CNS INFECTIONS WITH MOVEMENT DISORDERS SYMPTOMATOLOGY

NJIDEKA U. OKUBADEJO *MBCHB, FMCP*
FACULTY OF CLINICAL SCIENCES,
COLLEGE OF MEDICINE, UNIVERSITY OF LAGOS
NOKUBADEJO@UNILAG.EDU.NG

To disseminate knowledge and promote research to advance the field of Movement Disorders

http://www.movementdisorders.org

Objective

Highlight the spectrum of CNS infections manifesting movement disorders phenomenology

Outline

- Overview – some basics of movement disorders
- Overview of aetiologies of movement disorders
- Infectious causes of movement disorders
- Parainfectious movement disorders
- General approach/summary

Definition

Neurologic syndromes in which there is either **an excess of movement or**

a **paucity of voluntary and automatic movements**, unrelated to weakness or spasticity

- Hyperkinesias (*aka dyskinesias*)
- Hypokinesias

Hypokinesias

- Parkinsonism
- Apraxia
- Blocking (holding) tics
- Cataplexy and drop attacks
- Catatonia, psychomotor depression and obsessional slowness
- Freezing phenomenon
- Hesitant gaits
- Hypothyroid slowness
- Rigidity
- Stiff muscles

Fahn S, Jankovic J, Hallett M. Principles and Practice of Movement Disorders. 2nd ed. Philadelphia: Elsevier; 2011.

Hyperkinesias

- Tremor
- Dystonia
- Chorea/Ballism
- Athetosis
- Hemifacial spasm
- Myoclonus
- Ataxia/asynergia/dysmetria
- Tics
- Abdominal dyskinesias
- Akathitic movements
- Hyperekplexia
- Jumping disorders
- Jumpy stumps
- Moving toes and fingers
- Myokymia and synkinesis
- Myorhythmia
- Paroxysmal dyskinesias
- Periodic movements in sleep
- REM sleep behavior disorder
- Restless legs
- Stereotypy

