injection. Later that day he was admitted to regional hospital due to progression of sciatica. He recieved second intramuscular analgesic inejction. Second hospitalization day the patient developed acral left leg weakness and difficulty urinating; symptoms progressed to complete urinary retention, erectile dysfunction, saddle, L5 and S1 hypesthesia and left leg acroplegia. He was transferred to our hospital to rule out cauda equina syndrome. An MRI did not demostrate compression of neural elements within the spinal canal. An electrophysiological examination showed signs of sciatic nerve neuropathy in the pelvic region, which led to pelvic CT demonstrating piriformis muscle intramuscular hematoma.

Results: The surgery was performed. During the postoperative period, the patient regularly attended physiotherapy. His neurological deficit improved; after 26 mohths he is able to walk independently. He has no urinary or sexual dysfunction and his sensory deficit completely resolved.

Conclusion: Diagnosis of piriformis (plus) syndrome in an acute setting is a difficult feat as their clinical presentation may be quite similar to the more common cauda equina syndrome. Local hematoma should be strongly considered in an anticoagulated patient after local trauma.

Disclosure: I do not have a conflict of interest.

EPO-697

Video-Head Impulse test findings in peripheral neuropathies

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Background and aims: Study analysed the vestibulo-ocular reflex (VOR) as measured by the video-head impulse test (v-HIT) and refixation-saccade characteristics in patients with genetically confirmed Charcot-Marie-Tooth disease 1A (CMT1A) and chronic inflammatory demyelinating polyneuropathy (CIDP).

Methods: 22 patients (age 51.9±13.8 years, 17F/5M) with CMT1A with a mean disease duration of 25.2±17.5 years, and 10 patients with CIDP (age 54.7±21.8 years, 5F/5M) mean disease duration of 4.2 years were studied. VOR-gain, first-saccade amplitude, onset latency, peak velocity and duration were examined and compared against age-matched normal-controls (NC).

Results: In CMT1A group, 18 (82%) patients reported severe imbalance resulting in recurrent falls in 14 (64%) patients. VOR-gain was reduced (mean-2SD) in 10 (45%) patients, and was associated with longer disease duration and higher Charcot-Marie-Tooth Examination Score (CMTES). First-saccade onset latency was longer in all three canal planes in CMT1A compared to NC (p<0.05). In the HC plane first-saccade amplitude, peak velocity and duration were significantly different from NC (p<0.05). In CIDP group, 6 (60%) patients reported severe imbalance resulting in recurrent falls in four (40%) patients. VOR-gain was reduced in five (50%) patients and was associated with history of recurrent falls (p<0.05). First saccade onset latency was longer in the HC and PC plane (p<0.05).

Conclusion: Gait imbalance, recurrent falls and reduced VOR-gain are common CMT1A and CIDP. Prolonged onset latency of first-saccade in both conditions may indicate underlying demyelinating process of the vestibular nerve. Complementary otolith function testing is necessary to better characterise pattern of vestibular impairment and its correlation with v-HIT findings.

Disclosure: Nothing to disclose.

EPO-698

Vasculitic neuropathy associated with checkpoint inhibitors

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Background and aims: An 86 years old patient treated with Ipilimumab and Nivolumab for a pleural mesothelioma presented with a quickly progressive amyotrophic sensory-motor deficit since august 2021. It involved initially the left foot, then the hands and was associated with balance disorder and deep tendon areflexia.

Methods: The electromyogram revealed severe axonal neuropathy of the four limbs, predominant on the left limbs. It also showed some rare demyelinating abnormalities. CSF presented 1GB/mm^3, 0.63g/l protein and no abnormal cells. Blood tests showed negative infectious serologies, positive 1/640 NAAs with positive anti-SSA but negative cryoglobulinemia, negative ANCA and negative antineuronal antibodies. The neuromuscular biopsy showed signs of necrotic vasculitis: perivascular inflammatory infiltrate with thrombosis and fibrinoid necrosis in small and medium caliber vessels. (cf Image 1,2). Immunotherapy was stopped and corticosteroid treatment was introduced, after 10 days of which the patient improved both clinically and on the electromyogram.
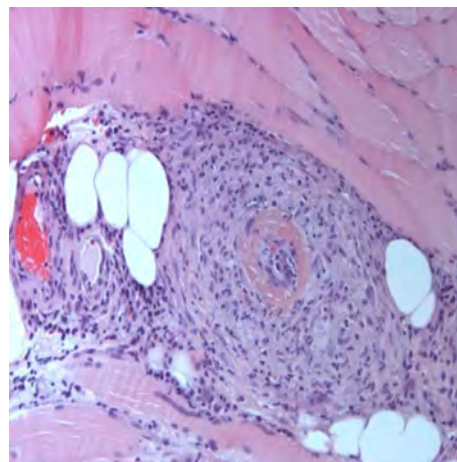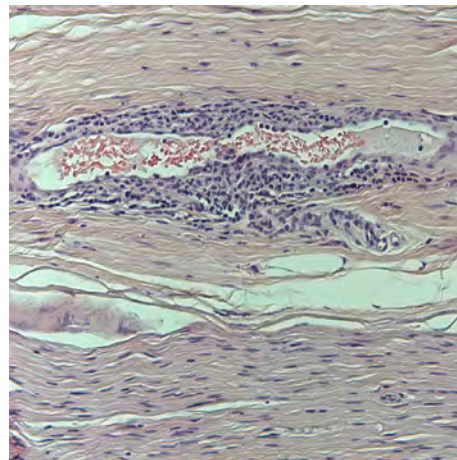
Results: Immune checkpoint inhibitors (ICI) are recently used in cancer therapy. Their direct immune system regulation may cause some immune related adverse events. Neurological adverse events are rare and consist mainly of myositis, myasthenic syndrom or acute or subacute polyradiculoneuritis. Descriptions of multiple mononeuropathy with vasculitis induced by ICI are extremely rare.

Conclusion: We hypothesize that this peripheral nervous system vasculitis is an exceptional immune adverse event attributable to immunotherapy, with a favorable prognosis after discontinuation of immunotherapy and corticosteroid therapy.

Disclosure: The patient signed un consent for publications.

EPO-699

Serum biomarkers of diabetic polyneuropathy

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Background and aims: Early stages of diabetic polyneuropathy (DPN) can be asymptomatic. A long subclinical period of DPN complicates a timely diagnosis of the disease.The aim of research was to study serum levels of brain derived neurotrophic factor (BDNF), its high-affinity tropomyosin receptor kinase type B (TrkB), vascular endothelial growth factor (VEGFA) and its high-specific receptor VEGFR2 as biomarkers of subclinical stage of diabetic polyneuropathy

Methods: We examined 54 patients with diabetes mellitus (DM) type 2. Presence of DPN was assessed by neurological examination according to the Michigan neuropathy screening instrument (MNSI) , Neuropathy disability Score (NDS) and electroneuromiography (ENMG) of lower extremities. Serum levels of BDNF, TrkB, VEGFA and VEGFR2 were measured by enzyme immunoassay. Control group consisted of 15 healthy persons.

Results: The 1st group included 28 patients with clinical and ENMG-sighs of DPN, 12 patients without clinical symptoms and with polyneuropathy confirmed by ENMG entered the 2nd, subclinical group, as shown in Table 1. In 14 patients with DM of 3rd group there were no revealed clinical or instrumental sighs of polyneuropathy According to the results of ELISA, represented in table 2, the serum levels of BDNF, TrkB and VEGFA in the 1st and 2nd groups were significantly higher than the corresponding values in the 3rd and control groups. There were no significant differences in serum VEGFR2 in the studied groups.

	Group 1	Group 2	Group 3	p-value
Glycaemia , mmol1	9,10±2,84	9,41±3,97	8,55±2,94	0,745
HbA1c, %	7,98±2,05	7,43±1,95	7,64±6,15	0,811
NDS	**17,83±5,83**	2,42±1,17	2,28±1,86	0,000*
MNSI	**6,50±1,91**	2,33±2,31	3,5±2,71	0,004*
N.Suralis S-amplitude, mkV	4,39±2,97	4,83±2,92	**9,37±2,92**	0,000*
Nerve conduction velocity, m/s, n.suralis	34,29±19,71	35,40±19,07	**63,33±4,46**	0,011*
N.peroneus, M-amplitude, mkV	2,84±1,80	2,23±1,39	**5,69±1,27**	0,004*
Latency M-amplitude, mc	3,83±1,30	4,23±0,98	**2,86±0,55**	0,017*
NCV, n.peroneus, m/s	45,33±7,95	48,56±17,19	**67,6±16,58**	0,003*

* statistically significant differences
*Values that differ from those of other groups indicated in **bold type***

Table 1. The results of clinical and instrumental examinations of the studied groups

Laboratory test	Group 1	Group 2	Group 3	Control group	p-value
BDNF, ng/ml	**4,70±2,68**	**2,74±1,89**	0,85±0,44	1,07±0,64	0,000*
TrkB, ng/ml	**4,72±2,75**	**4,68±1,93**	1,95±1,01	1,66 ± 0,63	0, 000*
VEGFA, pg/ml	**49,41±28,78**	**37,62±17,10**	28,36±9,81	25,22±12,86	0,000*
VEGFR2, ng/ml	21,29±8,27	20,42±7,69	17,49±5,03	16,59±4,53	0,016

*statistically significant differences
Values that differ from those of other groups indicated in **bold type**

Table 2. The results of an enzyme immunoassay of the studied groups

Conclusion: Serum levels of BDNF, TrkB and VEGFA may be considered as biomarkers of subclinical stage of diabetic polyneuropathy

Disclosure: The authors declare that they have no competing interests.

EPO-700

COVID-19 vaccine-related Guillain-Barré syndrome in Liguria, region of Italy: a multicenter case series

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Background and aims: Guillain-Barré-Syndrome (GBS) is a rare immune-mediated neurological disorder affecting peripheral nerves and nerve roots. GBS is one of the neurological adverse events that can be associated with post-COVID-19 vaccination, with frequency and features still to be precisely assessed. Herein we report a case-series of 13 patients affected by GBS after different kind of SARS-CoV2 vaccination.

Methods: Patients with GBS after COVID-19 vaccination admitted to six hospitals that cover the whole Liguria region (North-West Italy), from February 1st 2021, to October 30th 2021, were included in this study. Clinical and paraclinical data were retrospectively collected.

Results: 13 patients were included in the study (9 males; mean age at onset 64.1 year). Five patients were vaccinated with Oxford-AstraZeneca, seven with Pfizer-BioNTech and one with Moderna. The mean time between vaccination and GBS onset was 11.5 days. Ten patients (77%) developed GBS after the first vaccination dose and three patients after the second dose. As previously reported AIDP was the predominant variant and patients with bilateral seventh cranial nerve involvement were all vaccinated with Oxford-AstraZeneca. Three patients presented Treatment-Related-Fluctuation. A poor prognosis, calculated as GBS-DS ≥3, occurred in 38.4% of the patients, with a mortality rate of 15.4%, and a disability rate of 23,1% (walking with support).

Conclusion: Investigating causal relationships between COVID-19 vaccination and GBS was not the aim of our study even if the temporal correlation and the absence of previous infectious episodes supports the hypothesis of a close relationship between the vaccine and GBS.

Disclosure: There aren't competing relationships/activities/interests related with this manuscript.

EPO-701

Abstract withdrawn

EPO-702

A retrospective analysis of the long-term course of chronic inflammatory demyelinating polyneuropathy

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Background and aims: Chronic inflammatory demyelinating polyneuropathy (CIDP) is characterized by a progressive or relapsing course of the disease, leading to temporal or permanent disability and requiring maintenance of long-term immunotherapy. We assessed clinical and paraclinical outcomes in patients with CIDP history of more than 5 years.

Methods: We included 46 adult patients that fulfilled EAN/PNS diagnostic criteria for CIDP 2021. Outcome measures included Neurological Impairment Scale (NIS), Inflammatory Neuropathy Cause and Treatment (INCAT) disability scale, CIDP Disease Activity Status (CDAS), chronic acquired polyneuropathy patient-reported index (CAP-PRI). Electrophysiological examination and nerve ultrasound (UPPS, Grimm et al, 2015) were performed.

Results: Median follow-up period was 10 [7.0;13.45], average age 48.1±13.4 years. There were 32 (70%) typical CIDP patients and 14 (30%) multifocal CIDP. 50% typical CIDP had CDAS 1 (≥5 years off treatment), 64% multifocal CIDP - CDAS 5 (unstable active disease). For multifocal CIDP NIS motor score (p=0.002), INCAT score for arms (p=0.006), CAP-PRI score (p=0.025) were higher compared to typical CIDP. 80% of patients had neurophysiological signs of a chronic dysimmune nerve process, fulfilled criteria of EAN/PNS 2021 and nerve enlargement in proximal ulnar and median nerves segments and brachial plexus.

Conclusion: The typical CIDP is characterized by a favorable long-term course. The progressive unstable course of the disease with more severe neurological deficit and degree of disability are significantly more common in multifocal CIDP.

Disclosure: The authors have nothing to disclose.

EPO-703

No association between RFC1 repeat expansion and inflammatory neuropathies

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Background and aims: Biallelic expansion of the AAGGG repeat in the replication factor C subunit 1 (RFC1) has recently been described to cause CANVAS characterized by cerebellar ataxia, peripheral sensory neuropathy and vestibular areflexia. This genetic alteration is also seen in one third of patients having idiopathic sensory neuropathy; however, its frequency in inflammatory neuropathies is unknown. Therefore, we aimed to screen patients with acute and chronic inflammatory demyelinating polyneuropathy (AIDP, CIDP) and multifocal motor neuropathy (MMN) for RFC1 repeat expansions.

Methods: We screened 21 patients with AIDP, 152 with CIDP (including 5 with sensory variant), 63 with MMN and further 94 controls without neuropathy for the pentanucleotide AAGGG repeat expansion using short-range flanking PCR and repeat-primed PCR. Cases without amplifiable PCR product on flanking PCR and positive repeat-primed PCR were also tested for the non-pathogenic expansions of AAAGG and AAAAG repeat units.

Results: None of the 236 patients showed biallelic AAGGG expansion of RFC1. The frequency of AAGGG carrier status in the heterozygous state was 4.8% in AIDP, 4.9% in CIDP and 5.5% in MMN patients, respectively. The carrier frequency for AAGGG and AAAGG expansions were comparable to controls without any statistically significant difference.

Conclusion: Data suggests that pathologic expansion of AAGGG repeats does not contribute to the development of inflammatory neuropathies. Our results reinforce the understanding that RFC1 is specific to sensory but not to sensory-motor or motor neuropathy. Further, the data highlights the true frequency of AAGGG expansion of ~ 5% being one of the most common pathogenic alleles in the population.

Disclosure: Nothing to disclose.

EPO-704

Quality of life in patients with multifocal motor neuropathy: a 4-year follow-up study

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Background and aims: Multifocal motor neuropathy (MMN) is a rare immune-mediated disease, which is characterized by slowly progressive asymmetric muscle weakness. Several cross-sectional studies analyzed quality of life (QoL) in MMN patients. Aim of this study was to observe changes in QoL of MMN patients during time.

Methods: Our study included 17 MMN patients at baseline, while 12 patients were retested after four years. Three patients died, while two did not want to participate in follow up study. Following scales were used: Inflammatory Neuropathy Cause and Treatment (INCAT) scale, Rasch-built Overall Disability Scale (R-ODS), Beck's depression inventory (BDI), Fatigue Severity Scale (FSS) and SF-36.

