



Neuroradiology in sub-Saharan Africa – what can, should, must be done in 1st ever seizure & epilepsy

12th Regional Training Course (RTC)

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My Message to Young African Neuroscientists

- Dare to be the **BEST**
- Don't be satisfied in being the **FIRST**

- If our generation has failed, **you should not fail!**
- If our generation has survived, **you should not only survive but succeed!**
- If our generation has succeeded, **you shouldn't only succeed but be significant.**

- **Dare to DREAM**
- **Dare to work as a TEAM.**

AKN



Outline

1. Introduction: Definition of terms
2. Etiologies of Seizures
3. Diagnostic strategy in first seizure and Neuroimaging in epilepsy
4. Indications of Neuroimaging
5. The African Context
6. Conclusion: Take-home message

Definition of Terms

Epileptic seizure

- A clinical event presumed to result from an abnormal and excessive cerebral neuronal discharge.
- Clinical symptoms are paroxysmal and may include: impaired consciousness and motor, sensory, autonomic, or psychic events perceived by the subject or an observer.

Definition of Terms

Epilepsy (ILAE 2014)

Epilepsy: a disease of the brain defined by any of the following conditions:

1. At least two unprovoked (or reflex) seizures occurring >24 hrs apart;
2. One unprovoked (or reflex) seizure and a probability of further seizures similar to the general recurrence risk (at least 60%) after two unprovoked seizures, occurring over the next 10 years;
3. Diagnosis of an epilepsy syndrome.

Definition of Terms

Epilepsy is considered to be resolved

For individuals who:

- had an **age-dependent epilepsy syndrome** & passed the applicable age
- have remained **seizure-free for the last 10 years**, with **no seizure medicines for the last 5 years**.

Definition of Terms

An acute symptomatic seizure:

- Occurs after a recent acute disorder such as: a metabolic insult, toxic insult, CNS infection, stroke, brain trauma, cerebral haemorrhage, medication toxicity, alcohol withdrawal, or drug withdrawal.
- Occurs **within one week** of the insult.

A remote symptomatic seizure:

- Occurs **beyond 1 week** following a disorder known to increase the risk of developing epilepsy. Examples: traumatic brain injury, stroke.

Etiologies of Seizures

Differential Diagnosis of First ever seizure	
Infections	Meningitis, encephalitis, abscess Parasitic: Neurocysticercosis
CNS Disease	Structural – tumor, congenital malformation (cortical dysplasia, lissencephaly)
	Vascular – hemorrhage, stroke, AVM, venous thrombosis
	Increased ICP, herniation
	Neurocutaneous syndrome – tuberous sclerosis
	Trauma
Metabolic disorders	Hypoglycemia, Electrolyte imbalance, Renal failure, hepatic disorder
Toxic	Alcohol intoxication, Alcohol withdrawal, Benzodiazepine withdrawal Drugs: buspirone
Fever	Febrile convulsions

Diagnostic Approach to First-Ever Seizure

Detailed clinical Evaluation

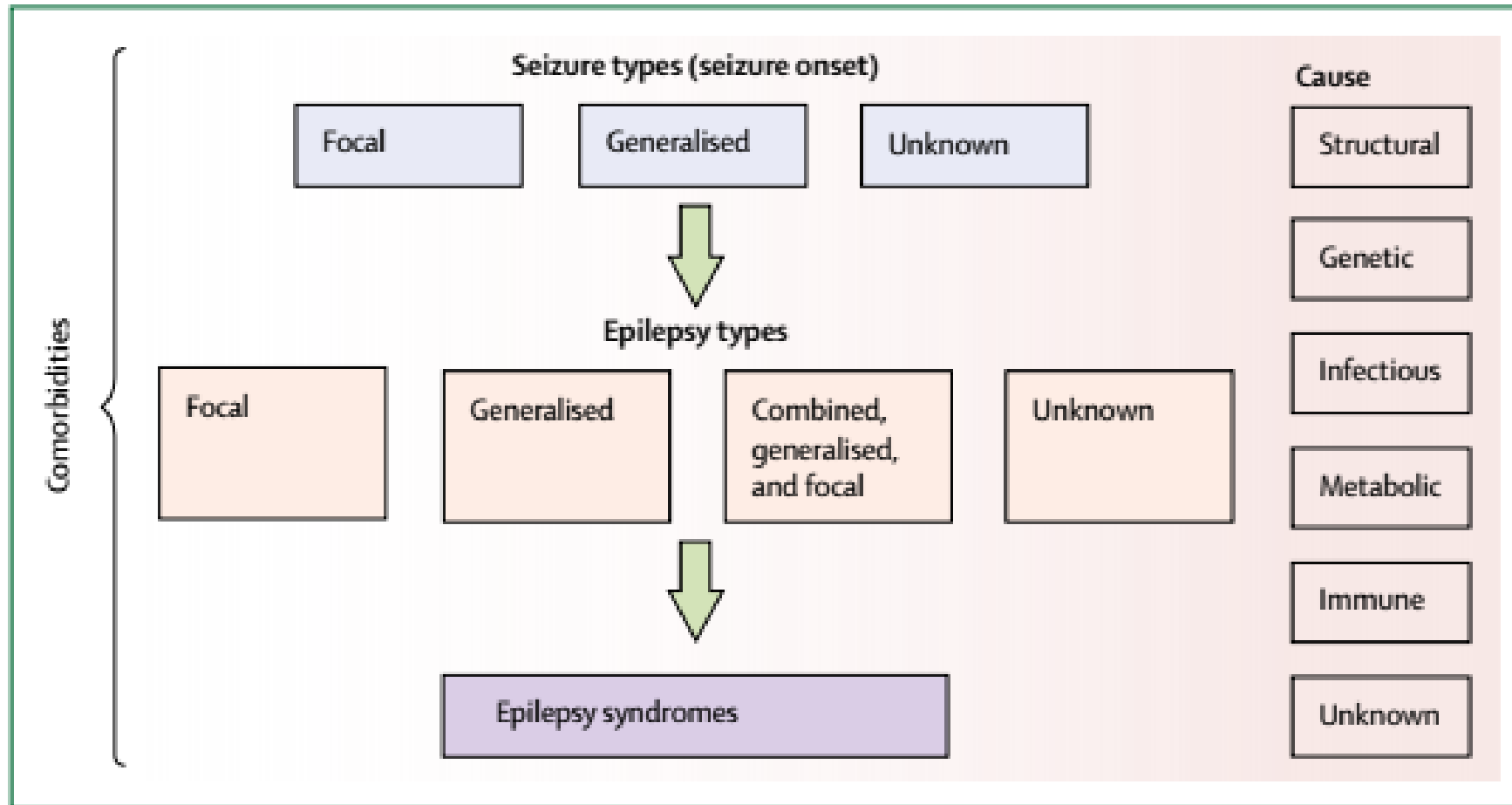
- Detailed history of seizure event
- Past medical history: severe head injury, etc
- Growth & developmental history: cerebral palsy, mental retardation
- Geographical residence: proximity to fast running streams, pig rearing area..