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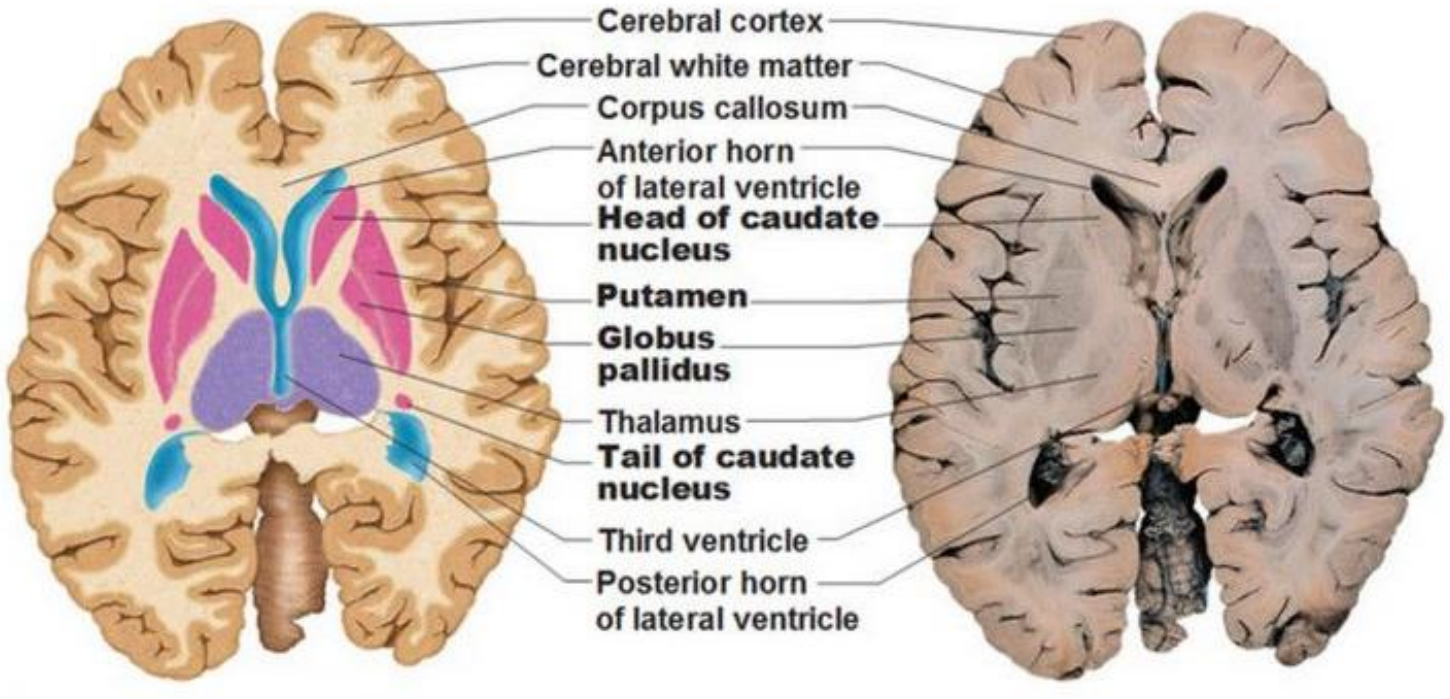