Results: Age at disease onset of 12 patients was 37.8 ± 12.9 years, with male to female ratio 2:1 and disease duration of 11.4 ± 5.0 years at first examination. Four patients were without any therapy, while the rest were treated with intravenous immunoglobulins (IVIG). Improvement of at least one point on INCAT total score was observed in 25% of patients. RODS score improvement of at least four points was observed in 50% of patients. Worsening in both BDI and FSS was noted during follow-up period. Among eight SF-36 subdomains, only physical functioning (PF) (76.67 ± 29.87; 57.50 ± 31.65, $p < 0.05$) worsened during the follow up period.

Conclusion: During a four-year follow-up period, 25–50% of MMN patients had improvement in their functionality based on INCAT and I-RODS score. However, worsening in physical aspects of QoL (PF and BP subdomains) should not be underestimated.

Disclosure: Nothing to disclose.

EPO-705

Diagnostic challenges of a TUBB3 R262H syndrome: resemblance with Moebius syndrome and a demyelinating polyneuropathy

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Background and aims: Congenital fibrosis of extraocular muscles (CFEOM) is a condition caused by a maldevelopment of oculomotor nerve. Tubulin isotype 3 (TUBB3) mutations cause CFEOM3A, frequently associated with non-ocular features. Patients harboring the c.785G>A missense mutation present with a specific phenotype, called TUBB3 R262H syndrome, with ptosis, ophthalmoplegia with divergent strabismus, facial paralysis, joint contractures, intellectual disabilities, Kallmann syndrome and progressive axonal polyneuropathy presenting during the first decade of life. This syndrome shares many features with other entities, such as Moebius or TUBB3 E410K syndromes.

Methods: We report an 18-year-old male patient that was considered to have, during infancy, an atypical Moebius Syndrome, due to severe facial bilateral paresis. As he grew up, additional features became evident, such as complex ophthalmoplegia (only able to abduct both eyes) with divergent strabismus, anosmia, fingers contractures, valgus knees and ankles, hypogonadotropic hypogonadism with associated global development delay and progressive sensorimotor polyneuropathy. MRI showed a thin corpus callosum, frontal lobes asymmetry, non-detectable oculomotor nerves and hypoplasia of the olfactory bulbs. EMG showed a sensorimotor polyneuropathy with intermediate velocities (35m/s for proximal median motor nerve).

Results: Genetic testing confirmed a heterozygous TUBB3 c.785G>A variant.

Conclusion: To our knowledge TUBB3 R262H syndrome was not previously associated with a demyelination pattern. There is evidence of TUBB3 expression on rat Schwann cells. Mutations of TUBB3 might cause disfunction of Schwann cells in humans which would explain the EMG pattern of our patient. Patients harboring TUBB3 mutations might present severe facial diparesis and be mistaken as Moebius syndrome, especially during early childhood.

Disclosure: There are no conflict(s) of interest that may have a direct bearing on the subject matter. This research didn't have any commercial or institutional support.

EPO-706

Guillain-Barrè syndrome associated with Neurofascin-155-IgG1 autoantibodies after SARS-CoV-2 vaccination

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Background and aims: Many cases of Guillain-Barré syndrome (GBS) have been reported to be associated with COVID-19. The clinical picture of COVID-19-associated GBS seems to resemble that of classic GBS. Clinical and laboratory data suggest a prominent post-infectious immune-mediated mechanism rather than a para-infectious one. Vaccines have also been associated to the pathogenesis of GBS as putative triggers. COVID-19 vaccine–related GBS has been rarely reported to date and some researches disavow the existence of this association. Some cases of GBS with positivity of anti-NF155 antibodies are described, but the role of these antibodies and of IgG subclasses in the pathogenicity and in the diagnostic work up of GBS needs to be further studied. We report the clinical and immunological characteristics of two patients who developed GBS within 3 weeks after Sars-CoV2 vaccination in whom NF155-IgG1 autoantibodies were detected.

Methods: Patient sera of four patients who manifested GBS after administration of SARS-CoV-2 vaccine were tested for the presence of anti-IgG1, anti-IgG3 and anti-IgG4 antibodies binding to NF-155 performing live cell based assay on HEK 293 cells transfected with human NF-155.

Brain magnetic resonance showing cauda equina contrast enhancement of patient 2

Results: Two patients showed marked reactivity mainly of IgG-1 subclass antibodies.

Conclusion: Patients' clinical findings did not differ substantially from common forms of GBS. The presence of a strong reactivity of the IgG1 antibodies in positive patients suggests that this subclass could have a specific pathogenic role. NF155-IgG1 assay may be a useful diagnostic test in patients with post- vaccine GBS.

Disclosure: The authors declare no competing interests.

Brain magnetic resonance showing left cranial VII nerve contrast enhancement of patient 1

EPO-707

Peripheral nervous system involvement in post-acute sequelae of COVID-19

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Background and aims: Post-acute sequelae of COVID-19 (PASC) refers to a wide range of symptoms experienced by COVID-19 survivors. Here, we aimed to investigate peripheral nerve system (PNS) in survivors of COVID-19 by means of electrophysiology.

Methods: All consecutive patients of COVID-19 outpatient clinics during October-November 2021 with COVID-19 at least four weeks ago were invited to complete a predesigned form composed of the Composite Autonomic Symptom Scale-31, the modified Toronto Neuropathy symptom score and fatigue severity scale. Patients with high scores in one and who volunteered to participate in the study were invited for a detailed examination and neurophysiological studies, which included nerve conduction studies, cutaneous silent period, repetitive nerve stimulation, needle electromyography, quantitative electromyography (QEMG) and single fiber electromyography. The findings of patients were compared to those of healthy subjects.

Results: Among 172 patients applied, 106 of them completed the form. Among 106 patients, 25 had autonomic symptoms, 10 had fatigue syndrome, 22 defined generalized weakness, 30 had paresthesia and 23 had myalgia. Patients are grouped according to COMPASS-31 scores into PASC and non-PASC (Table 1). Among these patients, ten patients agreed to participate in the electrophysiological analysis. Myopathic motor unit potentials were detected in three, in whom the percentage of polyphasic potentials were significantly high by QEMG. Nerve conduction studies, repetitive nerve stimulation and single fiber analysis were normal in all.

	Non-PASC patients n=81 (75.7%)	PASC patients n=25 (23.4%)	p value
Age, Median (IQR)	37 (18)	42 (17)	0.27
Female, n (%)	34 (42%)	13 (52%)	0.37
Duration between COVID-19 and questionnaire, day (IQR)	46 (202)	40 (40)	0.20
COMPASS-31 score, Median (IQR)	2.14 (5.4)	20.21 (12.34)	<0.001
FSS score, Median (IQR)	4.22 (3)	5.67 (1.33)	<0.001
Neuropathic complaints n (%)	13 (16%)	17 (68%)	<0.001
Muscle weakness, n (%)	11 (23.4%)	11 (73.3%)	<0.001
Anosmia, (%)	22 (27.2%)	14 (56%)	0.007

Table 1. Characteristics of patients with and without PASC

Conclusion: Although electrophysiological findings are relatively rare, symptoms of PNS are seen in up to 23.4% of COVID-19 survivors.

Disclosure: Nothing to disclose.

EPO-708

Abstract withdrawn

Sleep-wake disorders & Autonomic nervous system diseases 2

EPO-709

Comparison of pain provoked versus standard 40 min tilt table test for the conformation of vasovagal syncope

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Background and aims: Tilt table test represents a valuable diagnostic method in assessing patients with transient loss of consciousness and confirming the diagnosis of vasovagal syncope. However, the test lacks standardization, and various protocols exist in different centers. The aim of this study was to compare the difference in sensitivity and time-to-syncope of tilt table test with a painful stimulus provocation compared to standard test with no provocation.

Methods: This was a prospective study that included consecutive patients diagnosed with vasovagal syncope who were referred for tilt table testing. Patients were randomly assigned to two groups, group 1 with pain provocation after the first 10 minutes of upright position and group 2 with no provocation with further 30 minutes of tilt in both groups.

Results: In group 1, 66 (78.6%) patients developed syncope while in group 2, 35 (44.3%) patients had syncope (p<0.001). This represents an increase of 34.3% in TTT sensitivity with the application of painful provocation. There was no statistically significant difference in time to syncope between the two groups, although group 1 presented with shorter time-to-syncope (12 minutes (3-37) vs. 18 minutes (1-39), p=0.052). According to survival analysis, group 1 had shorter survival time in comparison to group 2 (p<0.001).
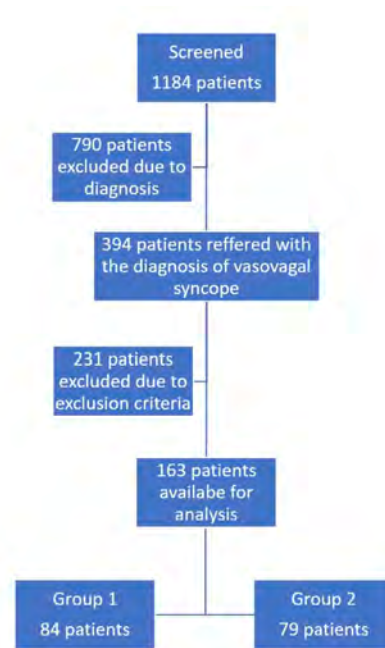
Figure 1: Flow chart of the study. There were 1184 patients that were referred for tilt table testing during the study period. 790 patients were excluded due to referral diagnosis other than syncope. Of the 394 patients that had a referral diagnosis of s
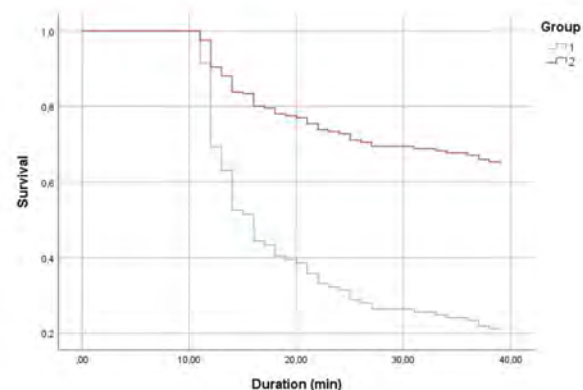
Figure 2: The model-predicted time to syncope occurrence related to type of the protocol. Results of the Cox regression analysis.

Conclusion: Pain provocation is a useful method for increasing sensitivity and shortening the duration of tilt table testing.

Disclosure: Nothing to disclose.

EPO-710

Sleep spindle analysis in children with snoring and/or sleep disordered breathing

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Background and aims: Obstructive sleep apnea syndrome (OSAS) in children is associated with the changes in the macro- and micro-structure of the sleep, which lead to the neurocognitive and developmental consequences. The possible effects of snoring on sleep and spindle activity have not been established yet.

Methods: We analyzed the clinical data, polysomnographic parameters and the sleep spindle activity in children with primary snoring and/or OSAS in compared to healthy children.

Results: A total of 51 children were included; 8 children had primary snoring, and 27 children had OSAS; of these, 16 OSAS patients had snoring and 11 patients did not. Sixteen children were the healthy controls and did not have snoring or OSAS. The mean age and the gender were similar between children with and without OSAS, while the children with OSAS had a higher body mass index z score (p=0.042). In sleep spindle analysis, the density (p=0.034) and the duration (p=0.019) of spindles were decreased in children with OSAS in compared to healthy controls. The sleep spindle activity did not show significant changes between children with primary snoring and healthy controls, or between OSAS children with and without snoring.

Conclusion: We may conclude that it is not snoring per se but OSAS that affects sleep spindle activity in children. Whether primary snoring is a normal variant or a disease with consequences requires further studies with larger samples. OSAS with and without snoring also deserve greater attention if they are different phenotypes of the disease with different pathophysiologic mechanisms.

Disclosure: Nothing to disclose.

EPO-711

The Effects of Smoking on Metabolic Parameters in the Treatment of Obstructive Sleep Apnea Syndrome

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Background and aims: The relationship between the obstructive sleep apnea syndrome (OSAS) and metabolic syndrome is quite complex. Smoking contributes to the development of metabolic syndrome by increasing the severity of OSAS, and disturbing the macro- and micro-structure of sleep. In this study, we aimed to investigate the effects of smoking on metabolic parameters in OSAS patients treated with the positive airway pressure (PAP) therapy.

Methods: Patients diagnosed with OSAS in our Sleep Disorders Unit were prospectively and consecutively included. Demographic parameters such as body mass index (BMI), neck, waist and hip circumference values, PSG parameters including apnea-hypopnea indices (AHI), and metabolic parameters were noted before and after 3-month PAP treatment in OSAS patients, and the effects of PAP therapy were compared in smokers and non-smokers.

Results: A total of 115 OSAS patients, 72 males and 43 females, were included in the study. 53.3% of them were smokers. There was no significant difference between smokers and non-smokers in terms of demographic parameters, BMI, neck, waist and hip circumference values and AHI scores. The analysis of fasting blood glucose, oral glucose tolerance test, HOMA index, HbA1c, insulin, triglyceride, LDL and total cholesterol showed no significant differences between the smoker and non-smoker groups. On the other hand, leptin values were increased in smokers but decreased in non-smokers, and the difference between two groups was highly significant (p=0.029).

Conclusion: We demonstrated that despite the beneficial effects of PAP treatment on metabolic parameters in OSAS, smoking plays a preparatory role for the leptin level increase and leptin resistance.

Disclosure: Nothing to disclose.

EPO-712

The clinical picture of idiopathic hypersomnia ten years after the initial diagnosis

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Background and aims: Idiopathic hypersomnia (IH) is a rare disorder of hypersomnolence. Considering that many frequent diseases and treatments may induce sleepiness, we wanted to determine whether our patients met IH diagnostic criteria years after the initial diagnosis.

Methods: The patients diagnosed with IH in two sleep centers at least three years ago were contacted, and their clinical status was reevaluated by an interview. The IH diagnosis was based on the persisting presence of excessive sleep or sleepiness and simultaneous absence of better explanation by reported conditions, medication, and other illnesses.

Results: In total, 50 subjects (34 females, average age 47.6 SD=12.8 years) were reexamined. The long sleep duration was initially found in 24 of them. The interval between the original diagnosis and the reevaluation was 9.6 (SD=7.8) years. 19 reevaluated subjects (38%) did not meet the aforementioned IH criteria for the following reasons. The disappearance of sleepiness (5 subjects), the diagnosis change to narcolepsy type 2 (1 subject), significant RLS combined with severe polymorbidity (2 subjects), severe OSA without treatment (3 subjects), mood disorder (bipolar-1, depression, and anxiety – 5) extensively medicated without considerable improvement, chronic cardio-respiratory failure (1 subject), and sedating medication for essential tremor and polyneuropathy (1 subject).

Conclusion: Our findings show that (a) IH might, after years, lose its original clarity due to the development of various previously absent conditions making diagnosis confirmation hard or even impossible, and (b) excessive sleepiness may disappear in some patients.

Disclosure: Supported by Ministry of Health of the Czech Republic, grant nr. NU20-04-00088.

EPO-713

The Bernese Retrospective Cohort to Study Rest-Activity Patterns in RBD-Patients

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Background and aims: Isolated REM-Sleep behavior disorder (iRBD) is a prodromal state of α-synucleinopathies. Symptoms like dream enactment may emerge years before manifesting an overt α-synucleinopathy. Changes in the rest-activity pattern have been identified in iRBD patients and associated with an increased phenoconversion risk. This study established a retrospective cohort of RBD patients to investigate alterations in the rest-activity pattern as biomarkers of increased phenoconversion risk.

Methods: Patients diagnosed with RBD according to the ICSD-3 criteria who had undergone on average 10 days (range 3–22) of actigraphy were included. Actigraphy summary variables (length of nighttime rest period, inactivity index, frequency of daytime rest periods, and nighttime activity) were extracted from the actigraphy report and analyzed with t-tests.