Diagnostic Approach to First-Ever Seizure

Detailed Clinical Evaluation

- Family history.
- Social history: exposure to lead or drugs of abuse, as well to the practical impact on employment and lifestyle.
- Physical Exam
 - Detailed systemic exam
 - Detailed neurologic exam
 - Search for signs of focal neurologic deficit

Diagnostic Approach to First-Ever Seizure



From: *Epilepsy*, Orrin Devinsky et al, *Nature Reviews Disease Primers*. 2018

Diagnostic Approach to First Ever Seizure

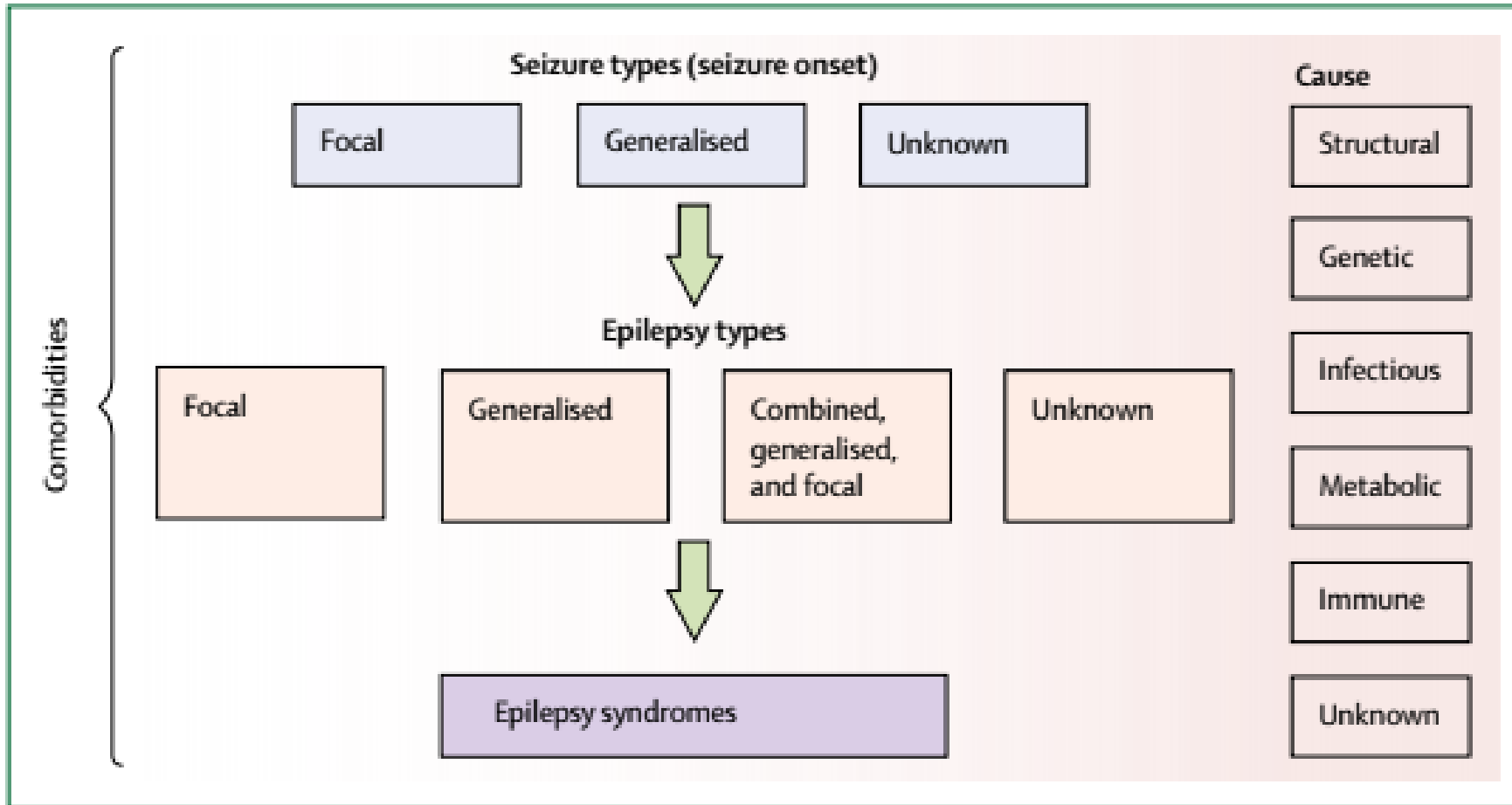
Rule out Seizure Mimicking Conditions

- Syncope
- Breath holding spell
- Aspiration/GastroEsophageal Reflux Disease (GERD)
- Psych – panic attack, day dreaming, ADHD
- Conversion, pseudo seizures
- Benign sleep myoclonus
- Complex migraine
- Motor tics

Approach to Known Epilepsy

- Known patient or newly diagnosed?
- Syndrome?
- Etiology?
- Detailed clinical history and evaluation
- Detailed description of seizures:
 - Stereotype seizures?
 - New clinical manifestations?

The goal of the clinical approach:



From: *Epilepsy*, Orrin Devinsky et al, *Nature Reviews Disease Primers*. 2018

Indications of Neuroradiology

Remote Symtomatic seizures/epilepsy



Neuroradiology Technologies

- Used in combination with seizure history and electroencephalography (EEG)
- To diagnose some specific epilepsy syndrome (Pohlmann-Eden and Legg, 2013)
- Major objective of Neuroimaging:
 - detect any underlying structural explaining the seizure and
 - diagnose epilepsy in some cases (Fisher et al., 2014).

Neuroradiology Technologies

- Influence clinical decisions:
 - initiation of antiseizure drug therapy or
 - expedited referral for surgical consideration.
- Priority should be given to patients with:
 - focal findings in the neurologic exam and
 - focal abnormalities on EEG

Computed tomography (CT)

- 1st line imaging tool in most acute care settings
 - Rapidly available
 - Relatively low cost
 - Excludes emergency lesions (exclude ICH, abscess or intracranial mass requiring neurosurgery (Hess and Barkovich, 2010))
 - Can effectively guide seizure management (Harden et al., 2007)
 - CT is sensitive for detection of calcified lesions and bone lesions.



Magnetic Resonance Imaging (MRI)

- 2nd line imaging tool in most settings
 - Not readily available
 - High cost
 - Not usually available in emergency care setting
 - Ideal for lesion detection: malformations, dysplasias, etc
 - Can effectively guide seizure management and surgery.