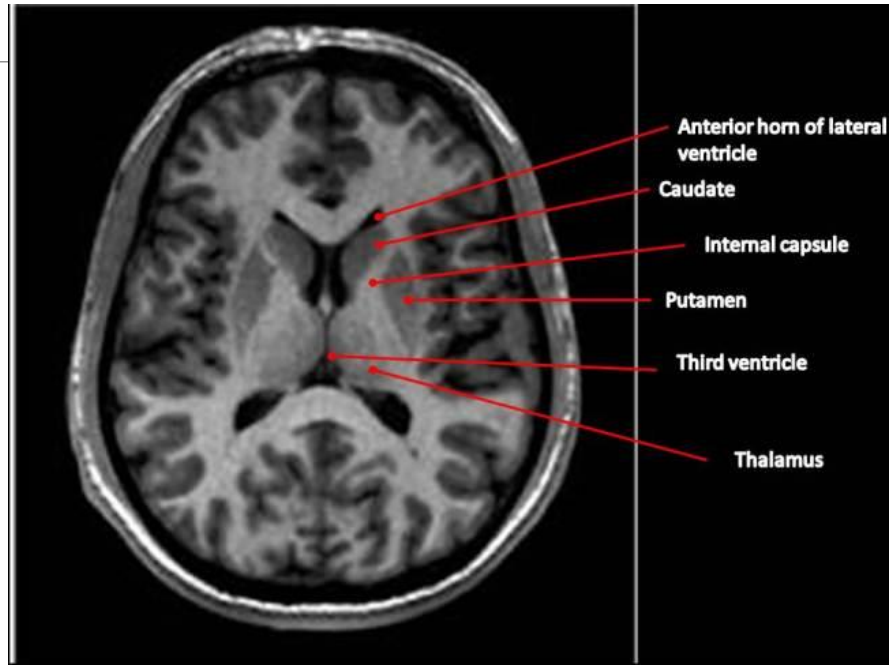
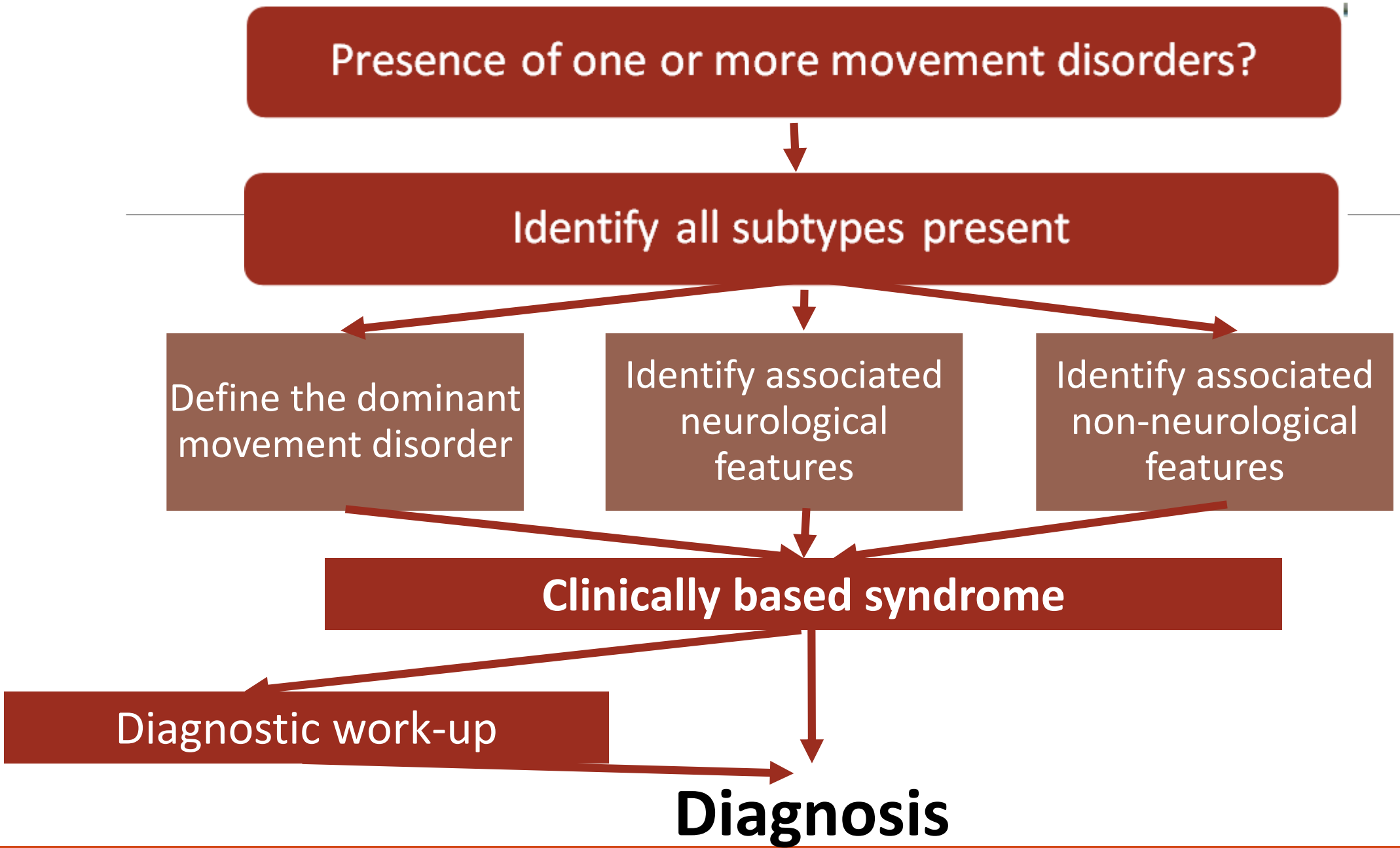
Localization of movement disorders