Results: 88 patients were included. The mean age was 62y (range 18–78), 69% were male. In 26% of patients, no underlying neurodegenerative disease was present (probable iRBD). No significant differences were found in the actigraphy summary variables between iRBD and patients with manifest α-synucleinopathy.

Conclusion: These preliminary results are in line with previously published studies. Non-parametric analysis based on the raw actigraphy data will be used further to characterize rest-activity patterns of RBD patients in the cohort to identify putative biomarkers of increased phenoconversion risk.

Disclosure: The authors declare that they have nothing to disclose.

EPO-714

The socioeconomic burden and value of treatment of insomnia and excessive daytime sleepiness – a multi-step approach

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Background and aims: Insomnia (IN, prevalence in the general population: 10–20%) and excessive daytime sleepiness (EDS, 5–15%), are the most frequent sleep-wake disturbances. Few reports suggest an important impact on individual's health, but also on efficiency, workability, and quality of life, and thereby on health systems and economic performance. Prospective and systematic studies on burden and value of treatment (VOT) of IN and EDS are lacking.

Methods: A European multi-society study was initiated by the EAN with the European Sleep Research Society (ESRS), European Psychiatric Association (EPA), Alzheimer Europe, European Brain Council (EBC), European Pediatric Neurology Society (EPNS) and European Federation of Neurological Associations (EFNA). A multi-step approach with 4 work packages (WP) is planned: WP 1: a systematic review of the burden and VOT of IN and EDS using the GRADE system. WP 2: a pilot study followed by a multi-center, multi-national study in which general practitioners (GP's, 6 per site) in collaboration with a specialized sleep center will prospectively assess (50 patients per GP) adult and pediatric patients with IN and EDS for 12 months. WP 3: a cost-of-illness evaluation study taking into account the results from WP 1 and 2. WP 4: a white paper with recommendations to improve the management of IN and EDS.

Results: Results of the meta-analysis of high-quality studies on IN and EDS will be presented (WP1). Further details on the methodology of WP2 will be presented at the congress.

Conclusion: This study together will provide insights into the possibilities of involving general practitioners in the diagnosis and management of patients with IN and EDS and the related cost implications. This study will influence the policy towards better treatment and care for people with IN and EDS.

Disclosure: No conflicts of interest to declare.

EPO-715

Clinical and electrophysiological recovery with immunotherapy in Sjogren Syndrome-linked severe autonomic neuropathy

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Background and aims: The autonomic system is frequently affected in Sjogren's syndrome (SS), but presentation with severe autonomic neuropathy is very rare. This report presents a patient with SS-associated severe autonomic neuropathy, which is significant clinical and electrophysiological responsive to immunotherapy.

Methods: N/A

Results: A 29-year-old female patient was admitted to our neurology clinic with recurrent syncope attacks and postural light-headedness. Episodes of syncope required the patient to lie in the supine position all day and were even triggered by a slightly sitting position. Heart rate variability (HRV) analysis revealed marked cardiovagal and sudomotor dysfunction. The patient was diagnosed with SS after detailed investigations. A 5-day course of intravenous immunoglobulin (IVIg) (total dose 2 g/kg) was given, and then she was able to straighten from the supine position. She continued IVIg treatment at a 0.4 g/kg dose once a month. After six months, she could walk long distances without support, and syncope attacks were almost entirely resolved. After approximately 1.5 years, control HRV analysis showed recovery in SDRR (standard deviation of the RR interval) and RMSSD (mean square root of consecutive RR interval differences).

Table 1: Heart rate variability analysis

	Normal Breathing	Deep Breathing
a)Initial examination 16.12.2019		
SDRR	0.017 s	
RMSSD	0.011 s	
b) Control examination 08.07.2021		
SDRR	0.032 s	0.061 s
RMSSD	0.029 s	0.036 s

SDRR: Standart deviation of RR interval

RMSSD: Root mean square of successive RR interval differences

Table 1

Conclusion: When patients present with symptoms suggestive of autonomic nervous system disorder, the diagnosis of SS should be kept in mind. In SS-associated severe autonomic neuropathy, immunotherapy can provide electrophysiological recovery in addition to excellent clinical response. If clinical and electrophysiological tests indicate severe autonomic neuropathy, IVIg and/or anti-CD20 monoclonal antibody therapy should be considered.

Disclosure: The authors have nothing to disclose.

EPO-716

Low specificity of screening questionnaires for REM sleep behavior disorder

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Background and aims: Validated screening questionnaires for REM sleep behavior disorder (RBD) have shown limited usefulness outside the context of validation studies. Aim of this study was to assess the diagnostic value of RBD screening questionnaires in a large sample of patients referred to a sleep center.

Methods: This prospective study included 400 consecutive patients referred for the first time for evaluation of any type of sleep disorder to Innsbruck or Barcelona. Patients filled consecutively prior to the routine clinical interview: RBD screening questionnaire (RBDSQ), RBD single question (RBD1Q) and Innsbruck RBD inventory. All patients positive for at least one questionnaire were invited to undergo video-polysomnography (V-PSG). Patients negative for all questionnaires underwent V-PSG whenever indicated. Sensitivity, specificity, accuracy, negative and positive predictive value of the RBD questionnaires were calculated.

Results: One patient from each center refused participation. Mean age of the 398 participants (54.8% male) was 50.4±17.1 years. 59.5% were positive for at least one questionnaire. 88.6% underwent V-PSG. RBD was diagnosed in 13.3%. Of the 161 patients negative for all RBD questionnaires, 92 underwent V-PSG. 1.1% of them had RBD. Sensitivity/specificity/accuracy were: 79.3%/47.3%/50.3% for the RBDSQ; 75.9%/66.1%/67% for the RBD1Q; 89.7%/54.6%/57.9% for the Innsbruck RBD inventory. Combining the three questionnaires, sensitivity was 96.6%, specificity 33.3%, accuracy 39.4%. Negative predictive value was 98.9%, positive predictive value 13.3%. Sleep experts identified RBD with 72.4% sensitivity, 96.3% specificity and 94.2% accuracy.

Conclusion: Specificity and positive predictive value of the RBD screening questionnaires were low to very low, underlying the need of V-PSG for RBD diagnosis.

Disclosure: Nothing to disclose.

EPO-717

Effects of acute exposure to altitude on Restless Legs Syndrome

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Background and aims: Next to genetic factors, brain iron dysregulation and dopaminergic dysfunction, a role of hypoxia has been suggested in restless legs syndrome (RLS) pathogenesis. Aim of this study was to investigate the effect of acute exposure to high-altitude on periodic leg movements during wakefulness (PLMW) and RLS symptoms during a suggested immobilization test (SIT) in RLS.

Methods: 28 RLS individuals underwent 1-hour SIT twice: in randomized order, double-blinded, in a simulated altitude of 3,000 m, and at 574 m. PLMW, subjective discomfort and urge to move the legs were recorded.

Results: 28 RLS patients (45.1±10.8 years, 53.6% female) were included: ten untreated, 10 under dopaminergic treatment and eight under non-dopaminergic treatment/polytherapy. PLMW index was higher at 3,000 m (p=0.289). Discomfort and urge to move the legs increased during SIT, and were worse at 3000m. Statistically significance was reached only for urge to move the legs at 30 (p=0.043) and 45min (p=0.039) after SIT onset. When stratifying for sex, a significant difference was present only in males: I. subjective discomfort and urge to move were higher at 3,000 m 30 min after SIT onset (p=0.045 and p=0.006, respectively); II.urge to move the legs was stronger at high-altitude 45 min after SIT onset (p=0.019); III.PLMW index during SIT was higher at 3,000 m (p=0.029).

Conclusion: In RLS patients, urge to move the legs is stronger at high-altitude. This effect was present only in male patients, with worse sensory and motor symptoms, and higher PLMW index at high-altitude. These data support the role of peripheral hypoxia in RLS.

Disclosure: This study was supported by the Swedish RLS Foundation and by the German Restless Legs Association.

EPO-718

INFLAMMATORY BIOMARKERS IN SLEEP-RELATED BRUXISM

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Background and aims: Sleep-related bruxism (SRB) is defined as the repetitive jaw-muscle activity characterized by clenching or grinding of the teeth or by bracing or thrusting of the mandible during sleep. SRB is associated with psychophysiological factors as well as drug use or sleep-related breathing disorders. The role of inflammation in the pathophysiology of SRB has not been demonstrated as in other sleep-related movement disorders like restless legs syndrome. We aimed to investigate the role of inflammation in the pathophysiology of SRB.

Methods: Patients with SRB diagnosed with clinical findings and polysomnography (PSG) and a healthy control group without bruxism were included in the study. Sleep-related breathing disorders were excluded. Demographic information, routine PSG data compared with the count of neutrophil, white blood cell (WBC), lymphocyte, and neutrophil-lymphocyte ratio (NLR), ferritin, and vitamin B12 in venous blood samples.

Results: Patients with SRB (n=31) were younger than control (n=20) group (35.7+12.2 years vs. 46.5+13.2 years; p=0.011). Periodic limb movement index was higher in patients with SRB than the control group (6.5+11.2/h vs 4.5+11.8/h; p=0.001). WBC count was higher in the patients than controls (7.4+1.2/mm^3 vs. 6.3+1.4/mm^3; p=0.018). Lymphocyte count was also higher in bruxism patients (2.6+0.6/mm^3 vs. 2.1+0.6/mm^3; p=0.058), but the level of significance remained at the limit. Serum levels of ferritin, vitamin B12, and NLR were similar between the two groups.

Conclusion: Higher WBC observed in SRB may suggest a common inflammatory mechanism. Further studies with larger samples are needed to explore the presence of inflammation in SRB.

Disclosure: All authors have no disclosure.

EPO-719

Easy TElemedicine for NARcolepsy (TENAR): 1-year feasibility study on televisit during COVID-19 epidemic in Italy

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Background and aims: Narcolepsy is a rare chronic central disorder of hypersomnolence often associated with endocrine-metabolic issues. The need of a multidisciplinary management, the scarcity of reference centers, the long diagnostic delay increase disease burden. We applied a multidisciplinary telemedicine approach during COVID-19 epidemic to allow patient access to the multidisciplinary consultations.

Methods: During the first COVID-19 epidemic peak and the related lockdown we applied a multidisciplinary care protocol through televisit to consecutive narcolepsy patients planned to attend routine follow-up visit. We conducted a baseline clinical sleep and endocrinological assessment, the former repeated at month 2, 4, 6 and 12 from study inclusion.

Results: 39 out of 44 (88.6%) eligible patients (30 adults, 9 children/adolescents), from 12 different Italian regions (Figure), were included (Table 1); 36 were residents outside the city of Bologna (median distance from the patients' city of residence: 234 Km, range 48–1,221) (Figure). At baseline (Table 2), median Epworth sleepiness scale score (ESS) = 10 (range 8–13); median BMI=25.6 (range 22.1–30.9). At 1-year follow up, the ESS score improved reaching statistical significance (median 8, range 6–13, p=0.013), and the proportion of patients with overweight and obesity significantly decreased (p=0.008).

Easy-TENAR feasibility study: Italian regions of origin of patients

Baseline characteristics	Categorical variables: N (%) Continue variables: median (IQR) [min – max]
Sex	
Female / Male	17 (43.6) / 22 (56.4)
Age – years	27 (18 – 44) [14 – 57]
Body Mass Index – Kg/m²	25.6 (22.1 – 30.9) [16.2 – 43.8]
BMI	
underweight	2 (5.4)
normal	12 (32.4)
overweight	13 (35.1)
obese	10 (27.0)
Education	
elementary school	2 (5.1)
secondary school	11 (28.2)
high school	23 (59.0)
degree	3 (7.7)
Living situation	
alone	3 (7.7)
in family	33 (84.6)
in sharing	3 (7.7)
Narcolepsy type 1/ type 2	38 (97.4) / 1 (2.6)
Age onset – years	15 (9 – 20) [3 – 45]
Age diagnosis – years	18 (12 – 35) [7 – 46]
Orexin	
positive	34 (87.2)
negative	2 (5.1)
missing	3 (7.7)
Cataplexy frequency	
No cataplexy	5 (12.8)
< 1/years	2 (5.9)
1/years-1/month	8 (23.5)
1/month-1/week	8 (23.5)
1/week-1/day	10 (29.4)
>1/day	6 (17.7)
Other diseases	
Obstructive sleep apnea syndrome	2 (5.1)
Chronic lung diseases	3 (7.7)
Depression, Psychosis	3 (7.7)
Hypothyroidism	1 (2.6)
Rheumatoid arthritis	1 (2.6)
Cancer	1 (2.6)

Table 1. Easy-TENAR feasibility study: baseline characteristics of the included patients (N=39).

Outcome	N of responders	Baseline	12 months	p-value baseline vs. 12months
		Median (IQR) [min-max] Mean (SD)		
ESS/ESS-CHAD	34	10 (8 – 13) [3 – 20]	8 (6 – 13) [3 – 19]	0.013
Cataplexy – n (%)	39	34 (87.2)	34 (87.2)	1
NSS in adults	21	21.9 (14.1)	20.3 (11.6)	0.29
Global Impression Scale	37	4 (3-4) [2-5]	4 (3-4) [1-6]	0.43
BDI in adults	21	5.3 (5.1)	5.3 (6.3)	0.89
STAI-trait in adults	21	45.0 (4.6)	43.4 (4.7)	0.56
STAI-state in adults	21	38.7 (10.5)	36.4 (9.5)	0.20
Weight – Kg	37	78 (67 – 97) [43.5 – 145]	76 (67 – 93) [42 – 145]	0.244
BMI - Kg/m2	37	25.4 (22.1 – 30.4) [16.2 – 42.8]	24.7 (22.8 – 29.3) [15.6 – 42.8	0.217
BMI – n (%)	37			0.008
underweight		2 (5.4%)	2 (5.4%)	
normal		12 (32.4%)	18 (48.7%)	
overweight		13 (35.1%)	9 (24.3%)	
obese		10 (27.0%)	8 (21.6%)	
Caloric intake	35	1600 (1200-2000) [1000-6950]	1450 (1150-1750) [1000-2750] 4 missing	0.13
Physical activity – n (%)	39	23 (59.0)	18 (48.7) 2 missing	0.17
SF-36 PCS in adults	15	42.0 (3.8)	43.3 (4.5)	0.43
SF-36 MCS in adults	15	48.5 (5.1)	47.8 (6.2)	0.71
Compliance to treatment	39			
very good – n (%)		32 (82.0)	37 (97.4)	0.056
good – n (%)		3 (7.7)	1 (2.6)	
poor – n (%)		4 (10.3)	0	
Adverse drug reactions	39	11 (28.2%)	4 (10.5%) 1 missing	0.08
Accidents	20	1 (5.0%)	0 (0%)	1

Table 2. Easy-TENAR feasibility study: clinical outcomes at baseline and 12-month follow up.

Conclusion: Telemedicine was well received by narcolepsy patients during lockdown and allowed to improve sleep and endocrinological aspects at 1-year follow up. We are performing a two-arm, parallel, open randomized controlled trial (TENAR RCT) to demonstrate the non-inferiority of the televisit versus standard in-office visit, paving the way for innovative multidisciplinary management of narcolepsy and other rare diseases.
Disclosure: Nothing to disclose.

ePosters Virtual

EPV-001

Apathy in Dementia and its association with Depression

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EPV-002

Odour identification in early Alzheimer's disease

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EPV-003

Alterations in White Matter Microstructure in Cognitively Impaired Patients with Parkinson's Disease

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EPV-004

Cytotoxic lesion of the corpus callosum in a patient with early Alzheimer's disease

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EPV-005

The INCP – a Tablet-Based Self-Administered Neurocognitive Assessment: A Pilot Study Using Test-Retest Analysis

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EPV-006

Rapidly Progressive Dementia – a Retrospective Case Series

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EPV-007

Unusual presentation of Creutzfeldt-Jakob disease: a two-hit phenomenon?