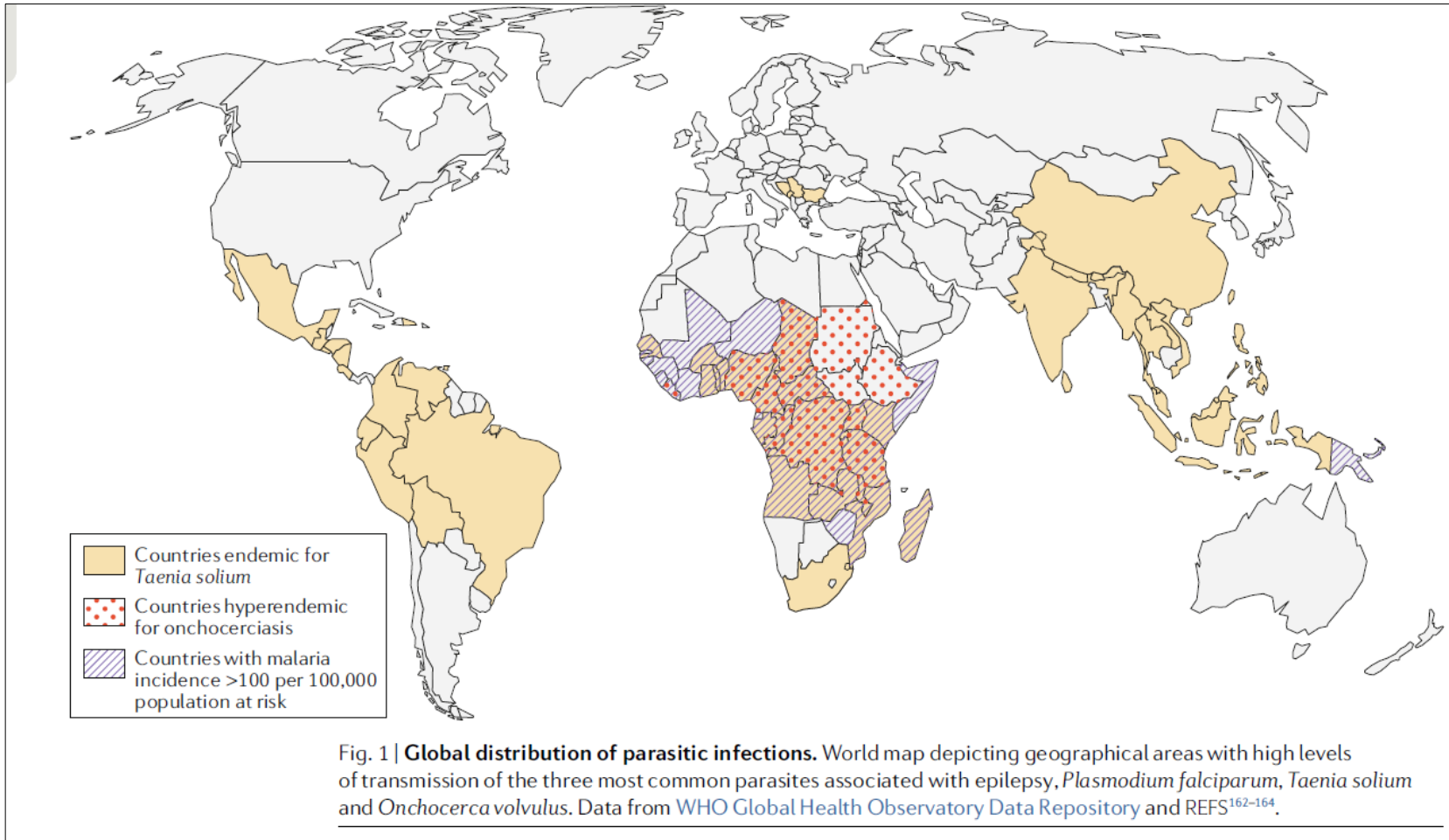
WHEN TO PERFORM AN MRI IN A PATIENT WITH SEIZURES

- All patients with epilepsy should undergo an MRI. Exceptions include:
 - Those with very typical forms of primary generalized epilepsy (e.g., JME, CAE)
 - Those with benign focal epilepsies of childhood with characteristic clinical and EEG features (ex: benign epilepsy with centrotemporal spikes, early-onset childhood epilepsy with occipital spikes (Panayiotopoulos type) and adequate response to antiseizure meds (ASMs) (Gaillard et al., 2011).
- There are **two indications**:
 - Newly diagnosed patients or patients with longstanding epilepsy who haven't been properly investigated.
 - Refractory seizures and therefore candidates for surgery (Berg et al., 2010).

IMPORTANCE OF MRI IN EPILEPSY

- MRI exam is crucial for the diagnosis and treatment of patients with epilepsy.
- MR images allow the characterization of the nature of the lesion:
 - progressive (e.g., cancer, Rasmussen's encephalitis) or
 - static (e.g., ischemic lesions, congenital malformations).
- MRI is an important tool for:
 - prognostic counseling and
 - defining treatment strategy.

Special Epidemiological & Clinical Situations in Africa: Endemic Parasitic Infections & Epilepsy



REVIEWS



Zoonotic and vector-borne parasites and epilepsy in low-income and middle-income countries

Gagandeep Singh^{1,2}, Samuel A. Angwafor², Alfred K. Njamnshi^{3,4}, Henry Framow⁵ and Josemir W. Sander^{6,7}

Abstract | Zoonotic and vector-borne parasites are important preventable risk factors for epilepsy. Three parasitic infections — cerebral malaria, *Taenia solium* cysticercosis and onchocerciasis — have an established association with epilepsy. Parasitoses are widely prevalent in low-income and middle-income countries, which are home to 80% of the people with epilepsy in the world. Once



Special Epidemiological & Clinical Situations in Africa: Onchocerciasis-Associated Epilepsy (OAE)

Articles

The temporal relationship between onchocerciasis and epilepsy: a population-based cohort study

Cédric B Chesnais, Hugues C Nana-Djeunga, Alfred K Njamnshi, Cédric G Lenou-Nanga, Charlotte Boullé, Anne-Cécile Zoung-Kanyi Bissek, Joseph Kamgno, Robert Colebunders, Michel Boussinesq

Summary

Background Many studies have suggested that onchocerciasis might be associated with epilepsy. Therefore, we did a cohort study to assess the incidence of epilepsy relative to *Onchocerca volvulus* skin microfilarial density (MFD) measured during childhood and to assess the possibility of a temporal relationship.



Lancet Infect Dis 2018
Published Online
September 26, 2018
<http://dx.doi.org/10.1016/>