- Structural lesions
- Functional (neurochemical) abnormalities

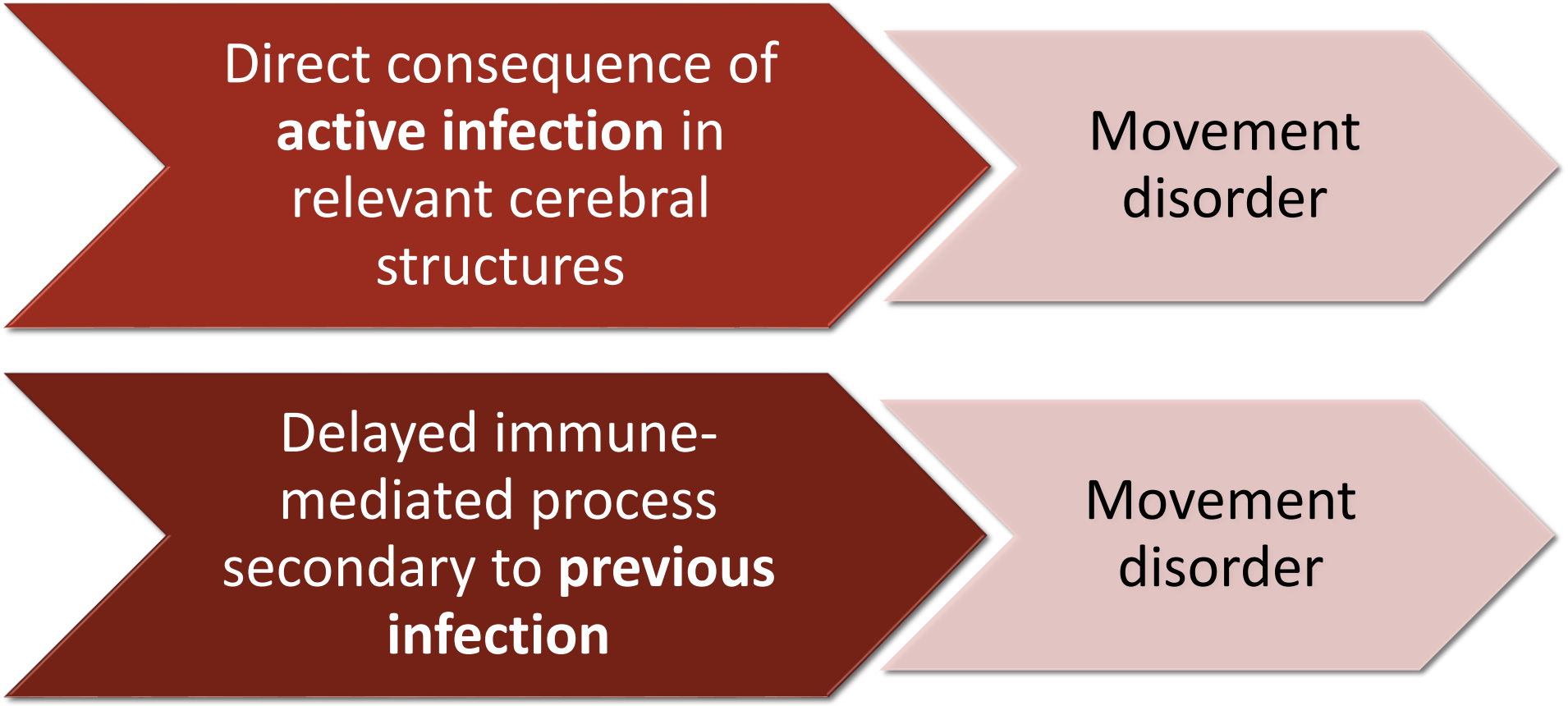


Adapted from: Abdo, W. F. *et al. Nat. Rev. Neurol.* 6, 29–37 (2010)

Aetiologies of movement disorders

Primary	Hereditary	Secondary
• Neurodegenerative		• Metabolic • Vascular • Tumors • Trauma • **Infections** • Inflammatory • Demyelinating • Paraneoplastic • Toxins

Infection-related MD mechanisms



Characteristics i

~ 20% (1/5th) of all secondary movement disorders

Scenario: infectious or post-infectious

Hypokinetic or hyperkinetic, single or mixed

Commoner types: dystonia, hemichorea/hemiballism, tremor, tics, myoclonus, paroxysmal dyskinesias, parkinsonism

Aetiologies:

viral, bacterial, parasitic, fungal, prion

Characteristics ii

- **Demographic profile**
  - Typically young onset (<20), but any age; based on distribution of cause
- **Time from infection to MD**
  - Acute or subacute onset or delayed by months to years
  - Typically about 6 weeks from onset of infection (**but depends on cause**)
- **Phenomenology**
  - Dystonia (~50% ± choreoathetosis); mixed (~23%); parkinsonism (~15%); generalized (~60%); also varies by aetiology (predilection)

** Data based on few published case series (mainly from Asia)

Aetiologies

Viral:
HIV, Others

Bacterial

Parasitic

Fungal

Prion-related:
Kuru, CJD

Some considerations….

- Fever and constitutional symptoms may be absent
- Evidence of infection may be remote
- Immune status may be normal or impaired
- Immunosuppression goes beyond associated HIV infection
- Readily available imaging (CT) may be normal
- Travel history, dietary habits, risk factors require eliciting
- The MD may be the major presenting complaint or masked by other neurologic or systemic features

HIV/AIDS-associated MD

- Clinically relevant MD in ~3% only (but on prospective follow up~50%)
- Most common hyperkinesias: **hemiballism/hemichorea and tremor**
- May have other associated neurological problems

Aetiologies

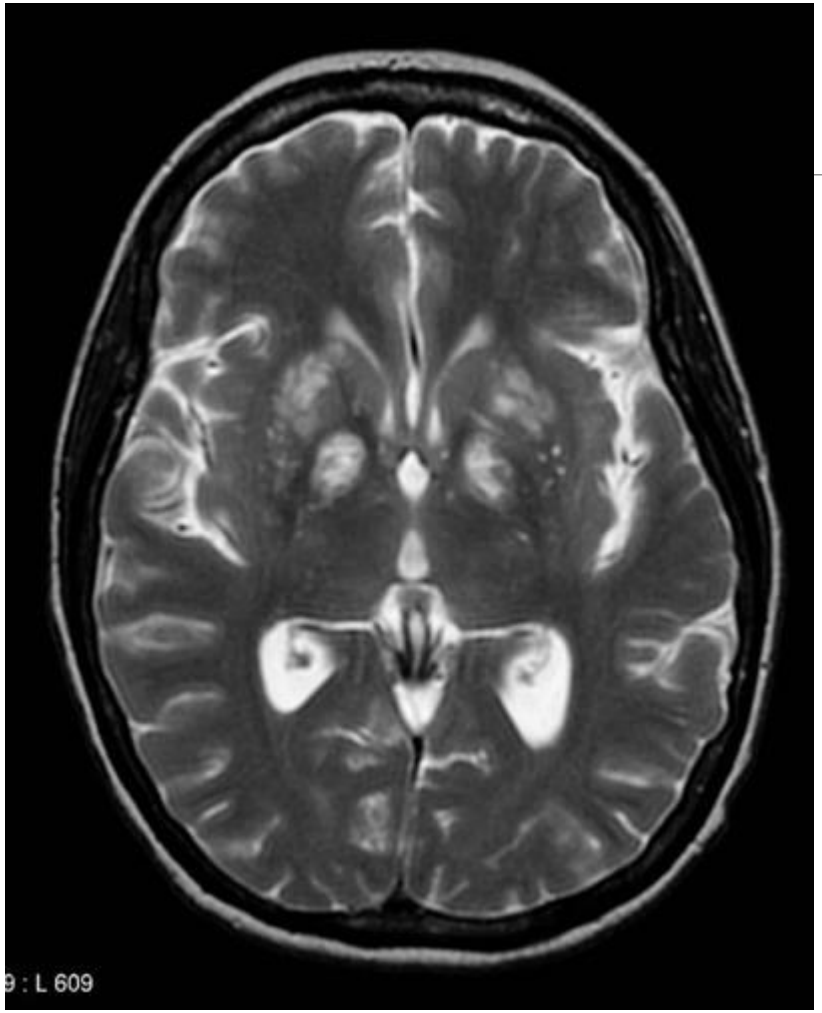
- Opportunistic infections and diseases
  - (esp. toxoplasmosis, T. pallidum, Crypt. neoformans, PML, primary lymphoma)
- Direct effect (HIV encephalopathy, dopaminergic dysfunction) → parkinsonism
- Drug induced e.g.antidopaminergic drugs, enhanced physiologic tremor