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EPV-008

Semantic dementia presenting with anorexia nervosa: a case report

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EPV-009

Capgras Syndrome: From Hashimoto's Encephalopathy to Alzheimer's Disease

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EPV-010

CAG repeats within the non-pathological range in the HTT gene influence personality traits in SCD patients

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EPV-011

Sporadic lateonset nemaline myopathy with dermatological manifestation, a challenge for diagnosis and treatment.

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EPV-012

Neuron-derived exosomal hemoglobin level in mild cognitive impairment

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EPV-013

Posterior Cortical Atrophy and Logopenic Variant of Primary Progressive Aphasia: A spectrum of the same syndrome?

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EPV-014

Evaluation of orthostatic hypotension among the community dwelling older persons

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EPV-015

Behavioral variant of Alzheimer's Disease: correlation to newly proposed diagnostic criteria

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EPV-016

Peripheral markers of inflammation in Mild Cognitive Impairment

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EPV-017

Autonomic nervous system dysfunction in patients with post-covid.

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EPV-018

Meningitis-retention syndrome (MRS): an unrecognized clinical condition

L. Quiros Illan [1], L. Ruiz Escribano-Menchen [1], F. Villanueva Ruiz [1], I. Martin Sobrino [1], M. Nieto Palomares [1], A. Garcia Maruenda [1], A. Franco Salinas [1], D. Grande Murillo [2], J. Muñoz-Torrero [1], A. Hernandez Gonzalez [1]

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EPV-019

Risk factors for cryptogenic stroke in people under sixty-five years

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EPV-020

Cardiac myxoma presenting with pituitary apoplexy and multisystem involvement

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EPV-021

Doctor, why can't I stop laughing? Pathological laughter as manifestation of pontine infarction.

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EPV-022

Posterior Reversible Encephalopathy Syndrome (PRES) as a Complication of Meningitis: Case Report and Literature Review

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EPV-023

Vertical one-and-a-half syndrome in a patient with pecheron artery ischemia: A case report

T. Azevedo [1], C. Batista [1], A. Ponceano [1], F. Alves [2], E. Júnior [3], R. Barreira [4], J. Santos [5]

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EPV-024

Incidental diagnosis of Familial Hemiplegic Migraine type 1 (FHM1) after genetic tests for cerebral small vessel disease

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EPV-025

Carotid web as a rare cause of stroke in young patients

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EPV-026

Combined acute revascularization in early bilateral carotid stent occlusion - case report

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EPV-027

Recurrent catastrophic antiphospholipid syndrome: what to do then?

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EPV-028

Ischemic stroke after diagnosis of Takotsubo Syndrome

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EPV-029

Frontal meningioma as a rare cause of anterior cerebral artery stroke: a case report

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EPV-030

A PUFF OF SEIZURES

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EPV-031

Short neck as a cause of stroke? Bilateral vertebral artery dissection in a patient with Klippel-Feil syndrome.

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EPV-032

DURAL ARTERIOVENOUS FISTULA: THERE MAY BE MORE THAN WHAT MEETS THE EYE

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EPV-033

Cerebral venous thrombosis following an immunoglobulin-E mediated anaphylactic reaction

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EPV-034

Occlusion of the Internal Carotid artery as a manifestation of unicentric Castleman's disease

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EPV-035

Infarction in the splenium of the corpus callosum associated with two mutations PAI-1 4G / 5G and ACE 1 / D

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EPV-036

Presentation of a lobar hemorrhahe related to cerebral amyloid angiopathy

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EPV-037

Multiple acute ischemic strokes : a study of clinical, radiological and etiological profile About 14 patients

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EPV-038

Cortical dysprosody

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EPV-039

Cerebellar stroke leading to akinetic mutism

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EPV-040

Decompression Sickness after repetitive Breath-Hold diving: A Case Report and systematic review of the literature

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EPV-041

Migraine as the main cause of the development of chronic cerebral ischemia (significant criteria, signs of neuroimaging)

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EPV-042

Contralateral recombinant tisular plasminogen activador-related angioedema in a patient with right hemispheric stroke

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EPV-043

Secondary prevention and outcome after acute ischaemic stroke in three different socio-economic environments

H. Hammer [1], A. Scutelnic [1], H. Sarikaja [1], T. Zdrojewski [2], K. Chwojnicki [3], B. Karaszewski [3], P. Lowiec [3], A. Yagensky [4], H. Saner [5], C. Bassetti [1], M. Arnold [1], M. Heldner [1]
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EPV-044

Characteristics of the pre-stroke risk factor profile and its influence on disqualification from mechanical thrombectomy

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EPV-045

Two brothers, two strokes, two different types of decisions at the same time

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EPV-046

Symptomatic cerebral arterial gas embolism – a rare complication of carotid angiography

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EPV-047

Transvenous embolization of a carotid-cavernous fistula in a patient with vascular Ehlers-Danlos syndrome

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EPV-048

"Upside-down": The room-tilt illusion

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EPV-049

Stroke Mimics Diagnosed By Emergency Medical Services In Kyrgyzstan: Is There A Way To Improve Logistics?

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EPV-050

Dyslipidemia as an indicator of severity of neurological deficiency in ischemic stroke in Dagestan women

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EPV-051

Carotid stenosis: when the eye is the sneak.

M. Martínez Zarco [1], A. González Romero [1], E. Marín Conesa [1], R. Ramírez Toledo [1], E. Gómez López [2], E. Giménez López [3], I. Pellicer Espinosa [4]
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EPV-052

Opercular syndrome with unilateral ischemic lesion: a stroke chameleon

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EPV-053

The frontal-occipital gradient as a neuroimaging biomarker of probable cerebral amyloid angiopathy

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EPV-054

Neutrophil-to-lymphocyte ratio (NLR) as a negative outcome predictor in Caucasian stroke patients treated with IV rtPA

M. Nowak, M. Karliński, M. Śnieżyński, N. Pożarowszczyk, I. Kurkowska-Jastrzębska, A. Członkowska
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EPV-055

Cerebral infarction in patients with cancer: treatment ploblems

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EPV-056

Transient Mustism Followed by Dysarthria with Pontine Ischemic Stroke

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EPV-057

Vasculitis with central nervous system involvement in adulthood: a review of 2 clinical cases

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EPV-058

Premorbid multidimensional frailty as predictor of short-term complications in acute stroke patients

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EPV-059

Critical stenosis of the intracraneal internal carotid artery due to extrinsic compression by parasellar Meningioma

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EPV-060

Moyamoya disease and paranoid schizophrenia: causality or casualty

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EPV-061

Takotsubo Syndrome and Ischemic Stroke: Cause or Consequence?

R. Rocha [1], L. Ribeiro [1], Â. Fonseca [1], T. Pinto [2], S. Silva [2], S. Tavares [2], N. Moreno [3], S. Moreira [1], C. Duque [1], V. Tedim Cruz [1]

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EPV-062

Cerebral venous sinus thrombosis and COVID-19. Where is the connection?

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EPV-063

Performance of ischemic stroke with large vessel occlusion treatment in a metropolitan area: a longitudinal analysis

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EPV-064

Wet And Dry Biomarkers To Predict Secondary Injury In Stroke: From Bench To Bedside. Nimble Study Protocol

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EPV-065

Threading the needle: a case of infarction in a middle cerebral artery displaced by an adjacent glioblastoma multiforme.

N. Giagkou, V. Tentolouris-Piperas, V. Papadopoulous, G. Zorbas, T. Mavridis, A. Tountopoulou, S. Vassilopoulou, D. Mitsikostas

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EPV-066

Heterozygous HTRA1 related cerebral small vessel disease: two case reports from Italy

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EPV-067

Endovascular treatment of carotid artery fibromuscular dysplasia in acute ischaemic stroke – a case report

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EPV-068

Case report: Congenital absence of the internal carotid artery – a rare anatomical variant

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EPV-069

Cognitive Functions among children with Isolated Growth hormone Deficiency in Khartoum-Sudan

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EPV-070

Vibrance-mg: Clinical Trial of Nipocalimab in Pediatric Myasthenia Gravis

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EPV-071

Sturge-Weber syndrome without port-wine stain, a case report

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EPV-072

Idiopathic Intracranial Hypertension (IIH) in children during the COVID-19 Pandemic

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EPV-073

Pharmacological aspect in managing refractory dystonia in Glutaric Aciduria Type 1

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EPV-074

Are different bioelectrical activities in hemifacial spasm related to facial nerve excitability?

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EPV-075

Neurophysiological and psychological features in the epilepsy with dissociative disorders

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EPV-076

The effect of N-Pep-12 therapy on brainwaves following an ischemic stroke

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EPV-077

Pattern analysis of the periaquedutal gray matter's FOS protein activation in rats submitted to withdrawal

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EPV-078

Quantitative electroencephalography (QEEG) as a biomarker for post-stroke depression

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EPV-079

FTI: a neuropsychological marker to discriminate different cortical forms of dementia

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EPV-080

Preliminary results of antisaccades in individuals with ultra high-risk psychosis and bipolar disorder

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EPV-081

Effect of parasellar invasion of pituitary adenoma on quality of life,intelligence, memory before and after surgery

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EPV-082

Identification of potential microRNA targets for the diagnosis of cognitive decline

R. Novobilský [1], M. Roubec [1], M. Sabela [1], P. Bártová [1], P. Kušnierová [2], O. Machaczka [3], A. Zatloukalová [3], P. Ambroz [3], J. Janoutová [3], M. Bar [1], D. Stejskal [2], V. Janout [3]

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EPV-083

Social Cognition deficits in Amyotrophic Lateral Sclerosis: a pilot cross-sectional population-based study.

F. Palumbo, B. Iazzolino, L. Peotta, A. Canosa, U. Manera, M. Grassano, F. Casale, P. Giorgio, R. Mario Giorgio, R. Vasta, C. Moglia, A. Chiò, A. Calvo
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EPV-084

The relation of cognitive reserve with cognitive impairments in different types of multiple sclerosis course

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EPV-085

Utility of the MoCA-Memory Index Score (MoCA-MIS) in distinguishing Alzheimer's disease from frontotemporal dementia

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EPV-086

Methods and considerations in the investigation of sleep and circadian disturbances in disorders of consciousness

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EPV-087

COVID-19 and Cognitive Impairment: a Cross-Sectional Study

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EPV-088

Effects of COVID-19 Pandemic on Daily Life of MS Patients

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EPV-089

Olfactory and Gustative Dysfunction in Iot study

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EPV-090

Neurological impacts of COVID-19: a bibliometric analysis

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EPV-091

Is epilepsy associated with a severe course of COVID-19?

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EPV-092

Myocarditis due to ChAdOx1 nCov-19 vaccination: a rare cause of cardioembolic stroke

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EPV-093

Differences in mortality rates in hemorrhagic strokes during the 4 waves of COVID-19

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EPV-094

Acute myelitis and Guillain-Barré Syndrome Overlap secondary to concurrent triple vaccination and SARS-COV-2 infection

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EPV-095

Peripheral neuropathy following COVID-19 mRNA vaccination – 2 Case Reports

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EPV-096

Clinical and electrophysiological characteristics of COVID and post COVID polyneuropathies in adults and pediatrics

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EPV-097

Circulating CGRP Levels in Headache Attributed to COVID-19 Infection

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EPV-098

Characteristics of stroke patients on wave 4 of COVID-19

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EPV-099

Post SARS-CoV2 myoclonus tremor: a case after a mild infection without metabolic alterations.

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EPV-100

Clinical case of acute encephalitis probably associated with SARS-CoV-2

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EPV-101

The neurological adverse effects of anti-covid vaccines: a mini-series of 10 cases

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EPV-102

The role of saliva in the defeat of oral cavity structures in coronavirus infection

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EPV-103

Neuromyelitis Optica Spectrum Disorder after COVID-19 Vaccination

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EPV-104

Our epilepsy unit throughout the COVID-19 pandemic

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EPV-105

Impact of COVID-19 and lockdown on neuropsychological status of MS population.

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EPV-106

The course of COVID-19 infection against the background of natalizumab therapy

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EPV-107

Is COVID-associated parosmia/parosmia a cortical disorder with trigeminal pathogenesis?

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EPV-108

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection as a trigger for the debut of myasthenia gravis

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EPV-109

A COVID-19 Patient Presenting with bilateral foot-drop and white matter abnormality: a case report.

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EPV-110

A rare case of bilateral caudate ischemia in a 60-years-old woman associated with CoVid-19

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EPV-111

Typical manifestations of mitochondrial disease in the epidemiological context of SARS-CoV-2 infection.

M. Martínez Zarco [1], E. Marín Conesa [1], A. González Romero [1], R. Ramírez Toledo [1], E. Gómez López [2], I. Pellicer Espinosa [3], P. Herrero Bastida [4], E. Giménez López [5], R. Morcillo [6]

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EPV-112

Acute encephalitis following COVID-19 vaccination

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EPV-113

Vaccination coverage against SARS-CoV-2 in Portuguese adult patients with Multiple Sclerosis

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EPV-114

Impact of delaying botulinum toxin treatment in patients with migraine during the COVID-19 pandemic

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EPV-115

Coronavirus (COVID-19) Vaccinations in patients with multiple sclerosis - The experience of one center

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EPV-116

COVID-19 Cytokine Storm in Myasthenia Gravis Treated with Mesenchymal Stem Cells: The First Philippine Experience

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EPV-117

Traumatic brain injury during COVID-19 epidemy

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EPV-118

Nerve conduction study results in patients recovering from COVID-19

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EPV-119

Post-COVID-19 cognitive functioning in people with type 1 diabetes mellitus

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EPV-120

Facial diplegia: a complication to consider in adenovirus-based SARS-CoV-2 vaccination

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EPV-121

Asymmetrical inflammatory myositis after ChAdOx1 nCov-19 vaccine

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EPV-122

Assessment Of Cognitive Functions In Patients With Post-Covidal Cerebroastenic Syndrome

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EPV-123

Purulent meningoencephalitis in post-covid-19 paediatric patient - complication of sinusitis

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EPV-124

Amantadine treatment in Parkinson's disease patients as a modulatory factor of SARS-Cov-2 infection

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EPV-125

Impairment of trigeminal function in patients with COVID-19 and smell disturbances. An electrophysiological study

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EPV-126

Postinfectious opsoclonus-myoclonus syndrome in COVID-19 unvaccinated patient

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EPV-127

Education Needs in Diagnosing Rare Diseases With Neurological Manifestations: A Clinician Survey

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EPV-128

Junior doctor-led neurology teaching to address neurophobia in medical students

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EPV-129

Project PEARL: raising the profile of mitochondrial disease

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EPV-130

Prevalence and Risk Factors of Functional Seizures Among Adult Sudanese Patients with Epilepsy

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EPV-131

Cognitive Functions, Depression and Anxiety symptoms in southern Indian Rural Epileptic Patients in COVID-19 Pandamic

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EPV-132

Epileptiform activity index in initial therapy of oxcarbazepine and controlled-release carbamazepine in focal epilepsy

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EPV-133

Nothing comes easily talking about NORSE.

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EPV-134

Does the gender of a patient with drug-resistant epilepsy determine readiness for surgery?