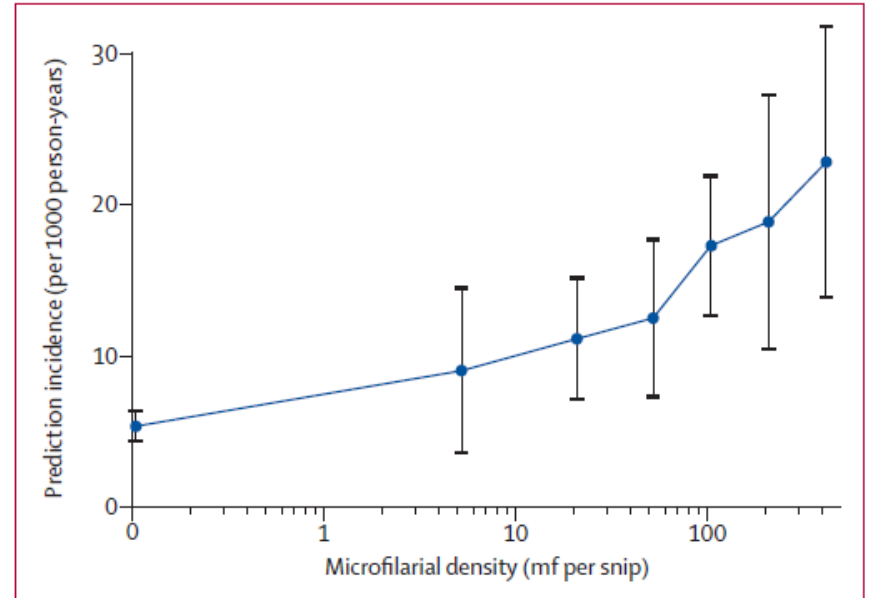
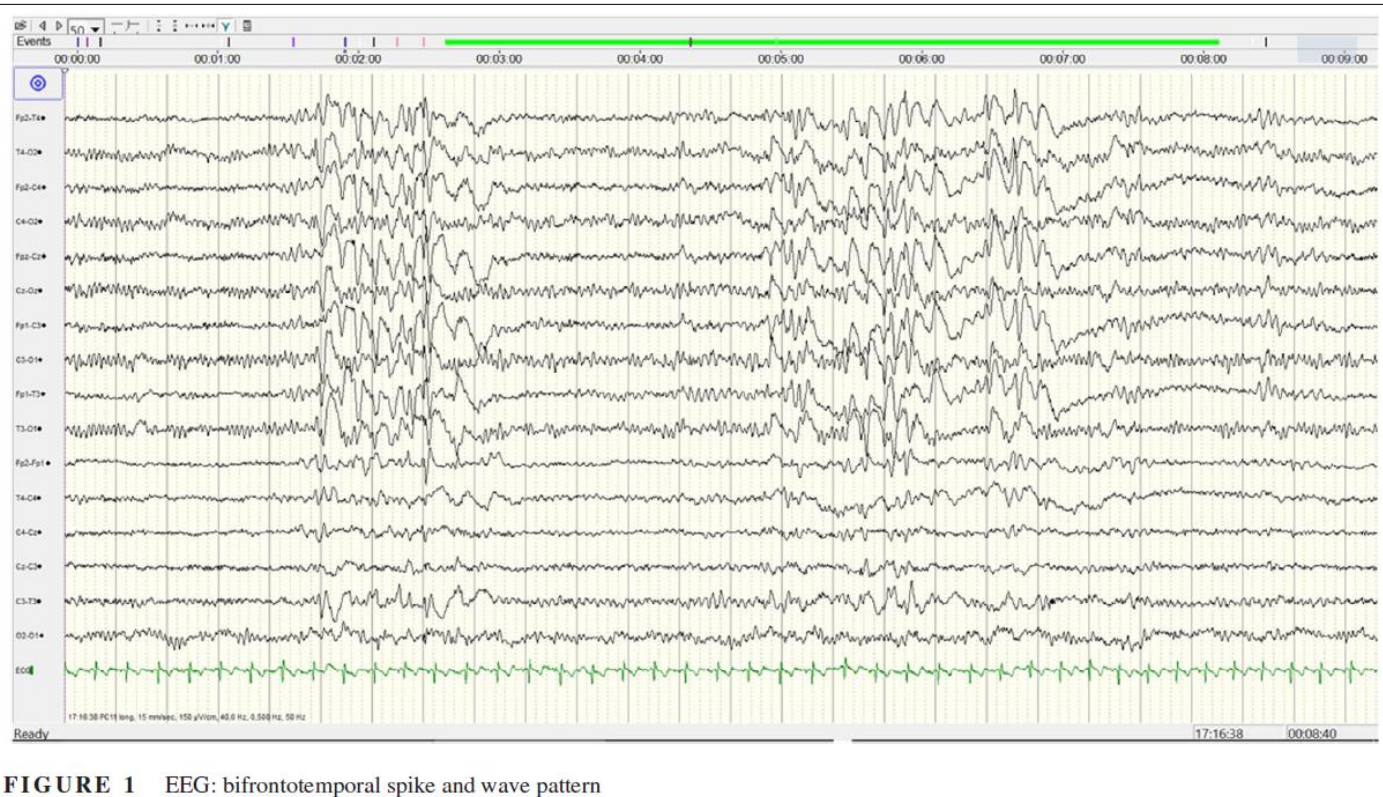


Figure 1: Predicted incidences of epilepsy according to individual microfilarial densities
Vertical lines indicate the 95% CI for each point of measure from the final model. X axis is presented in a logarithm scale. Mf per snip= microfilariae per skin snip.

From: Chesnais, Nana-Djeunga, Njamnshi et al., 2018, Lancet-Infectious Dis.



Special Epidemiological & Clinical Situations in Africa: Onchocerciasis-Associated Epilepsy (OAE)



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FULL-LENGTH ORIGINAL RESEARCH

Epilepsia Open®
Open Access

Epilepsy in the Sanaga-Mbam valley, an onchocerciasis-endemic region in Cameroon: electroclinical and neuropsychological findings

Alexandre Morin¹ | Maxime Guillaume¹ | Leonard Ngarka^{2,3,4} | Godwin Y. Tatah^{2,3,5} | Joseph Nelson Siewe Fodjo^{2,3,6} | Guillaume Wyart⁷ | Ghislain Nokam⁸ | Thierry Tchoumi⁹ | Mary Bello Nkinin⁴ | Wepnyu Y. Njamnshi^{2,3,4} | Eric-Samuel Chokote^{2,3} | Michel Boussinesq^{10,11,12} | Robert Colebunders⁶ | Cédric B. Chesnais^{10,11,12} | Gilles Gargala¹³ | Dominique Parain¹⁴ | Alfred K. Njamnshi^{2,3,4}

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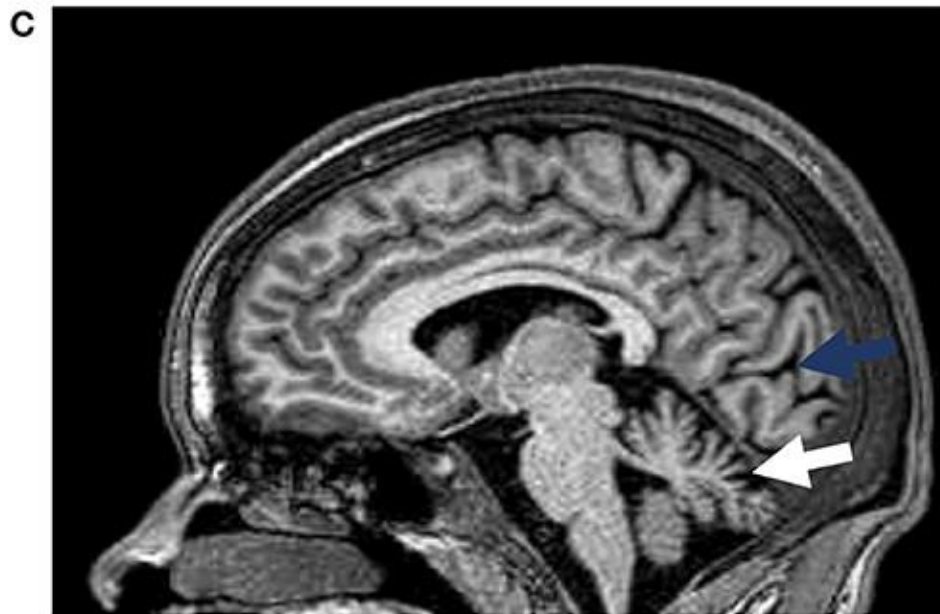
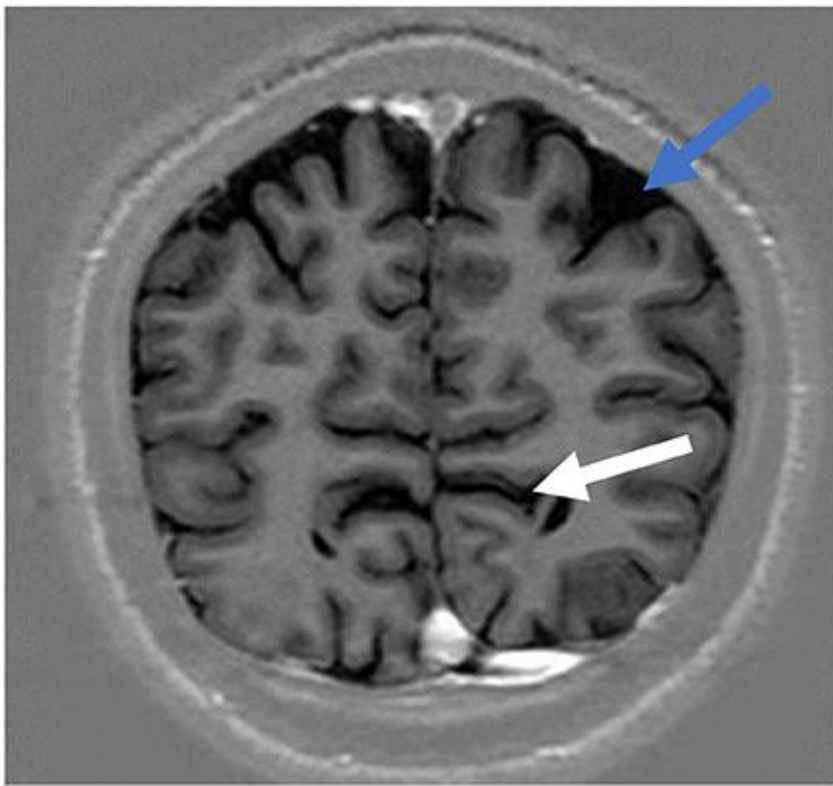