HIV/AIDS-associated MD

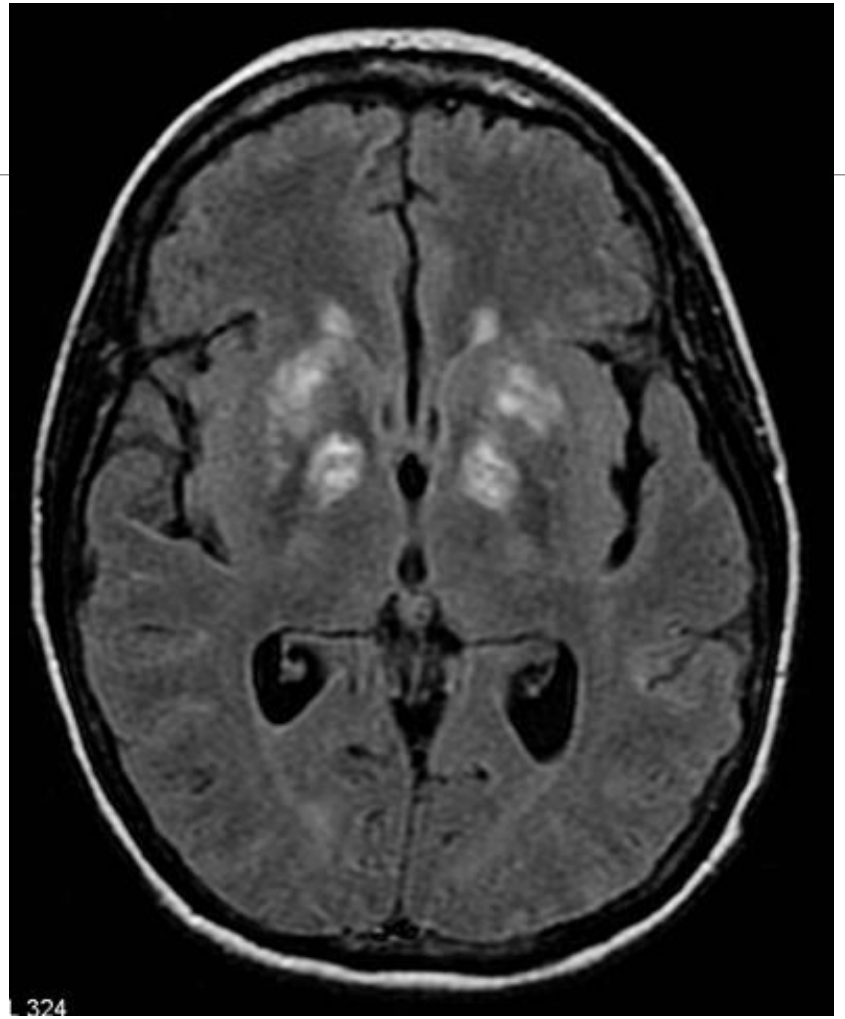
- **Hyperkinetic movement disorders**
  - Hemichorea-hemiballism most often
    - Acute onset in known AIDS or first presenting feature
  - Generalized or focal dystonia
  - Paroxysmal dyskinesias (non-specific trigger)
  - Myoclonus: action cortical, spinal or peripheral segmental
  - Others: oculomasticatory myorrhythmia (Whipple's), tics, akathisia, NMS