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EPV-135

The course of epilepsy in a female patient with a mutation in the KIAA2022 gen

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EPV-136

Long-term comparative efficacy of Valproic acid and Levetiracetam in children and adults with focal epilepsy

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EPV-137

Late onset Rasmussen encephalitis presenting as status epilepticus

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EPV-138

Patterns of Clinical Presentations of Epilepsy among Sundaes Patients with Tuberous Sclerosis

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EPV-139

Telemedicine versus face-to-face follow-up in patients in remission or with stable epilepsy: a comparative study

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EPV-140

Status epilepticus revealing a Paget's disease of the bone

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EPV-141

Phosphate levels as a biomarker for seizures at the Emergency Department

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EPV-142

Treatment optimalization can improve cognition in patients with epilepsy – experiences with EpiTrack

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EPV-143

Factor structure of the Russian-language version of the Epilepsy Anxiety Survey Instrument

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EPV-144

Occipital epilepsy and capnon. Differential diagnosis of calcified lesions

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EPV-145

Epilepsy secondary to cobblestone lissencephaly in an adult patient with merosin-deficient congenital muscular dystrophy

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EPV-146

Epilepsy in Cowden syndrome: beyond Lhermitte-Duclos disease

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EPV-147

Does bariatric surgery have an impact on epilepsy? A retrospective cohort study

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EPV-148

A case of seizures precipitating by specific triggers in a patient with Panayiotopoulos syndrome

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EPV-149

EEG seizures onset patterns and duration in focal status epilepticus

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EPV-150

Features of the course of epilepsy in patients after neurosurgical treatment of ruptured cerebral arterial aneurysms

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EPV-151

Intracranial hypotension syndrome following a spinal dural tear

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EPV-152

N95 face masks as aggravator factors of primary headaches in a grrek healthcare personnel during the COVID-19 pandemic

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EPV-153

Bifocal pain in Nummular headache – An extra rare phenotype

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EPV-154

Headache in autoimmune encephalitis: prevalence, characteristics, and outcomes

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EPV-155

COVAX: Post COVID-19 vaccination headache: a clinical and epidemiological evaluation.

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EPV-156

Idiopathic intracranial hypertension in pregnancy

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EPV-157

Exhalated CO2 with three different face masks in subjects with headache associated with personal protective equipment

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EPV-158

Delayed-on and wearing-off of OnabotulinumtoxinA in preventive treatment of Chronic Migraine

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EPV-159

Responsiveness Of COVID-19 Induced De-Novo Headaches To NSAIDs.

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EPV-160

A headache that pretends to be primary, about a case

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EPV-161

Efficacy of Erenumab in high-frequency episodic migraine: Russian real-life study by Research Center of Neurology

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EPV-162

Recurrent alternating Tolosa-Hunt syndrome – case report with prolonged follow-up and literature review.

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EPV-163

Epidemiology of a primary headache in university students in Slovakia

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EPV-164

Chronic paroxysmal hemicrania: great effect of nVNS in a patient with contraindication for indomethacin

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EPV-165

Abstract withdrawn

EPV-166

Gut Microbiome in Patients with Migraine

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EPV-167

Voxel Based Morphometry analysis to assess structural brain changes during NTG-induced migraine attacks

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EPV-168

Trigeminal schwannoma presenting as chronic cluster headache

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EPV-169

VISUAL SNOW SYNDROME: A case by case unveiling of a novel entity.

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EPV-170

Fremanezumab in resistant chronic migraine. A descriptive analysis from our Headache Unit

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EPV-171

A case of cerebral vasculitis mimicking RCVS

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EPV-172

Impact of SARS-Cov-2 infection in migraine. Case series

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EPV-173

Adding Eptinezumab to Brief Patient Education to Treat Chronic Migraine and Medication-Overuse Headache: Study Design

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EPV-174

Enlarging the spectrum of cluster headache: Extracranial autonomic involvement revealed by voice analysis

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EPV-175

No wearing-off effect in migraine patients treated with galcanezumab in a real-life setting

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EPV-176

Nocardial brain abscess in a mistreated patient with steroids

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EPV-177

Study of non primary CNS infections preceding stroke

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EPV-178

Rapidly progressive ataxia with cognitive impairment: Oppenheimer-Brownell variant of sporadic Creutzfeldt Jakob disease

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EPV-179

Peripheral neuropathy due to neuroborreliosis: Insensitivity for CXCL13 as early diagnostic marker

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EPV-180

Cryptococcus neoformans meningitis associated with testicular cancer in an apparent immunocompetent patient.

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EPV-181

A case of Motor Neuron Disease (MND) with extrapyramidal signs related to ANG mutation

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EPV-182

Motor neuron disease-like clinical picture in an Italian family with TFG p.Pro285Leu substitution

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EPV-183

Psychological support for family caregivers of ALS patients: telemedicine approach at the time of COVID-19 pandemic

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EPV-184

Serum Vitamin D in Amyotrophic Lateral Sclerosis patients: a marker of clinical and reasoning and executive impairment.

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EPV-185

Oculomotor dysfunction in motor neuron disease: a case report and literature review

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EPV-186

A patient with ALS and atypical Brugada ECG pattern: a case report

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EPV-187

Piriformis syndrome as amyotrophic lateral sclerosis (ALS) mimic

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EPV-188

Optimization of diagnostic errors in the amyotrophic lateral sclerosis

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EPV-189

Effects of Safinamide on cognitive and behavioral symptoms in fluctuating Parkinson's disease patients.

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EPV-190

Is perfusion in the mesencephalon and pons a differentiating feature of variants of progressive supranuclear palsy?

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EPV-191

Prevalence and clinical characteristics of movement disorders at the UNIEMTG

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EPV-192

Outcomes of pregnancy in Wilson's disease: a systematic literature review and meta-analyses.

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EPV-193

mRNA biomarkers for Parkinson's disease progression

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EPV-194

Hemichorea-Hemiballismus revealing an inaugural diabetes mellitus

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EPV-195

Are intestinal infections important for Parkinson's disease development?

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EPV-196

Hemifacial spasm and botulinum toxin: what we have learned so far.

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EPV-197

Multicenter,validation study of monitoring advanced Parkinson´s disease under Levodopa/Carbidopa Intestinal Gel

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EPV-198

Neuroleptic Malignant Syndrome: an undiagnosed neurologic emergency?

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EPV-199

Assessment of motor symptoms of Parkinson's disease in the long-term follow-up after the cell therapy

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EPV-200

Combined approach in the diagnostics of Parkinson's disease and other neurodegenerations

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EPV-201

Tremor and bradykinesia are two distinct side effects induced by valproate intake

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EPV-202

Heterogeneity in phenotypical and treatment response in a cohort of normal pressure hydrocephalus patients

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EPV-203

Are we addressing the emotional burden? recognition of mood disorders in patients with essential tremor

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EPV-204

Levodopa-Carbidopa-Entacapone-Intestinal Gel induced mania

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EPV-205

DBS in Parkinson's disease, Tremor and Dystonia – the experience of a center over the last 20 years

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EPV-206

Information provision during diagnostic consultations about Parkinson's disease

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EPV-207

Belly Dance Dyskinesia as a manifestation of B12 deficiency in MTHFR gene mutation. Videographic record of a case

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EPV-208

Hypertension in PSP-Parkinsonism Predominant and Corticobasal Syndrome.

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EPV-209

Association between helicobacter pylori infection and patients with Parkinson's disease.

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EPV-210

Genetic Parkinson disease associated with upper motor neuron disease

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EPV-211

Bezoar and catheter knotting as rare complications of levodopa carbidopa intestinal gel therapy

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EPV-212

Acute parkinsonism following a routine haemodialysis session

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EPV-213

STN DBS improves balance disorders in Parkinson's disease patients and impacts the disease progression

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EPV-214

Analysis of risk factors with a multistep process model in Parkinson's disease

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EPV-215

Spinal Cord Lesions as Predictor of Lack of Response to First-Line Therapies in Treatment-Naïve MS Patients

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EPV-216

Prominent D-Dimer Elevation and Pretibial Edema Related to Alemtuzumab Treatment: A Case Report

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EPV-217

Feasibility of the smartphone app haMSter to monitor patient reported outcomes in multiple sclerosis

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EPV-218

Influence of some single nucleotide polymorphisms on multiple sclerosis severity in people receiving Natalizumab

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EPV-219

Ocrelizumab versus Cladribine for Treatment of Highly Active Multiple Sclerosis: A Tertiary Center Experience

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EPV-220

Healthcare-related regret in multiple sclerosis: a psychometric analysis of a new assessment battery

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EPV-221

Better symptomatic management and patient education are in the focus of interest of pwMS–an exploratory survey

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EPV-222

Effect of stabilometric training and transcranial magnetic stimulation on motor defect in multiple sclerosis patients

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EPV-223

Immunogenicity and safety of mRNA COVID-19 vaccines in people with MS treated with different DMTs

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EPV-224

Quality of life in Austrian relapsing multiple sclerosis patients on de novo fingolimod treatment

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EPV-225

Anti-CD20 treatment in Multiple Sclerosis patients in time of pandemic: COVID-19 infection and vaccines

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EPV-226

Working productivity in patients CIS/ CDMS treated with Avonex® or Plegridy®: real-word evidence from the Czech republic

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EPV-227

Abuse in Adulthood and Pregnancy in Women with Multiple Sclerosis. A Population-based Cohort Study

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EPV-228

Cost-minimisation Analysis of Natalizumab Extended Interval Dosing Compared with Standard Interval Dosing in Italy

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EPV-229

Ocrelizumab, from phase III studies to real-world evidence: a single-center experience

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EPV-230

SWISSMASIA: Swiss Study of the Impact of siponimod (Mayzent) on SPMS Patients in a Long-term Non-interventional Study

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EPV-231

Brain Activation Patterns During Actual and Imagined Movement to Rhythmic Auditory Stimulation

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EPV-232

A relationship of dietary habits of patients with multiple sclerosis with physical and psychological symptoms

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EPV-233

Abstract withdrawn

EPV-234

Fatigue in patients with multiple sclerosis in an Algeria cohort

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EPV-235

Clinical characteristics and outcomes of multiple sclerosis patients with COVID-19 in Kosovo

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EPV-236

Are psychological factors risk factors for developing Multiple Sclerosis?

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EPV-237

Impact of information processing speed on episodic memory in multiple sclerosis (MS): a survival analysis

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EPV-238

Autoimmune phenomena in HIV+ patients: Neuromyelitis Optica Spectrum Diseases (HIV-NMOSD)

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EPV-239

Predicting cognitive impairment in multiple sclerosis: between cognitive reserve and brain volume

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EPV-240

Demyelinating disease due to Adalimumab in a patient with Ankylosing Spondylitis (AS)

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EPV-241

Executive disfunction and its correlation with quality of life at patients with multiple sclerosis

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EPV-242

Clinical characteristics, neuroimaging features and long-term outcome in early onset multiple sclerosis

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EPV-243

Low-specificity of Multiple Sclerosis Diagnostic Criteria for Perivenular Demyelination detected by brain MRI

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EPV-244

Potential Therapeutic Utility of Direct AMP Kinase Activation for X-Linked Adrenoleukodystrophy (ALD)

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EPV-245

ADEM-like tumefactive multiple sclerosis with MOG-antibodies post COVID-19 vaccination: a case report

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EPV-246

Impact of Multiple Sclerosis and ethnicity on clinical outcomes: evidences from African American and Caucasian patients

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EPV-247

Clinical and demographic analysis of MS patients treated with natalizumab or fingolimod: 5- year observational study

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EPV-248

Determinants of Health-Related Quality of Life in mildly disabled multiple sclerosis patients.

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EPV-249

Impact of physical and psychoemotional factors on a perceived social support in patients with multiple sclerosis

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EPV-250

Abstract withdrawn

EPV-251

Skin infections associated with natalizumab usage – a potential new adverse reaction to be aware of

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EPV-252

Best supportive care for patients with PPMS in Germany prior to ocrelizumab treatment: Final results of RETRO PPMS

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EPV-253

Relapsing multiple sclerosis onset in a patient with atopic dermatitis on dupilumab: are two coincidences a clue?

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EPV-254

SARS-CoV-2 infection and vaccination: its influence on a NMOSD and MOGAD population

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EPV-255

Online Education Yields Significant Gains in Physicians' Knowledge of B-Cell-Targeted Therapies for Multiple Sclerosis

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EPV-256

Validation of the Fatigue Impact Scale in Serbian patients with multiple sclerosis

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EPV-257

Rationale for off-label treatments use in primary progressive multiple sclerosis: a review of the literature

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EPV-258

Pain impact on Health-related quality of life in neuromyelitis optica and multiple sclerosis patients

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EPV-259

Vestibular Evoked Myogenic Potentials and Video Head Impulse Test Studies in Multiple Sclerosis

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EPV-260

The combination among VEP, OCT and functional TCD data in patients with RRMS during attack-free period.

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EPV-261

Prognostic role of visual evoked potentials at multiple sclerosis diagnosis.

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EPV-262

Caracteristics of MuSK Antibody-Positive Myasthenia Gravis : A Tunisian cohort study

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EPV-263

An axonal Charcot-Marie-Tooth disease associated with a homozygous GDAP1 gene mutation: a less severe phenotype

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EPV-264

Antibodies in Stem Cell Experimental Therapy of Spinal Muscular Atrophy and Duchenne Muscular Dystrophy

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EPV-265

Clinical features, treatment options and follow-up in patients with late-onset myasthenia gravis

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EPV-266

Myopathic Ehlers-Danlos syndrome in a patient with monogenic obesity: a case report

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EPV-267

Generalized Myasthenic Syndrome induced by Lithium intoxication – a case report

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EPV-268

Delirium in patients with subarachnoid hemorrhage

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EPV-269

A case diagnosed with hypomyelinating leukodystrophy 2 with homozygous mutation in the GJC2 gene

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EPV-270

A rare case of Adult-onset Neuronal Ceroid Lipofuscinosis

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EPV-271

Spinocerebellar Ataxia Type 5: an Unusual Infantile Onset with Development Delay

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EPV-272

Late-onset myopathy Maskerbery-Griggs-Udd type or tibial muscular dystrophy

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EPV-273

Methylation status of SNCA gene in synucleinopathies with cognitive impairment

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EPV-274

The role of GBA1 rare variants in a Hungarian Parkinson's Disease Cohort

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EPV-275

Friedreich ataxia affecting 2 consecutive generations: importance of very late presentations and high carrier

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EPV-276

Myopathy presenting as foot drop in a young adult; first case of GNE myopathy in Pakistan

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EPV-277

Two brothers with cerebellar ataxia and cognitive dysfunction: first traces of Spinocerebellar Ataxia type 40 in Italy

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EPV-278

A case of ataxia and optic atrophy caused by NDUFA1 mutation

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EPV-279

Identification of potential microrna targets in patients with significant internal carotid artery atherosclerosis

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EPV-280

Identification of genes involved in folic acid synthesis in mothers of children with congenital cerebral malformations

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EPV-281

A case of resistant mitochondrial myoclonus epilepsy with status epilepticus associated with novel NARS2 mutations

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EPV-282

Abstract withdrawn

EPV-283

Pseudotumoral Neuro Behçet's disease: a single-center cohort from Tunisia

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EPV-284

Gas Geyser Syndrome – A preventable menace in developing world

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EPV-285

Superior oblique myokymia: A multi-sequence MR imaging case study

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EPV-286

Primary central nervous system lymphoma (PCNSL) with a relapsing presentation and open-ring enhancement

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EPV-287

Influence of amyloid deposition on glucose metabolism during neurocognitive tests in older adults with MCI

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EPV-288

MCP-sign, an infrequent and reversible finding in Marchiafava-Bignami Disease.