From: Morin, Guillaume, Ngarka, Njamnshi et al., 2021, Epilepsia Open

Neuroradiology in African Context: OAE

MRI in Onchocerciasis-Associated Epilepsy (OAE): 10 participants

- Most participants (8/10) had structural abnormalities on brain MRI
- Commonly observed abnormalities:
 - mild to moderate cerebellar atrophy (6/10)
 - regional cerebral atrophy (5/10): bilateral medial parieto-occipital (2/10), bilateral fronto-parietal (1/10), bilateral parietal (1/10), bilateral medial occipital (1/10).
- No hippocampal atrophy nor hippocampal sclerosis
- No Enhancement with gadolinium.



Representative magnetic resonance images from possible OAE epilepsy cases showing regional atrophy

From: R Ogwang et al. 2021

MRI in PWE and Nodding Syndrome

- Normal cerebral MRI scans were found in 10/32 patients (31.3%)
- Common findings
 - Hippocampal changes (9/22)
 - Gliotic lesions
 - Signal abnormalities : subcortical hyperintensities that did not fulfil the criteria for gliotic lesions
 - Cysts
 - Other lesions: cortical dysplasia

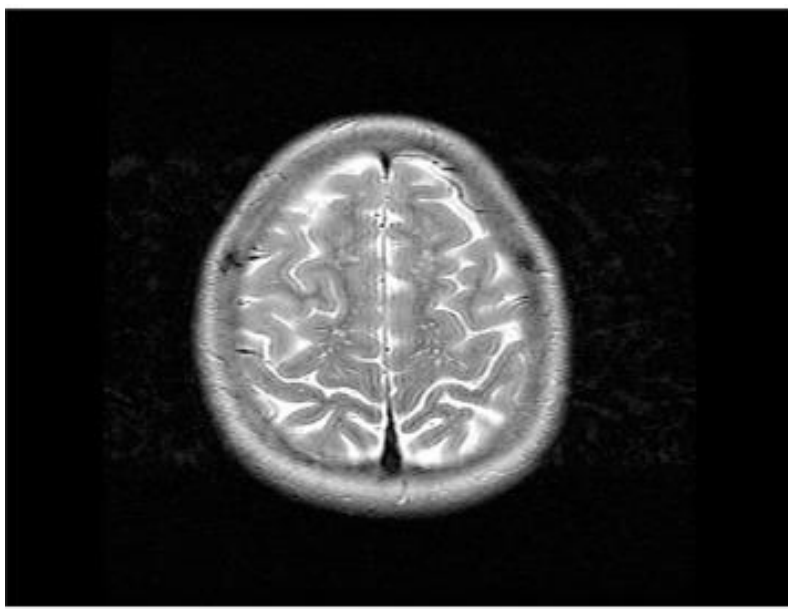


Figure 1a T2W1

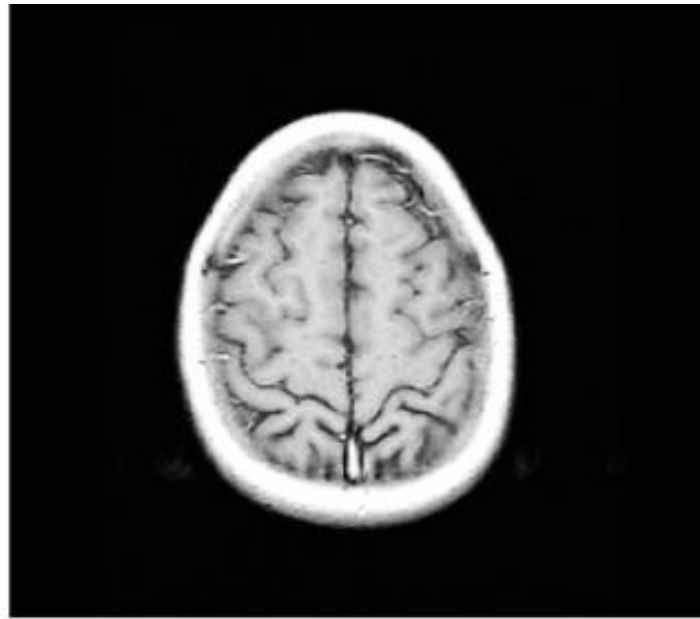
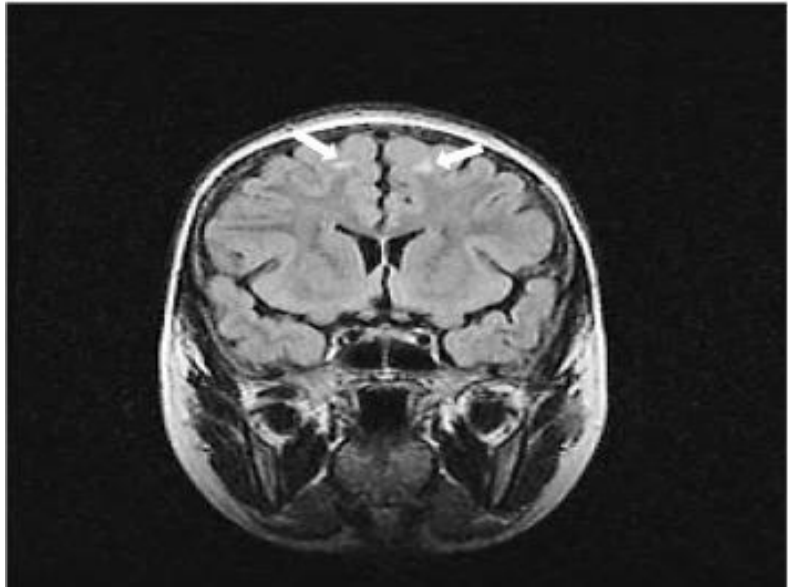
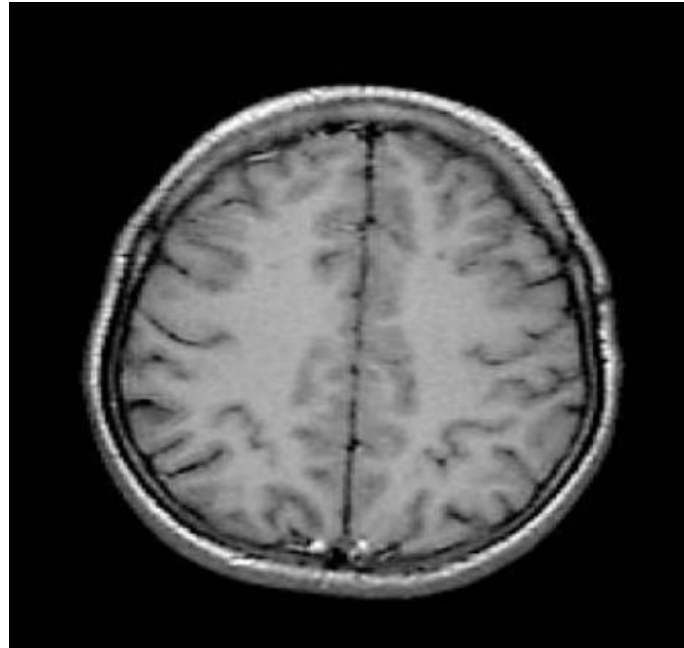
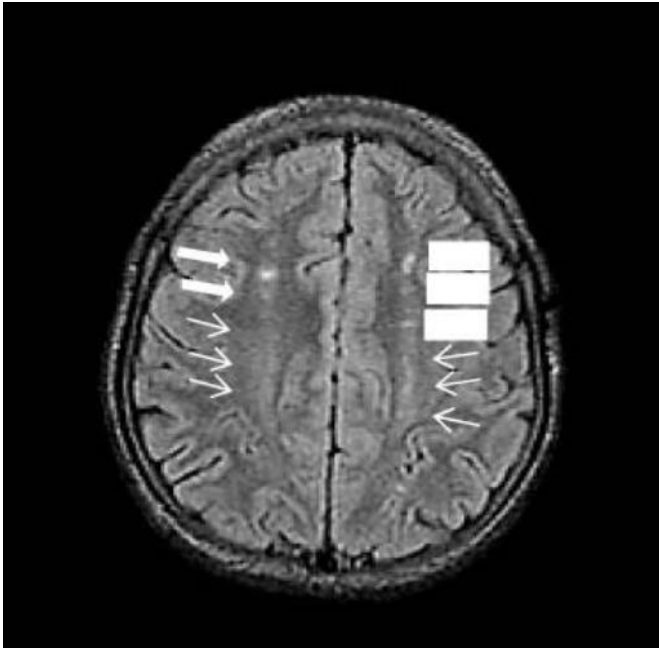
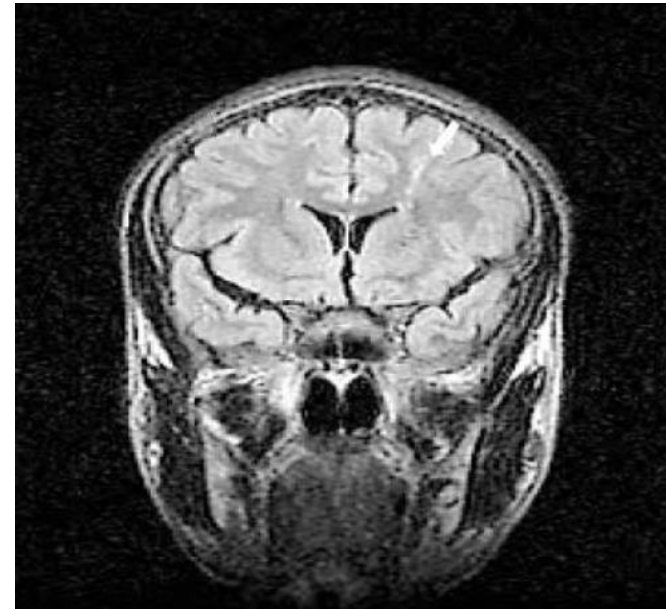
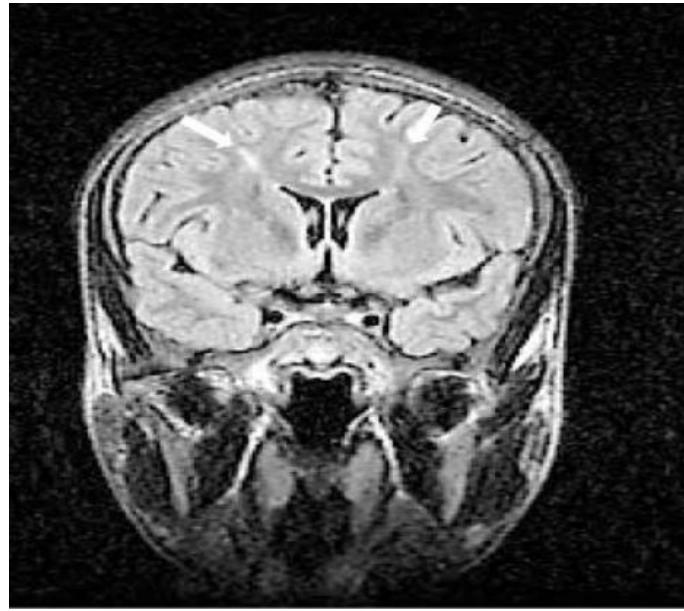
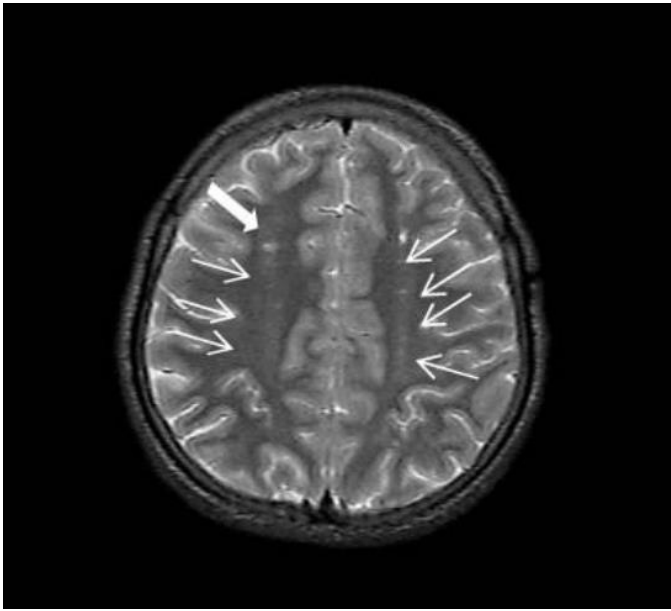