- **Parkinsonism and tremor – usually due to HIV encephalopathy**

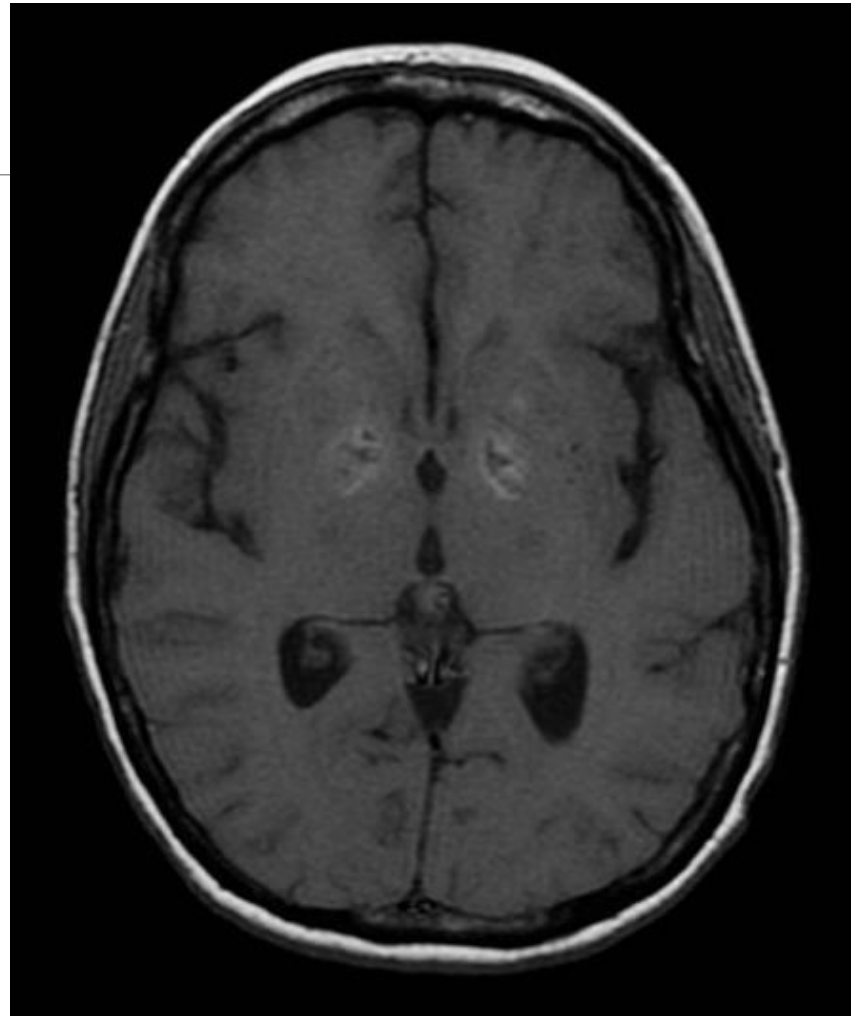
Cryptococcomas in the basal ganglia



Axial T2



Axial FLAIR



Axial T1

HIV/AIDS-associated MD ii

- **Treatment**
  - Specific to suspected aetiology (e.g. sulfadiazine + pyrimethamine in toxo)
  - HAART*
  - Symptomatic treatment
    - reserpine, valproic acid or tetrabenazine for hemiballism-hemichorea
    - Tremor: levodopa, anticholinergics, propranolol, clonazepam, etc
    - Parkinsonism: levodopa/carbidopa (? Efficacy)

***HAART drugs with CNS activity may prevent MD or improve symptoms (zidovudine, stavudine, lamivudine, abacavir, nevirapine, efavirenz, indinavir)**

MD associated with other viral infections

Hyperkinetic movement	Virus
Tremor	WNV (static, kinetic) Kuru (cerebellar) JEV (postural, rest, intermittent CJD (rest, postural)
Chorea	Variant CJD, WNV, Kuru, HSV, JEV
Dystonia	WNV, JEV, Variant CJD,
Myoclonus	Variant CJD, WNV, Kuru, JEV

WNV – West Nile virus
CJD – Creutzfeldt-Jakob disease
JEV – Japanese encephalitis virus
HSV – Herpes simplex virus