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EPV-289

Subcortical Nodular Heterotopia with presentation in adulthood

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EPV-290

Dynamic vertebral artery occlusion: a rare case of extensional Bow Hunter's syndrome

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EPV-291

MELAS Syndrome Neuroimaging: Perfusion CT at a stroke-like episode

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EPV-292

Giant perivascular Virchow-Robin spaces: a rare cause of adult onset progressive spastic paraparesis

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EPV-293

The man who went deaf with a tumour on his spine

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EPV-294

Neurosarcoidosis as a rare and reversible cause of hydrocephalus: a case report

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EPV-295

Distal Hypotrophy and Demyelinating Polyneuropathy as Presenting Symptom of Neurosarcoidosis

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EPV-296

Immunophenotyping of lymphocytes in patients with multiple sclerosis

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EPV-297

Predictors of disability in patients with multiple sclerosis

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EPV-298

Knowledge, current practice and attitude on autoimmune encephalitis among western China neurologists

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EPV-299

About the (anti-DNA) autoantibodies status in pregnant women with neurocirculatory dystonia in Uzbekistan.

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EPV-300

SARS-CoV-2 infection in patients with neuroimmunological disorders in a centre from the north of Portugal

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EPV-301

Isolated Myelopathy in Occult Breast Carcinoma with Negative Paraneoplastic Antibodies: a Case Report

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EPV-302

An elderly NMDA-R encephalitis with striatal lesions presenting as Dementia

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EPV-303

Combined central and peripheral demyelination after COVID-19 vaccination

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EPV-304

Do "Havana Syndrome" and Gulf War Illness Share Neuroinflammation as a Common Disease Mechanism?

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EPV-305

PRES secondary to Common Variable Immunodeficiency: the first case report in the literature

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EPV-306

Blood pressure variability and cognitive impairment in patients with type 2 diabetes

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EPV-307

Multiple intracraneal haemorrhages as a presentation of Pheochromocytoma

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EPV-308

Neurological symptoms caused by hiatal hernia

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EPV-309

Vesico sphincter and sexual dysfunction in Behcet's Disease: a rare but serious complication

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EPV-310

Different Patterns of Neurological symptoms amongst thyroid patients in the Ribat Hospital in Khartoum, Sudan 2021

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EPV-311

Isolated Central Nervous System Langerhans Cell Histiocytosis in an adult: a rare cause of neurocognitive deterioration

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EPV-312

Pellagra and Marchiafava-Bignami disease in a patient with new-onset seizures

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EPV-313

Ischemic stroke and subarachnoid hemorrhage as first clinical presentation of Thrombotic thrombocytopenic purpura

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EPV-314

Vasculitis with nervous system involvement: A 20-years' experience in a tertiary hospital in Spain

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EPV-315

Rheumatoid meningitis as a rare reason of meningitis, do we recognize it?

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EPV-316

From a Patient to an Artist: Covid-19 Patient with Neurological Complications Who Started Painting

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EPV-317

The role of creativity in recovery from severe covid-associated toxic-metabolic encephalopathy

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EPV-318

Smouldering multiple myeloma: where do we draw the line? A case study

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EPV-319

Autoimmune encephalitis with elevated P-type voltage gated calcium channel antibodies

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EPV-320

Syncope as a manifestation of lymph node metastasis from breast cancer – case report

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EPV-321

Glioblastomas: An oncologic hospital series

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EPV-322

Abstract withdrawn

EPV-323

A Systematic Review and Case Report of Numb Chin Syndrome: Forewarning relapse in Multiple Myeloma

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EPV-324

Headache in a HIV patient – a common symptom hiding a rare diagnosis

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EPV-325

Early neurophysiology on sensitive neuron degeneration of pure Denny-Brown's syndrome. An asset to improve outcome.

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EPV-326

Tolosa-Hunt syndrome: a case series

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EPV-327

Awakening ptosis: to see to know

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EPV-328

Brown Syndrome or when a trochlear nerve palsy is not a trochlear nerve palsy

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EPV-329

Recurrent optic neuritis: an atypical case of Harding's disease? – a case report

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EPV-330

A rare pupillary phenomenon: tadpole pupil

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EPV-331

Optic nerve cavernoma : a less common cause of visual loss

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EPV-332

Quality of life assessment in patients with Charcot-Marie-Tooth disease type 1A

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EPV-333

Mononeuritis multiplex – broad range of etiology

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EPV-334

Acute nutritional neuropathies in high-income countries requiring hospitalization: A systematic review

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EPV-335

The use of TENS in the rehabilitation of patients after carpal tunnel decompression

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EPV-336

Effects of Neuropsychological Rehabilitation on Multiple Sclerosis Patients' Everyday Functioning

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EPV-337

The Effects of Neurorehabilitation on Sequence Effect in Parkinson's Disease Patients with and Without Freezing of Gait

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EPV-338

Feasibility of remote computerised cognitive assessment after out-of-hospital cardiac arrest

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EPV-339

Day-clinical care filling the PD treatment gap

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EPV-340

Evaluation of the effect of high and low frequency transcranial magnetic stimulation on neuroplasticity after stroke

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EPV-341

Indirect effects of physical rehabilitation intervention in patients in early recovery period of ischemic stroke

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EPV-342

Activity and efficacy of radial shock wave therapy in reducing spasticity in people with Multiple Sclerosis.

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EPV-343

Correlation bond between hand functioning, cognition and quality of life of CP children: prospective randomized study

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EPV-344

PI variations in medium cerebral artery during haemodialysis after SARS-COV 2 infection.

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EPV-345

The Controversy of Floating Carotid Plaque

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EPV-346

Lead and Mercury Poisoning Neurotoxicity in the Middle Size Industrial City

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EPV-347

Long-term results of microsurgical reconstruction of distal traumatic median and ulnar nerve lesions

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EPV-348

Concussion: Getting Evidence of Neuronal Dysfunction Into Practice Using Brainstem Auditory Evoked Potentials.

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EPV-349

Grey matter volumes as marker of low pain-related quality of life in multiple sclerosis patients

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EPV-350

Brain-blood barrier dysfunction in Complex Regional Pain Syndrome: a case report

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EPV-351

The pain is related with neurocognitive dysfunction and depression in patients with Parkinson's disease

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EPV-352

The role of pain in the semiotics of non-motor manifestations of Parkinson's disease

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EPV-353

Cranial nerve and root enhancement in bifacial weakness with paresthesias

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EPV-354

Guillain-Barre Syndrome in 220 patients with COVID-19

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EPV-355

Features of Chronic Inflammatory Demyelinating Polyneuropathy in different age groups at disease onset

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EPV-356

Characteristics of Guillain Barre Syndrome

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EPV-357

Abstract withdrawn

EPV-358

Cognitive impairment in patients with narcolepsy

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EPV-359

Anti-IgLON5 Disease Parasomnias and Obesity: Neuroimmune and Neuroendocrine Aspects

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EPV-360

Fatigue in CNS hypersomnolences

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EPV-361

Non traumatic hemorrhagic myelopathies, three different scenarios

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EPV-362

The ability of seated push-up test to determine body compositions of individuals with spinal cord injury

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EPV-363

Constitutive NOS production in Alzheimer's disease according to ε genotype: a human CSF-based in vivo analysis.

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EPV-364

A treatable cause of rapidly progressive dementia - amyloid beta related angiitis.

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EPV-365

Acute Inflammation impact on amyloid, neuronal and glial markers

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EPV-366

Corticobasal degeneration mimicking rhombencephalitis

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EPV-367

Accessibility of eldelrly with dementia to healthcare services in rural area of the ADRION Region: the SI4CARE Project

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EPV-368

Testamentary Capacity Assessment Tool (TCAT): An update report

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EPV-369

Effect of Taijiquan intervention on patients with Alzheimer's disease: Meta analysis

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EPV-370

Chronic gastrointestinal dysfunction as the initial presentation of Autoimmune Autonomic Ganglionopathy (AAG)

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EPV-371

Post-COVID-19 autonomic symptoms in neuropsychiatric patients

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EPV-372

Prognostic role of hematological inflammatory biomarkers in acute ischemic stroke

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EPV-373

The association between inflammatory biomarkers with dementia after acute ischemic stroke

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EPV-374

Assessment of AP structure and hemorheological parameters in patients with atherosclerosis of ICA

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EPV-375

Triglyceride-glucose index as a marker of advanced carotid atherosclerosis

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EPV-376

Does platelet count help predict the outcome of acute phase treatment in ischemic stroke?

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EPV-377

Can weightlifting cause a stroke? A case report of vertebral artery dissection.

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EPV-378

Stroke: social aspects of the disease in Brazil between the years 2015 to 2019

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EPV-379

Parkinson's disease and cerebrovascular changes: correlation or causation?

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EPV-380

Gender Related Differences in Lifestyle Risk Factors of Young and Middle – Aged Patients with Acute Ischemic Stroke

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EPV-381

Perioperative scenario after carotid endarterectomy at a reference hospital in Brazil

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EPV-382

Painting the ceiling and vertebral artery hypoplasia as risk factors for vertebral artery dissection: a case report

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EPV-383

Anton's Syndrome (visual anosognosia) due to acute stroke: A Case Report

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EPV-384

Are patients with ischemic stroke properly informed about this pathology and its secondary prevention?

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EPV-385

Asymptomatic carotid stenosis: when should screening be performed?

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EPV-386

Posterior reversible encephalopathy syndrome triggered by hypertension in a patient previously treated with pazopanib

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EPV-387

Diagnosis, assessment, and follow-up of a rare case with Sneddon's Syndrome in a remote greek island.

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EPV-388

Isolated cranial nerve palsy: Do not forget carotid artery dissection

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EPV-389

Negative pressure hydrocephalus: literature review

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EPV-390

D-Dimer as a predictor of disability after CVT

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EPV-391

Artery of Percheron Infarct Secondary to Antiphospholipid syndrome

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EPV-392

Role of Cerebral Small Vessel Disease Markers in Hematoma Expansion

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EPV-393

Burden of ischemic stroke associated with pre-stroke frailty in patients receiving intravenous thrombolysis

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EPV-394

Risk factors of restenosis, stroke and death after carotid revascularization: the importance of Chronic kidney disease

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EPV-395

Stroke of unusual etiology: intracranial isolated fibromuscular dysplasia

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EPV-396

Continuous partial epilepsy as a clinical manifestation of ischemic stroke

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EPV-397

Endovascular treatment of cerebral aneurysms in the acute period of subarachnoidal hemorrhage in severe hunt-hess

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EPV-398

Rare Hypertensive Brainstem Encephalopathy, HBE, in a male with almost total remission, in a month

E. Koumasopoulos [1], C. Michaletou [1], M. Kodounis [1], M. Brinia [1], I. Noulas [1], G. Velonakis [2], E. Gialafos [3], L. Stefanis [3], M. Evangelopoulos [1], M. Anagnostouli [1]
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EPV-399

The impact of carbohydrate metabolism disorders on post-stroke patients' prognosis

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EPV-400

Red blood cell morphodynamics in patients with Polycythemia Vera and brain infarcts

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EPV-401

Hyperglycemia Presenting as Left Middle Cerebral Artery Stroke: a Case Report

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EPV-402

A blinded, multicenter, randomized phase II trial of tetramethylpyrazine nitrone in patients with acute ischemic stroke

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EPV-403

Stroke acute care in the COVID-19 pandemic: a global perspective

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EPV-404

Unfolding the enigma of stroke in Rheumatoid Arthritis? A case series from a tertiary care centre in South India

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EPV-405

Atrial fibrillation in young stroke patients: associated factors and outcomes in a nationwide analysis

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EPV-406

The role of monocytic chemotactic protein-1-cytokin (MCP-1) in the pathogenesis and progression of atherosclerosis (AS)

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EPV-407

Recurrent venous occlusive events in patient treated with new-generation tyrosine kinase inhibitor

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EPV-408

Intracerebral haemorrhage associated with early-onset cerebral amyloid angiopathy 5 decades after a dura mater graft

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EPV-409

A neurological explanation for a recurrent traveling psychosis

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EPV-410

Atherosclerotic Carotid Plaque Vulnerability Characteristics and Risk of Stroke: Substudy Results of ANTIQUE Study

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EPV-411

Time Interval between NOAC last Intake and Ischemic Stroke Recurrence - Data from the RENO-EXTEND database

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EPV-412

Impact of vascular risk factors in the number of acute ischemic events.

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EPV-413

Ipsilateral symptoms caused by stroke

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EPV-414

Tenecteplase in central retinal artery occlusion study (TenCRAOS)

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EPV-415

Prevention of stroke and other thromboembolic events in primary care: alarming data from a Brazilian medium-size city

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EPV-416

Emergency neurology in the pre-COVID era in Lombardia: a survey of diagnostic and care resources in 33 Hospitals

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EPV-417

Cerebrovascular disease associated to hematological disorders

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EPV-418

Frequency and risk factors of in-stent restenosis following carotid artery stenting (CAS).

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EPV-419

A virtual reality system for the rehabilitation of post-stroke pain syndrome

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EPV-420

Risk Factors for Ischemic Stroke in young adults: A Case-Control Study

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EPV-421

Hypokalemia- stroke mimic. Case report

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EPV-422

Carotid web, an underrecognised cause of stroke

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EPV-423

Effects of blood pressure changes during mechanical thrombectomy on malignant brain edema in ischemic stroke patients.

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EPV-424

Chronic neurological deficits up to 6 months after large stroke in young and old mice

N. Zerva, A. Pavlopoulos, C. Petritsis, A. Kotronis, A. Chaviaropoulou, C. Pantos, I. Mourouzis, A. Lourbopoulos
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EPV-425

Clinical et paraclinical Characteristics of ischemic stroke in patients with cancer

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EPV-426

Identifying the signs of Pediatric Abusive Head Trauma: a real challenge

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EPV-427

Executive functions and visual-spatial gnosis in children with sensorimotor alalia and systemic speech underdevelopment

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EPV-428

Clinical features of arterial ischemic stroke types in Russian pediatric cohort

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EPV-429

Neuroimaging features of arterial ischemic stroke types in Russian pediatric cohort

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EPV-430

Frequency and risk factors of arterial ischemic stroke types in Russian pediatric cohort

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EPV-431

Differences in response to short-latency auditory evoked potentials in healthy children and children with Down syndrome

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EPV-432

Electrical Stimulation methods in carpal tunnel syndrome : a prospective comparative study

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EPV-433

Electrodiagnosis of ulnar neuropathy at the elbow

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EPV-434

Neurophysiological features of genetically proven neuronal intranuclear inclusion disease with vomiting and vocal tremor

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EPV-435

Neurophysiological validation of the combination of artificial gravity and aerobic training: A proof of concept study

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EPV-436

Thalamic auditory center activity in healthy children and patients with acute bacterial meningitis

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EPV-437

Visual scanning in patients with alzheimer's disease and mild cognitive impairment: kitchen scanning task

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EPV-438

Brain metabolism stratification of Stage of Objective Memory Impairment (SOMI) in aMCI-AD and early AD.

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EPV-439

Dementia due to structural injury of the mammillary bodies: an unusual case of Korsakoff-like

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EPV-440

Determinants of cognitive decline in Dementia with Lewy bodies

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EPV-441

A pilot study on the use of immersive Virtual Reality in a population of patients affected by neuromuscular diseases

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EPV-442

Psychogenic non-epileptic seizures (PNES) and Binge Eating Disorder: a cross-sectional study

A. Mammì [1], V. Bova [2], J. Martino [1], I. Sammarra [1], E. Ferlazzo [1], V. Cianci [2], S. Gasparini [1], S. Neri [1], D. Santangelo [1], M. Beghi [3], A. Gambardella [1], A. Pujia [1], U. Aguglia [1]
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EPV-443

Increase of EEG intrahemispheric synchronization during nocturnal sleep in patients with mild memory impairments

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EPV-444

Evaluation of cognition with the eyelink: visual search in healthy subjects

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EPV-445

CADASIL coma: an underdiagnosed acute encephalopathy key for a whole family.