Figure 3a T1W1 post contrast



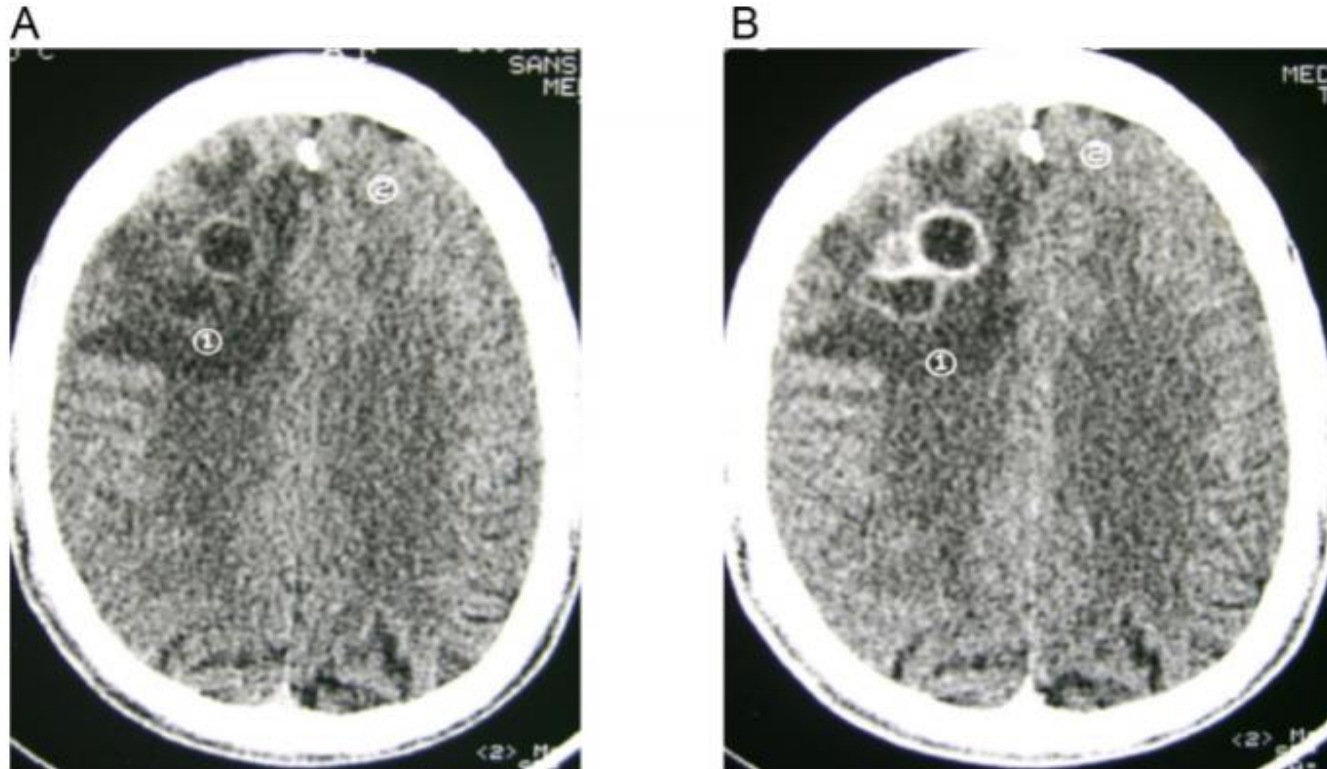
13 year-old male
with head nodding
and generalized tonic
clonic seizures

MRI findings:
bilateral punctuate
subcortical
hyperintensities in the
frontal lobe on T2W1
Non enhanced



14 year-old male with head nodding and generalized tonic-clonic seizures showing bilateral punctate subcortical hyperintensities in the frontal lobe, on T2W1 and axial as well as coronal FLAIR most likely corresponding to gliotic lesions

Neuroimaging in Neurocysticercosis



Colloidal and granular lesions of NCC associated with significant oedema

Millogo, A, Njamnshi, AK, & Kabwa-PierreLuabeya, M (2018). Neurocysticercosis and epilepsy in sub-Saharan Africa. *Brain Research Bulletin*



a)

b)

c)

Axial CT scan in a case of Neurocysticercosis

Note: Cortical epileptogenic lesions, lesions at different stages of development

From: A. S. Winkler, 2012 *Epilepsy and Neurocysticercosis in Sub-Saharan Africa*



Neuroradiology in sub-Saharan Africa – what can, should, must be done in 1st ever seizure & epilepsy

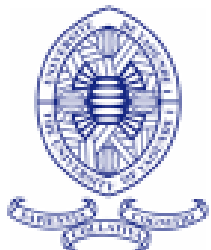
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Perspectives for Neuroimaging in Africa: Mobile MRI, Artificial Intelligence & Telemedicine

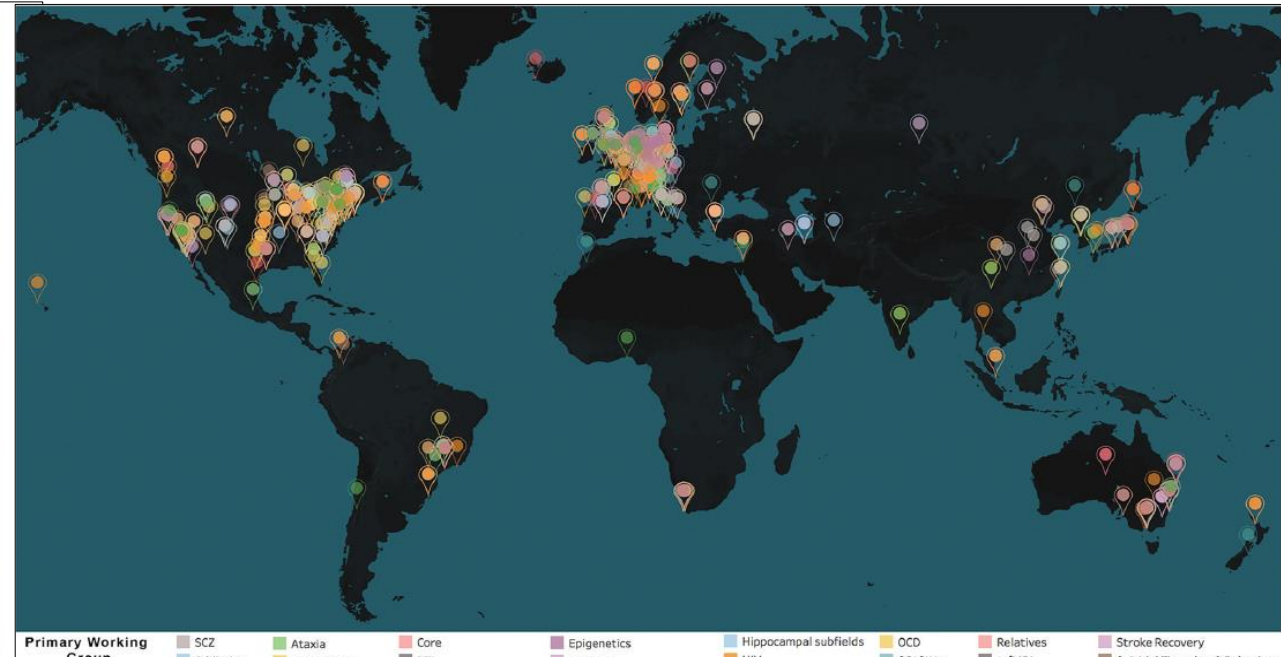


Fig. 2 ENIGMA founding sites. The first ENIGMA project (Stein et al. 2012) was initiated in 2009, by a consortium of research groups worldwide involved in neuroimaging and genetics. Several existing consortia and research networks are taking part, including IMAGEN, EPIGEN, SYS, FBIRN, and ADNI. Many of these efforts pre-dated

ENIGMA and continue today; each conducts its own projects in to their collaborative work within ENIGMA. ADNI collects data sites around the U.S.; for clarity, not all data collection sites are here. Each *symbol* represents a site contributing to ENIGMA of June 2013

Fig. 1 World Map of ENIGMA's Working Groups. The ENIGMA Consortium has grown to include over 1400 participating scientists from over 200 institutions, across 43 countries worldwide. ENIGMA is organized as a set of 50 WGs, studying 26 major brain diseases (see color key). Each group