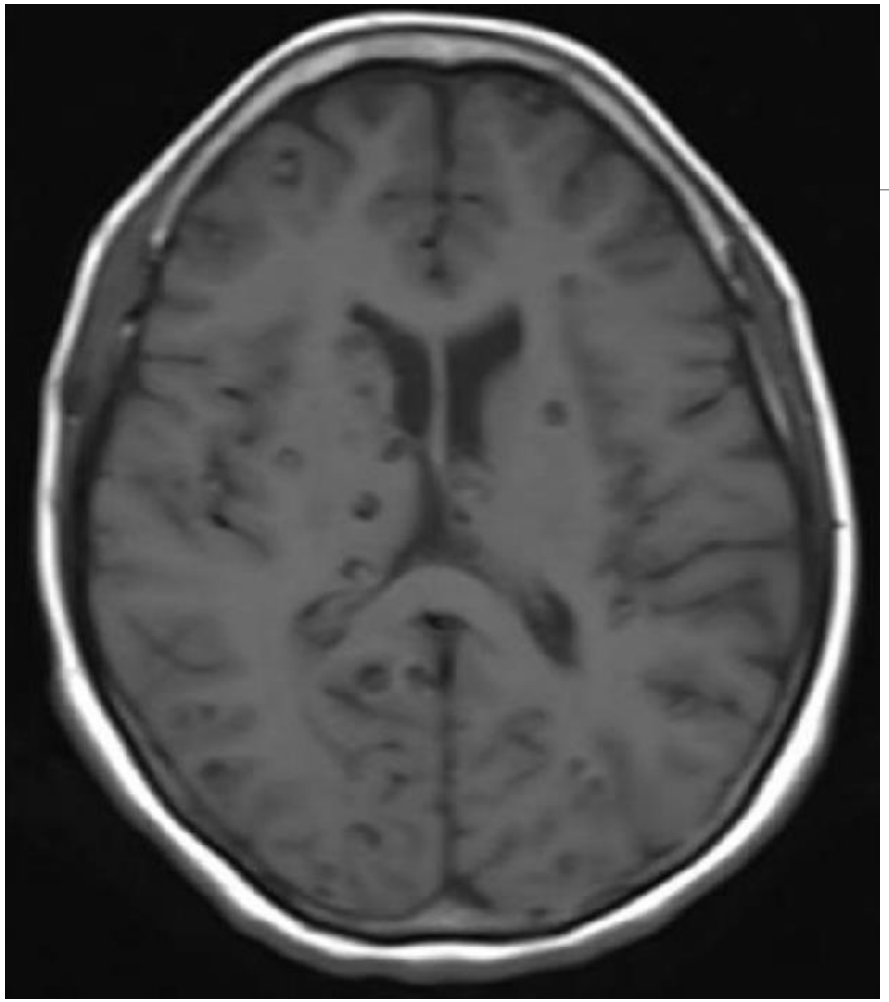
MD associated with tuberculosis

- **Mechanisms**
  - Space occupying lesion
  - Vascular (stroke-like)
  - Inflammation
- **Phenomenology**
  - Hemichorea
  - Unilateral parkinsonism
  - Others
- **Treatment**
  - Antituberculous therapy
  - Surgery (if amenable)
  - Steroids
  - Antituberculous therapy