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EPV-446

Difficulties and needs of professional caregivers for patients with chronic disorders of consciousness: an online survey

L. Legostaeva [1], D. Sergeev [1], E. Iazeva [2], I. Bakulin [1], A. Poydasheva [1], Y. Ryabinkina [1], N. Suponeva [1], M. Piradov [1]
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EPV-447

Hypoxic-ischemic encephalopathy (HIE) associated with amniotic fluid embolism (AFE): a successful case report

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EPV-448

Sleep-wake changes in patients with Post-Covid syndrome, fatigue and excessive daytime sleepiness

L.G. Fregolente [1], L. Diem [1], J.D. Warncke [1], S. Bauer [1], S. Jung [1], M. Funke-Chambour [2], R. Hoepner [1], C.L.A. Bassetti [1]
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EPV-449

Neurological characterization of COVID-19 inpatients: A retrospective study in the Dominican Republic

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EPV-450

Clinical profile of COVID-19 in Algerian patients with multiple sclerosis

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EPV-451

Inflammatory neurological complications after COVID-19 vaccination: a retrospective multicenter study in Portugal

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EPV-452

Neurological involvement in patients with mucormycosis secondary to COVID-19 infection

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EPV-453

Incidence of post-acute COVID-19 brain fog in patients attended by a telemonitoring service

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EPV-454

Bilateral facial paralysis in times of pandemic

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EPV-455

Antibodies against SARS-CoV-2 in patients with relapsing remitting MS treated with disease modifying therapies

J. Kulikowska [1], K. Kapica-Topczewska [1], F. Collins [2], M. Gudowska-Sawczuk [3], A. Kulczyńska-Przybik [3], M. Bazylewicz [1], A. Mirończuk [1], A. Czarnowska [1], B. Mroczko [3], J. Kochanowicz [1], A. Kułakowska [1]

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EPV-456

Does Inactivated SARS-CoV-2 Vaccine Provoke Relapses in Multiple Sclerosis?

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EPV-457

Analysis of factors affecting the outcome of ischemic stroke associated with COVID-19

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EPV-458

The impact of SARS-COV2 pandemic in ambulatory neurological care demand: comparative cross-sectional cohort study.

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EPV-459

Neurological Manifestations of COVID-19 in Latin American population

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EPV-460

Peripheral hypoglossal nerve palsy after SARS-CoV-2 vaccination – report of two cases

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EPV-461

A case of Miller-Fisher and Guillain-Barre overlap syndrome that developed after sinovac-coronavac vaccine's second dose

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EPV-462

Acute necrotizing encephalopathy associated with COVID-19

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EPV-463

Long COVID Prevention in Nonhospitalized COVID Patients by Repurposing Isosorbide 5-Mononitrate and Cilostazol

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EPV-464

Post-COVID Immunosuppression in Patients with Parkinson's Disease

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EPV-465

How well did the healthcare system respond to the elderly with dementia during Covid-19? Results from SI4CARE Project

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EPV-466

Assessment of psychopathological disorders in those who have came through COVID-19

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EPV-467

Prevalence of headache after COVID-19 vaccination among Ukrainian students

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EPV-468

Neurological manifestations in Brazilian hospitalized patients with COVID-19 by age

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EPV-469

Aphasia and COVID-19: a review of case reports

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EPV-470

Some neurological manifestations of the post-COVID syndrome

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EPV-471

Electroencephalographic challenges in patients with epilepsy

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EPV-472

Surgical Outcome of Refractory Epilepsy Secondary to Polymicrogyria: Tertiary Centre Experience

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EPV-473

Use of perampanel as the first adjunctive therapy in patients with epilepsy

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EPV-474

Epilepsy in Children with Down Syndrome - A Review of the Last Decade

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EPV-475

EEG source localization accuracy for the detection of seizure onset zone in refractory epilepsy

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EPV-476

Epileptic seizures in Neuro-Behçet disease : an underestimated condition?

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EPV-477

Drug-resistant cavernoma - related epilepsy

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EPV-478

How do you support teenagers with epilepsy transitioning into adulthood?

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EPV-479

Morphological changes of neuroglia in epileptic focus in drug-resistant epilepsy

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EPV-480

Significance of neuroinflammation in the epileptic focus in drug-resistant epilepsy

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EPV-481

The significance of glial apoptosis and neuroinflammation in the pathogenesis of drug-resistant epilepsy

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EPV-482

Particularities of ictogenesis and epileptic seizures in individuals with diabetes

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EPV-483

Reflex Epilepsies

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EPV-484

Progressive myoclonic epilepsy secondary to a defect in glycosylation

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EPV-485

Radiological features of ischemic stroke resulting in post stroke seizures and post stroke epilepsy.

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EPV-486

Stroke-like episodes, epileptic seizures and metabolic disturbances: case report and differential diagnosis

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EPV-487

Differentiating between epilepsy and nonepileptic seizures using the analysis of semantic categories

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EPV-488

Factors associated with suicidal risk among adult patients with epilepsy: a large cross-sectional outpatient survey

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EPV-489

Dyke-Davidoff-Masson syndrome, a rare cause of refractory epilepsy

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EPV-490

Clinical and imaging predictors for early seizure after ischemic stroke

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EPV-491

The severity of psychopathological symptoms and suicidal behavior in patients with epilepsy

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EPV-492

Generalized epilepsy diagnosis admitted to video-EEG monitoring: an insightful look into this population

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EPV-493

VNS-induced synchronous vocal cord paralysis

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EPV-494

An unusual presentation of Gayet-Wernicke encephalopathy in a pregnant woman

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EPV-495

Headache after Covid 19 infection: Tunisian Cohort experience

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EPV-496

Inpatient Constipation in Migraine Patients Prescribed Preventive Medications in a US Electronic Health Record Database

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EPV-497

Episodic migraine without aura and alexithymia

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EPV-498

Erenumab discontinuation in migraine patients: interim analysis of the APOLLON study population

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EPV-499

Reversible cerebral vasoconstriction syndrome: a diagnostic challenge

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EPV-500

Migraine-like headache in a patient with dural carotid-cavernous fistula

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EPV-501

Onabotulinumtoxin A reduces serum CGRP levels and improves mood and cognitive function in Chronic Migraine patients

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EPV-502

Longitudinal experience with cluster headache over 40 years in a University Hospital in Spain

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EPV-503

Abstract withdrawn

EPV-504

Description of the effectiveness and safety of 12 months of fremanezumab in 104 patients with chronic migraine.

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EPV-505

Analysis of predictors of response to fremanezumab at 3 months of treatment in 82 migraine patients

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EPV-506

Role of the default mode network in episodic cluster headache: cerebral connectivity analysis with hd-eeg

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EPV-507

High Frequency Episodic Migraine and Chronic Migraine, Two Sides of the Same Coin?

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EPV-508

HaNDL Syndrome (Headache and Neurologic Deficits with cerebrospinal fluid Lymphocytosis): A case report.

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EPV-509

A case series on a rare diagnosis: Idiopathic Painful Nervus Intermedius Neuropathy

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EPV-510

By the steps of someone else`s fame

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EPV-511

Forensic psychiatry and its historical context

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EPV-512

The unusual suspects: meningoencephalitis and brain abscess as complications of chronic sinus and ear infection

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EPV-513

An unusual case of chronic meningitis caused by Granulicatella elegans

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EPV-514

Tuberculous meningitis: overview of the disease in Brazil between 2017 to 2021

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EPV-515

Meningitis in Brazil: etiological and outcome panorama between the years 2017–2021

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EPV-516

Neurobrucellosis: A broad clinical presentations and diagnostic challenges

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EPV-517

Pseudotumoral presentation of neurocysticercosis: a case report

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EPV-518

Serological screening for syphilis in non-compressive spinal cord deficiencies

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Epv-519

Neurosyphilis, diagnostic difficulties: a case report

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EPV-520

Hitting the target

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EPV-521

Chronic cryptococcal meningitis associated with cytomegalovirus infection in a HIV patient with severe immunodeficiency

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EPV-522

Leukocencephalopathy in HIV: not always as it seems

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EPV-523

Biopsy-proven Progressive Multifocal Leukoencephalopathy – case series with clinicopathological correlation

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EPV-524

SARS-CoV-2 related Meningoencephalitis

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EPV-525

Looking to the eyes: they can guide your diagnosis

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EPV-526

A case of hiv infection presenting as cerebellar ataxia

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EPV-527

A comparison between features of a Large Centre for Motor Neuron Disease in Italy and Literature data

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EPV-528

Assessing the efficacy of a smartphone app for remote monitoring of neuromuscular patients

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EPV-529

Anxiety - prognostic marker of ALS?

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EPV-530

Ocular ptosis and diplopia as the rare symptoms of ALS

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EPV-531

Safety and efficacy of onasemnogene abeparvovec in spinal muscular atrophy: a single-center experience.

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EPV-532

Contribution of Parkinson's Disease genes to Amyotrophic Lateral Sclerosis pathogenesis

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EPV-533

Continuous theta burst stimulation as a biomarker of levodopa-induced dyskinesias in PD patients: a preliminary report.

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EPV-534

Carabamazepine toxicity presenting with acute onset neuropsychiatric disturbance and generalised chorea

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EPV-535

Longitudinal evaluation of biochemical and clinical profile of GBA-Parkinson Disease: a 2-year follow-up study

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EPV-536

Alteration of expression of genes involved in the autophagy in the pathogenesis of GBA- associated Parkinson's disease

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EPV-537

Clinical features associated with the freezing gait phenomenon in patients with Parkinson's disease

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EPV-538

European Parkinson's Disease Association survey on Parkinson's – patient insights, knowledge and experience of treatment

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EPV-539

Corticobasal syndrome and Parkinson's disease at the beginning: usefulness of asymmetrical patterns for early diagnosis

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EPV-540

Initial experience with levodopa– entacapone–carbidopa intestinal gel infusion (LECIG) in clinical practice in Germany

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EPV-541

Early onset hemichorea-parkinsonism with POLG mutation without external ophthalmoplegia responsive to pallidal DBS

F. Garri [1], D. Calandrella [1], G. Sacilotto [2], M. Zini [2], C. Bolliri [1], V. Cereda [1], M. Barichella [2], G. Pezzoli [1]
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EPV-542

Fifteen years' experience with levodopa/ carbidopa intestinal gel infusion in advanced Parkinson's Disease

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EPV-543

Frequency and severity of autonomic disorders in patients with idiopathic cervical dystonia

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EPV-544

Dyskinesia and Parkinsonism in two patients treated with avapritinib

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EPV-545

Case of clozapine-induced camptocormia

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EPV-546

Blood serotonin as a marker of a favorable course of Parkinson's disease

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EPV-547

Association of hematological malignancies with sporadic and genetic forms of Parkinson's disease in the PPMI study.

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EPV-548

A randomised controlled trial on effectiveness and feasibility of sport climbing in Parkinson's disease

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EPV-549

Abstract withdrawn

EPV-550

Multidimensional Frailty predicts motor and cognitive progression in Parkinson's disease

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EPV-551

Parkinson´s Disease patients' perspective of telemedicine visits during COVID-19 pandemic

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EPV-552

Abstract withdrawn

EPV-553

Assesment of tolerability and efficacy of opicapone in older adult patients

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EPV-554

Psychotic features in early PD: prevalence, phenomenology and clinical correlates

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EPV-555

Negative DAT-SPECT in old onset Parkinson's disease: an additional pitfall?

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EPV-556

What could patients gain from remote deep brain stimulation programming?

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EPV-557

Differences in severity of motor and non-motor symptoms between early- and late-onset Parkinson's disease

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EPV-558

Acute onset oromandibular caused by Allopurinol

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EPV-559

Automated Quantification of Local Field Potentials Recorded with an Implantable Neurostimulator in Parkinson's Disease

A. Singer [1], T. Brionne [1], M. Case [1], T. Witt [2], F. Steven [3], K. Martinez [4], M. Schiess [5], H. Shah [6], F. Pagan [7], F. Farrokhi [8], T. Theys [9]
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EPV-560

Phenotypic characteristics of patients with ANO10 mutation from Serbia and a literature review

I. Stankovic [1], N. Dragasevic [1], A. Milovanovic [1], A. Marjanovic [1], M. Brankovic [1], V. Dobricic [2], I. Petrovic [1], M. Svetel [1], I. Novakovic [1], V. Kostic [1]
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EPV-561

Biochemical markers to predict shunt response in the management of idiopathic normal pressure hydrocephalus

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EPV-562

Combined VIM and GPi deep brain stimulation for dystonic tremor

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EPV-563

Tremor Characteristics of Movement Disorder Patients Based on Smartphone Application In Cipto Mangunkusumo Hospital

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EPV-564

Focal continuous hypertrophic myokymia is treatable with botulinum A toxin

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EPV-565

Rate of hospitalization of pregnant women with multiple sclerosis in Poland

B. Adamczyk [1], D. Walkiewicz [2], M. Maluchnik [3], J. Perwieniec [2], K. Podwójcic [4], M. Szeląg [2], M. Zakrzewski [2], K. Rejdak [5], A. Słowik [6], M. Wnuk [6], M. Adamczyk-Sowa [1]
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EPV-566

Central nervous system disease in primary Sjögren's syndrome

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EPV-567

Impact of Multiple Sclerosis on Caregivers: An Online Survey across the United States and Europe

R. Webb [1], D. Bury [2], E. Pain [3], K. Sharrock [2], C. Coulevrat [4], K. Higuchi [2], R. Kornfeld [2], J. Fine [4], M. Dupont [2], M. Chekroun [3]
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EPV-568

Characterization of the gait in patients with RRMS and SPMS measured by FeetMe®: Results of the MS Feet PRO study

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EPV-569

Real world evidence with Ocrelizumab in progressive and relapsing multiple sclerosis

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EPV-570

Neurogenic Bladder and Sexual Dysfunction Affect Self Perceptions of Health in Patients with Multiple Sclerosis

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EPV-571

Neural networks for rapid assessment of brain lesion patterns in multiple sclerosis

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EPV-572

Association of brain atrophy with disease progression and cognitive and mood outcomes in patients with MS

M. Cole [1], E. Jones [2], K. Gandhi [1], A. Keenan [2], H. Le [3], L. Adedokun [4], M. Berry [2], J. Pike [2], N. Grant [2], E. Trenholm [2]

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EPV-573

Natalizumab extended interval dosing experience in real world

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EPV-574

Autonomic dysfunction in Multiple Sclerosis

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EPV-575

Effect of proposed biosimilar natalizumab on MRI endpoints in RRMS patients: Data from the Phase III Antelope study

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EPV-576

Effect of proposed biosimilar natalizumab on clinical endpoints in RRMS patients: Data from the Phase III Antelope study

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EPV-577

Neurofilaments Light Chain levels and disease activity and outcome in patients with Multiple sclerosis

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EPV-578

Multiple sclerosis lesion distribution in 7 Tesla MRI - review of the literature and a case series study

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EPV-579

Abstract withdrawn

EPV-580

The immunological markers of secondary progressive multiple sclerosis.