ENIGMA 2013

ENIGMA 2019



Perspectives for Neuroimaging in Africa: Mobile MRI, Artificial Intelligence & Telemedicine

ENIGMA-Epilepsy

The ENIGMA-Epilepsy WG combined data from 24 centers across 14 countries to create the largest neuroimaging study to date of epilepsy⁹. Data from 2149 individuals with epilepsy were divided into four common epilepsy syndromes: idiopathic generalized epilepsies ($N = 367$), mesial temporal lobe epilepsies with hippocampal sclerosis (MTLE; left, $N = 415$; right, $N = 339$), and all other epilepsies in aggregate ($N = 1026$), compared to 1727 matched healthy controls. Compared to controls, all epilepsy groups showed lower volume in the right

thalamus ($d = -0.24$ to -0.73), and lower thickness in the precentral gyri bilaterally ($d = -0.34$ to -0.52). Both MTLE subgroups also showed profound volume reduction in the ipsilateral hippocampus ($d = -1.73$ to -1.91), and lower thickness in cortical regions, including the precentral and paracentral gyri ($d = -0.36$ to -0.52) compared to controls. Notably, the effect sizes for cortical differences in this neurological disorder were much greater than those seen in all complex psychiatric disorders. In an approach known as 'virtual histology', a follow-up study¹¹⁰ overlaid the cortical deficit maps on gene-expression data from the Allen Brain Atlas, and detected enrichment for microglial markers in regions with greater deficits. The WG is currently combining DTI data and exploring putative neuroanatomical biomarkers of medication treatment resistance and post-operative outcomes.

ENIGMA – EPILEPSY (24 centres, 14 countries; $n = 2149$ vs 1727 matched controls)

- Idiopathic gen. epilepsies
- Mesial temporal lobe epilepsies with hippocampal sclerosis
- All other epilepsies
- Results
 - Lower R. Thalamus volumes in all epilepsies
 - Lower pre-central gyri thickness (bilat)
 - “Virtual histology” shows microglial markers
- More markers: ttt resistance & post-op outcomes!



https://trends.medicaexpo.com/medicaexpo-e-magazine/project-118905-438125.html?token=114eae2712082b6296f91cfb154bd993dcc0dedd#utm_medium=email&utm_source=insight&utm_campaign=1-primary-care-24-08-2021&utm_content=photo&utm_term=TRENDS_recommendation

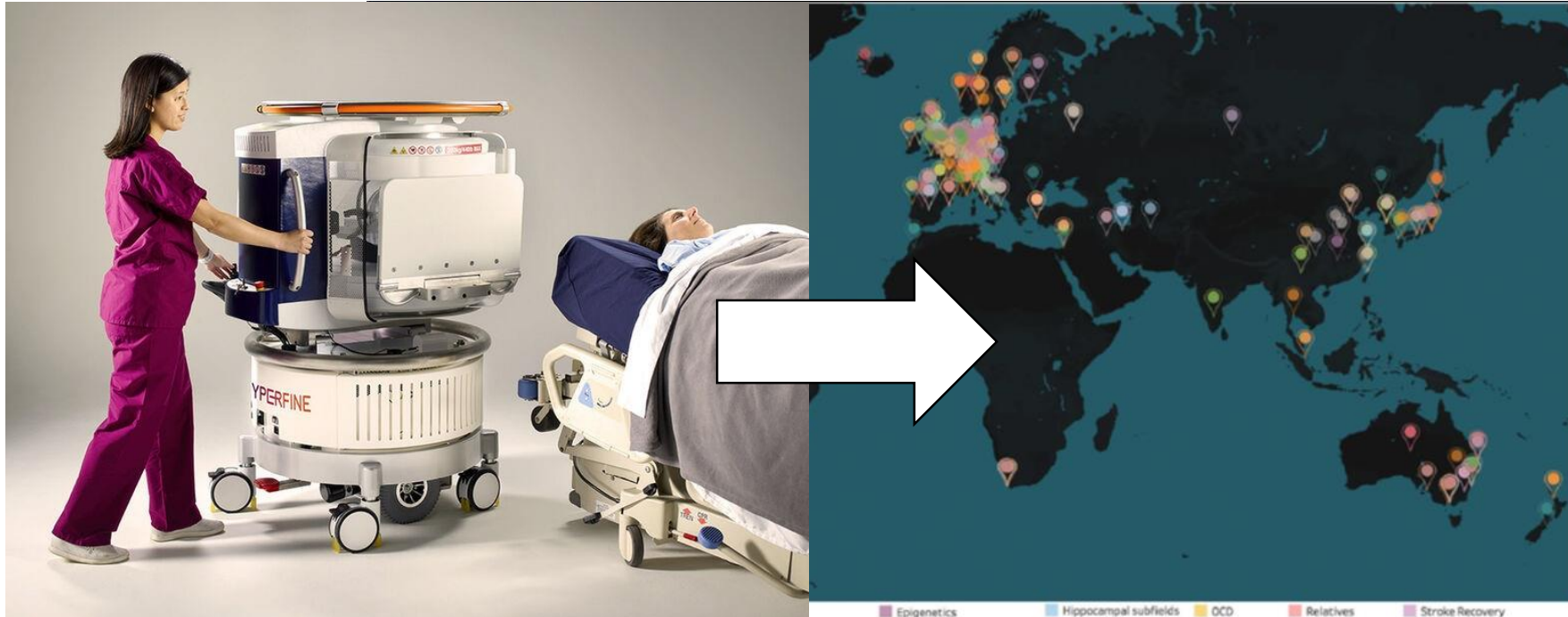


Conclusion: TAKE HOME MESSAGE

- **What can be done:**
 - Head MRI and/or CT depending on geographical & financial accessibility (**now**)
 - Mobile paediatric MRI (**near future**)
 - Mobile or fixed MRI (+ **functional MRI**) and/or CT with **AI** and Telemedicine (**near future**)
- **What should be done:**
 - At least head CT for **first-ever seizure** and **changing symptomatology for known epilepsy** (**Ex: Status epilepticus, additional seizure types**)
- **What must be done:**
 - Head MRI (and Electrophysiology + Neuropsychology) if indication for **epilepsy surgery**
 - **Thorough clinical evaluation** (and if possible EEG) and treatment (No imaging possibility)

Thank You

For Supporting the Future of Neuroimaging in Africa,
for better brain health



Group	Addiction	Brain Injury	DTI	Epigenetics	Hippocampal subfields	OC	Relatives	Stroke Recovery
22q Deletion Syndrome	ADHD	BrainAGE	Early Onset Psychosis	Epilepsy	HIV	DRIGINS	rs/fMRI	Suicidal Thoughts & Behaviors
MDD	Anxiety	Clinical High Risk	Eating Disorders	Evolution	Irritability	Parkinson's	Schizotypy	Sulci
BD	ASD	CNVs	EEG	Frontotemporal Dementia	Lateralization	Plasticity	Sleep Disorders	Tourette's Syndrome
				GWAS	Lifespan	PTSD	Storage Disease	Transgender Persons

Fig. 1 World Map of ENIGMA's Working Groups. The ENIGMA Consortium has grown to include over 1400 participating scientists from over 200 institutions, across 43 countries worldwide. ENIGMA is organized as a set of 50 WGs, studying 26 major brain diseases (see color key). Each group