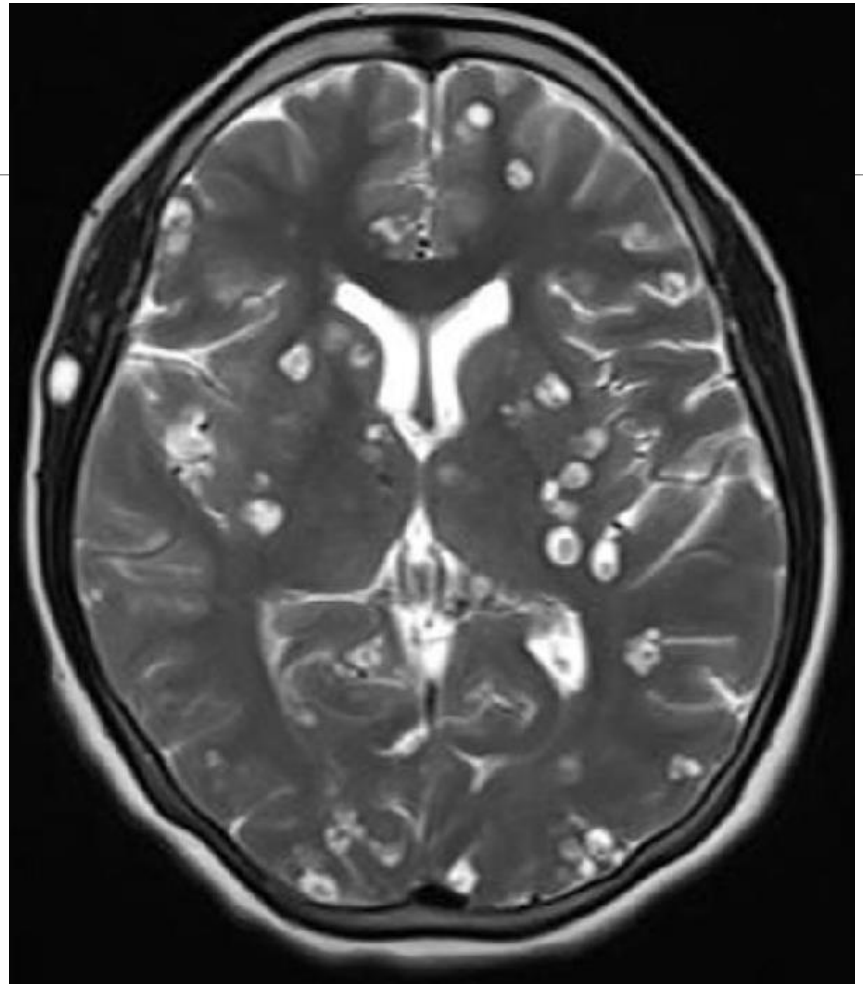
MD associated with neurocysticercosis

- Accidental ingestion of Taenia solium eggs
- Subacute onset typically
- Bilateral but often asymmetric
- Chorea and dystonia: closely aligned with pathology
- Treatment:
  - anthelmintic (albendazole)
  - May require steroid, surgery, symptomatic tx of the MD

Neurocysticercosis



T1 MRI



T2 MRI

Courtesy Radiopaedia

MRI findings in MD of infectious cause

- Abnormal in ~80%
- Signal changes in thalamus (~1/2)
  - Common location in cases with dystonia
- Signal changes in other parts of basal ganglia
- Signal changes in midbrain (~4%)

*Data based on few published case series (mainly from Asia)

Parainfectious (autoimmune) MD

Hyperkinetic or hypokinetic

Mechanisms

- Molecular mimicry (infectious agents v. neural agents
- Host susceptibility (HLA allelic differences)

Sydenham chorea

- Onset 8-9 years; mostly girls
- Autoimmune response to group A β-hemolytic streptococcal infection (often pharyngitis)
- Leading cause of paediatric chorea globally
- Isolated or with other acute rheumatic fever syndrome features (arthritis, carditis, skin rash)
- 4-8 weeks after GABHS

Sydenham chorea – clinical features

- Acute onset chorea (20% hemichorea onset, generalized in most)
- Chorea lasts 2-3 months then abates (may last up to 2 years)
- Motor impersistence, hypotonia, tics, abnormal EOMs
- Behavioral abnormalities (anxiety, OCD, depression, disruptive behavior)
- May recur (also in pregnancy – chorea gravidarum)

Sydenham Chorea – lab diagnosis

- **Laboratory diagnosis**
  - ↑ antistreptolysin O titer
  - ↑ antideoxyribonuclease B
  - Positive streptozyme
  - Throat culture for streptococcus pyogenes

- **MRI –** normal or signal changes in basal ganglia

Sydenham Chorea – treatment

- Antibiotics
- Valproic acid
- Neuroleptics
- Anti-depressant and anti-anxiety medications
- Immunotherapy – steroids, plasmapharesis, IVIG in severe cases

PANDAS

Paediatric Autoimmune Neuropsychiatric Disorder Associated with Streptococcal infection

- Sudden psychiatric onset
- Obsessive compulsive disorder ± tics, other motor abnormalities
- Inconsistent evidence of streptococcal infection or immune response
- ? Nonexistent → Paediatric Acute-onset Neuropsychiatric Syndrome (PANS)
- Symptomatic treatment

Other para-infectious MD

- Opsoclonus-myoclonus syndrome
  - Hep C, mycoplasma, dengue, influenza, HIV
- Dystonia (generalized, segmental; infantile bilat. striatal necrosis)
- Mixed: Anti-NMDA receptor encephalitis (post HSE); HIV
- Parkinsonism (post viral)
- Ataxia (post– varicella, enterovirus, EBV; mycoplasma)
- Infantile bilat. striatal necrosis post group A beta hemolytic strept. infxn
- **Treatment:** immunotherapy; symptomatic therapy

General approach

- High index of suspicion in acute/subacute-onset movement disorders
- **!!** Onset may be more insidious and associated infection may be remote
- **Clinical evaluation**: isolated MD, mixed MD, MD + other neurologic features, MD + other systemic features ± other neurologic features to determine the syndrome
- Additional diagnostic evaluation if indicated to explore aetiology further (blood labs, brain imaging, EEG, etc)
- **Treatment approach:**
  - typically combination of symptomatic, disease specific (infection-targeted) and immunomodulatory (if indicated)