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EPV-581

Evaluation of serum light chain neurofilaments in Relapsing Multiple Sclerosis patients NEDA-3

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EPV-582

Humoral and cellular immune response after SARS CoV-2 vaccine in Multiple Sclerosis patients immunosuppressed

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EPV-583

Clinical experience with Cladribine in Multiple Sclerosis Patients. A multicentre Study

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EPV-584

Evaluation of relationship between ABCG2 mutation and teriflunomide exposure and safety in Chinese RMS patients

C. Quan [1], H. Zhou [2], H. Yang [3], M. Zhang [4], B. Zhang [5], G. Tan [6], B. Bu [7], T. Jin [8], C. Li [9], Q. Xue [10], H. Dong [11], F. Shi [12], X. Qin [13], X. Zhang [14], F. Gao [15], H. Zhang [16], J. Wang [17], X. Hu [18], W. Qiu [18]

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EPV-585

Efficacy of switching from Tysabri® to a proposed biosimilar of natalizumab: Data from the Phase III Antelope trial

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EPV-586

Phase I PK/PD similarity study of proposed biosimilar natalizumab PB006: A single dose study in healthy individuals

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EPV-587

Clinical spectrum of biopsy-proven inflammatory CNS lesions

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EPV-588

Seronegative immune-mediated necrotizing myopathy. Distinctive features from other myopathies. A case report.

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EPV-589

Adult onset congenital myasthenic syndrome revealed by progressive wrist and fingers extensors deficit.

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EPV-590

Myasthenia Gravis due to COVID-19 vaccine?

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EPV-591

Botulism: Clinical suspicion over confirmatory studies

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EPV-592

Eculizumab in Patients with Generalised Myasthenia Gravis: Subgroup Analysis of Post-Marketing Surveillance in Japan

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EPV-593

Thymic Pathology in a Myasthenia Gravis cohort

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EPV-594

Genetic data and Muscle Biopsy Results of Patients with Duchenne Muscular Dystrophy in Our Clinic

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EPV-595

Epidemiological and clinical profile of patients with Myasthenia gravis in southern Brazil

P. Pascoal Rodrigues [1], C. Kamoi Kay [1], R. Ducci [1], M. Utiumi [2], O. Fustes [1], L. Werneck [1], P. Lorenzoni [1], R. Scola [1]
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EPV-596

A case of SMPX gene-related distal myopathy

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EPV-597

The diagnostic role of muscle biopsy: A 15 years single referral center experience

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EPV-598

Decompressive craniectomy techniques and their outcomes in reducing intracranial hypertension

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EPV-599

Higher APACHE II score is independent early predictor of mortality in patients with metabolic encephalopathy

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EPV-600

The risk factor of mortality among critically ill patients with metabolic encephalopathy

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EPV-601

Repercussions of the COVID-19 pandemic on the microsurgical treatment of neuroma in Brazil

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EPV-602

Central nervous system neoplasm in the last 10 years in Brazil: prevalence and mortality

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EPV-603

Descriptive Analysis of Chronic Inflammatory Demyelinating Polyneuropathy (CIDP) in the Northern Area of Tenerife

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EPV-604

Comparison of vascular risk factors between two different cohorts of high vascular risk from Tenerife

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EPV-605

Microsurgical treatment and aneurysm embolization: a descriptive analysis in a developing country

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EPV-606

Seasonality of Benign Paroxysmal Positional Vertigo – A retrospective study from Central Europe

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EPV-607

Screening of the FMR1 premutation in Greek patients with movement disorders

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EPV-608

Pachygyria in Russian monozygotic twins due to WASF1 mutation

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EPV-609

Mutational screening of Greek patients with axonal Charcot-Marie-Tooth disease using targeted Next-Generation Sequencing

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EPV-610

Heterozygous HTRA1-related cerebral small vessel disease: are we pointing towards a milder form of CARASIL?

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EPV-611

Mutation in TUBB4a causing from dystonia to spastic quadriparesis across one family

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EPV-612

CEP85L-related subcortical band heterotopia in an Irish family

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EPV-613

Neurological impairment and cytogenetic variations in klinefelter syndrome

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EPV-614

A heterozygous variant in RTN2 gene as a cause of hereditary spastic paraplegia: a case-report

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EPV-615

CONDSIAS – the long road to diagnosis

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EPV-616

Pronounced orthostatic hypotension in GBA-related Parkinson's disease

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EPV-617

Celiac disease and peripheral neuropathy: identifying pleiotropic SNPs among established genetic risk variants

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EPV-618

Role of Methionine PET in Differentiating Gliomas and Pseudo-tumoral Demyelinating Lesions in Multiple Sclerosis

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EPV-619

Giant arachnoid cyst, expectant attitude or surgery?

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EPV-620

A case of HHV6 infection with extensive neuroimaging findings in an immunocompetent patient

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EPV-621

Metronidazole-induced encephalopathy in a cirrhotic patient

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EPV-622

Neurocysticercosis: A rare cause of painless diplopia

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EPV-623

Anti-NMDA receptor encephalitis secondary to follicular lymphoma, an unusual association: By a clinical case.

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EPV-624

Selective caudate atrophy in multiple sclerosis is associated with cortical volume loss

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EPV-625

Neuropsychiatric and cognitive manifestations of paraneoplastic limbic encephalitis

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EPV-626

Neurofilament light chain as a biomarker for multiple sclerosis progression– investigations using a novel animal model

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EPV-627

Evaluation of empathy and its relationship with cognitive dysfunction in patients with multiple sclerosis

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EPV-628

Three cases of neuromyelitis spectrum disorder (NMOSD) with a late onset in the 80's

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EPV-629

Alzheimer's disease microglia and COVID-19 exosomes: a quasinfectious model of outside-in neurodegeneration

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EPV-630

Pembrolizumab for Progressive Multifocal Leukoencephalopathy. A case report and literature review

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EPV-631

Adult-onset leukoencephalopathy with axonal spheroids and pigmented glia (ALSP): Initial misdiagnosis

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EPV-632

Susac syndrome: a therapeutic challenge. High-intensity immunosuppressive treatment and clinico-radiological follow-up

C. Ribacoba Díaz, V. Cid Izquierdo, J. Alcalá Ramirez del Puerto, L. Portocarrero Sánchez, M. Sánchez Boyero, L. Palliotti, V. Gajate García, A. Marcos Dolado, E. López Valdés, R. Ginestal López

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EPV-633

Head drop and ophthalmoplegia: complications of check-point inhibitors

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EPV-634

Novel analysis of extracellular vesicles according to their cellular origin as biomarker of multiple sclerosis.

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EPV-635

Role of extracellular vesicles in monitoring the response to modifier treatments for multiple sclerosis

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EPV-636

Immune and nervous system-derived EVs provide clinical information in relapsing remitting Multiple Sclerosis

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EPV-637

Type I interferon and interferon beta 1a signalling in viral infections, Alzheimer's Disease and Multiple Sclerosis

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EPV-638

SARS-CoV-2 RNA binding proteins as primers of neurodegeneration

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EPV-639

The infection response molecular signalome of multiple sclerosis vs. viral infections, including SARS-CoV-2

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EPV-640

Personalized Integrated Care Promoting Quality of Life for Older People (ProCare4Life)

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EPV-641

The computational testing of diagnostic capabilities of Arsenic and Selenium in hair and nail samples in the elderly

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EPV-642

Nanotechnology in neurosurgery: state-of-the-art

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EPV-643

Development of a prognostication tool by analyzing the risk factors of Acute Ischemic stroke

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EPV-644

Smartphone-based app for Carpal tunnel syndrome testing – primary study.

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EPV-645

A comparative overview of the European neurology start-up landscape using an investment data platform

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EPV-646

The Clinical and Radiological Features and Prevalence of Neuro-Behçet's Disease: a Multicenter Study.

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EPV-647

ENCEPHALITIS AS THE FIRST MANIFESTATION OF SYSTEMIC LUPUS ERYTHEMATOSUS (SLE)

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EPV-648

Diabetic Striatopathy: A case series of rare and treatable movement disorder

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EPV-649

The great mimic: An elusive diagnosis for a multiple cranial polyneuropathy

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EPV-650

Atypical Presentation of An Atypical Pneumonia – A Case Report

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EPV-651

The forgotten, not so hidden behind the mask of the common: Lemierre syndrome mimicking an acute stroke

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EPV-652

Thyroid disturbances and Parkinson's disease in Croatian residents

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EPV-653

Endemic distal renal tubular acidosis (dRTA) with severe Hypokalemic Periodic Paralysis … A forgotten entity!

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EPV-654

Phenomenon of Kernohan-Woltman: Uncommon neurological sign, paradoxical and with possibilities of reversibility

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EPV-655

Primary central nervous system lymphoma: a diagnosis conundrum

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EPV-656

Multiple cranial mononeuropathy secondary to adecarcinoma in a young patient

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EPV-657

Diagnostic performance of machine learning algorithm vs conventional MRI for brain tumors.

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EPV-658

Unusual presentation of brain metastases from uterine cervical cancer. A case report.

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EPV-659

10 years of surgical treatment of spinal cord tumors in Brazil

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EPV-660

Autonomic evoked potential indices in children with cerebellar tumors

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EPV-661

Giant chondroma of the cerebral convexity: a rare report

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EPV-662

Leptomeningeal metastasis in a Neurology Department of a tertiary hospital: a case series

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EPV-663

Primary (isolated) diffuse meningeal melanomatosis: A case report and literature review

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EPV-664

Retinal findings in patients with MOGAD

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EPV-665

Acute painless right sided mydriasis; an unusual etiology

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EPV-666

Recurrent retinal vein thrombosis and styloid process: an unexpected association

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EPV-667

Eye movement study in essential tremor: A window on cognitive assessment

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EPV-668

IgG4-related disease with exclusive sinonasal involvement, an unusual etiology of progressive diplopia

M. Lara Gonzalez [1], B. Hidalgo Valverde [1], M. Garcia Ruiz [1], M. Sanchez Boyero [1], J. Otazu Moudelle [2], J. Gimeno Hernandez [3], J. Plaza Hernandez [4], V. Gajate Garcia [8], A. Marcos Dolado [8], E. Lopez Valdes [8], R. Ginestal Lopez [8]
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EPV-669

Pupil-sparing compression of oculomotor nerve by non-aneurysmal posterior cerebral and superior cerebellar arteries.

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EPV-670

Bilateral optic neuropathy secondary to Vitamin B12 deficiency

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EPV-671

Guillain–Barré syndrome: clinical presentation, diagnosis and management in the Maltese Population

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EPV-672

Report of Novel GJB1 mutation in a Charcot-Marie-Tooth female patient

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EPV-673

POEMS syndrome: A Colombian case series

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EPV-674

Patient Characteristics from the NEURO-TTRansform Study of Eplontersen in Transthyretin Amyloidosis Polyneuropathy

L. Obici [1], M. Waddington Cruz [2], F. Barroso [3], J. Berk [4], C. Chao [5], N. Dasgupta [6], P. Dyck [7], M. Gertz [7], Y. Parman [8], M. Weiler [9], J. Wixner [10], N. Viney [11], S. Jung [11], E. Schneider [11], T. Coelho [12]
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EPV-675

Anatomical Findings During Microsurgical Decompression for Classical Trigeminal Neuralgia

A. Santoyo-Pantoja, A. Munguía-Rodríguez, M. Segura-Lozano, A. Segura-Zenón, A. González-Silva, Y. Torres-Torres
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EPV-676

The effectiveness of a comprehensive program with biofeedback on the support reaction in the recovery period of a stroke

J. Egorova, V. Borisova, N. Filatov, S. Kotov, E. Isakova, E. Slyunkova

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EPV-677

Brain-computer interfaces with neurofeedback and computer trainings – efficiency comparison for patients with PICS

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EPV-678

Are our patients aware of the importance of neurorehabilitation treatment?

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EPV-679

Differences in effective rehabilitation between women and men

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EPV-680

Cognitive outcomes in patients treated with neuromuscular electrical stimulation after coronary artery bypass graft

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EPV-681

Neuroplasticity control by using brain-computer interface in immersive virtual reality in motor rehabilitation.

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EPV-682

A pilot study research effectiveness of rehabilitation patients after stroke with virtual reality

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EPV-683

Evaluation of the cost-effectiveness of digital rehabilitation services in patients with aphasia

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EPV-684

Cerebral hemodynamic changes to transcranial Doppler sonography in de novo patients with celiac disease

F. Fisicaro [1], G. Lanza [2], C. D'Agate [3], M. Pennisi [1], M. Cantone [4], G. Pennisi [2], M. Hadjivassiliou [5], R. Bella [6]
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EPV-685

Acute Stress Induces Cerumen Secretion: Case series of Four Medical Students during Exams

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EPV-686

IVIg responsive neuropathy associated with the treatment of cutaneous T-cell lymphoma with Brentuximab

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EPV-687

Disulfiram-induced multiple organ damage and pres with atypical presentation: a case report

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EPV-688

The role of beta-NGF in the maintenance of chronic neuropathic pain in post-traumatic neuropathies and plexopathies

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EPV-689

Quantitative analysis of conservative treatment for traumatic brain injury in Brazil

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EPV-690

An analysis of the economic impact of traumatic brain injury in childhood and adolescence in Brazil from 2011 to 2021

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EPV-691

Predictive factors of pain in Parkinson's disease

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EPV-692

Neuropathic pain in Parkinson's disease

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EPV-693

Central sensitization in adolescents with tension-type headache and nonspecific neck pain.

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EPV-694

Transcutaneous electric stimulation of the vagus nerve as a treatment for migraine – A systematic review

G. Sena, A. Kouassi, R. Pinheiro, A. Neves, T. Thomaz, J. Silva
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EPV-695

A single center experience of botulinum toxin A injections for the treatment of trigeminal neuralgia

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EPV-696

Anxiety and depression in different phenotypes of post-stroke pain syndrome

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EPV-697

The level of neurotrophic factors in patients with post-stroke pain syndrome

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EPV-698

Topographo-anatomical features of facial skull and bone metabolism in patients with persistent idiopathic facial pain

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EPV-699

Insulin resistance and risk of dementia in patients with Parkinson´s disease

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EPV-700

Peripheral neuropathy in myotonic dystrophy type 1 patients

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EPV-701

Chronic polyneuropathy associated with COVID-19 is chronic inflammatory demyelinating polyneuropathy (CIDP)?

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EPV-702

SPHYNCS: First glance at the gut microbiome in Narcolepsy type 1 and Narcolepsy Borderland

L.G. Fregolente [1], J.D. Warncke [1], J. Van der Meer [1], S. Bauer [1], M.H. Schmidt [1], SPHYNCS Investigators [1], A.J. Macpherson [2], B. Yilmaz [2], C.L.A. Bassetti [1]
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EPV-703

In-depth analysis of sleep, daytime sleepiness and autonomic function in MSA and PD: A prospective study

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EPV-704

Sleep disorders in myotonic dystrophy type 1 patients

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EPV-705

The relationship between sleep, anxiety and work productivity among white-collar employees during the COVID-19 pandemic

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EPV-706

Spinal cord compression revealing a chronic myeloid leukemia

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EPV-707

Vertebral hydatidosis: An uncommon cause spinal cord compression and with poor prognosis

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EPV-708

Elsberg syndrome: a tricky differential diagnosis case report

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EPV-709

Syringomyelia in rare forms of Chiari malformation type 1: CM0.5, CM1 without short bones, CM1 with Basilar invagination

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EPV-710

Idiopathic longitudinally extensive transverse myelitis: a case report

A. González Romero, M. Martínez Navarro, E. Marín Conesa, M. Martínez Zarco, E. Gómez López, R. Ramírez Toledo
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EPV-711

Progressive bulbomyelopathy as a presentation of dural arteriovenous fistula

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EPV-712

Nerve root injury from sacral Tarlov cysts and correlation with sensory and pelvic symptoms

C. Hentzen [1], I. Cabrilo [2], P. Malladi [3], S. Simeoni [3], G. Amarenco [4], N. Zaidman [2], M. Pakzad [5], S. Shah [6], A. Casey [2], J. Panicker [3]

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EPV-713

Clinical case of intermittent weakness of the medial rectus muscle of the eye.

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EPV-714

Side locked unilateral migraine with unilateral leukoaraiosis

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Index

A

I