Seizures in stroke, dementia and Parkinson’s patients
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Post-stroke seizures

- Stroke and stroke surviving is very prevalent in Africa (0.1% - >0.3%) and increasing (5-10% per 5 years).
- Stroke is the most identifiable cause of epilepsy in people above the age of 35 years.
- In elderly, stroke is the cause of seizures in > 50% of cases in which a cause can be identified.
- Seizures occur in about 9% of patients after stroke, recurrent seizures in 2-3% of patients.
- Seizures occur more commonly after hemorrhagic than ischemic stroke.

Akinyemi et al 2021; Lin et al, 2021; Pitkanen et al, 2017; Zöllner et al, 2021

Post-stroke seizures

- Cortical strokes are more likely to cause post-stroke seizures.
- Stroke involving multiple lobes are more likely to cause seizures than stroke involving one single lobe.
- Involvement of parietal and temporal lobe and the caudate nucleus is associated with a higher risk of seizures.
- Hemorrhagic stroke involving the cortex leads to seizures in 54%, in basal ganglia in 39% and in thalamus none.
Early post-stroke seizures
- Most seizures occur within 24 hours of stroke onset (early onset); late onset post-stroke seizures > 1 week post-stroke
- Causative mechanisms: accumulation of intracellular calcium and sodium; glutamate excitotoxicity, local ischemia (hippocampus), global hypoperfusion, metabolic disturbances

Late post-stroke seizures
- Persistent changes in neuronal excitability
- 90% of patients with ischemic stroke and late onset seizures may develop epilepsy compared to 35% with early onset seizures.
- Higher risk in “late early” seizures, larger stroke volumes and with more deficits and multiple early seizures.
- Figures are similar in patients with hemorrhagic stroke: 93% versus 29%.
- Gliotic scarring is often seen in late-onset seizures.
- More recent neuroimaging biomarkers: diffusion-based estimation of blood-brain barrier integrity and glutamate excitotoxicity

Semiology of post-stroke seizures
- Most post-stroke seizures are focal aware seizures (61%), only 28% are focal to bilateral tonic-clonic seizures.
- Early onset seizures are more likely to be focal; late-onset seizures are more likely to be focal to bilateral tonic-clonic seizures.
- 9% of patients develop status epilepticus.
Therapy post-stroke seizures

- Usually, no prophylactic antiseizure medication (ASM) therapy is needed in stroke patients without seizures.
- When seizures occur, ASM will be prescribed but long-term ASM are not needed in most patients with early post-stroke seizures.
- ASM are needed for patients with late-onset seizures.

Monotherapy is sufficient, 80% of patients achieve good seizure control.

LTG, LEV are preferred, when available.

While efficacious, older ASM are not preferred: hyponatremia, osteoporosis, drug interactions, cognitive side effects!
Therapy post-stroke seizures

- Post-stroke seizures necessitate individual risk assessment, accounting for effectiveness of ASM.
- The use of i.v. thrombolysis and mechanical thrombectomy does not increase the risk of seizures.

Seizures in Alzheimer’s disease

- AD is most common cause of memory impairment in the elderly.
- Ageing is a risk factor for both developing AD and seizures.
- Fluctuations of cognitive functions could be only manifestation of seizures in patients with AD, diagnosis may be challenging.
- Proposed mechanisms: neuronal loss (HC), alterations in neurotransmitters, amyloid plaques, concomitant strokes.

Seizures in Alzheimer’s disease

- Co-morbidity of epilepsy and AD: associated with mutations in the amyloid precursor protein (APP) amyloid beta (Ab) gene pathway.
- ASM could deteriorate the cognitive function or have other undesirable effects on patient’s other medical conditions.
Seizure types and treatment of seizures in AD

• Seizures most often occur in early stage or in the late stage of AD
• Generalized tonic-clonic seizures, focal seizures, myoclonic seizures and transient epileptic amnesia
• ASM indications: progressive memory deficit in the presence of overt seizures or epileptiform EEG discharges
• ASM without interactions and with renal clearance are preferred: LTG, LEV
  “Start low, go slow!”

Interaction between AD, stroke and epilepsy

Do seizures cause dementia?

• Elderly patients (55-70y) with chronic epilepsy (>20y) screened for cognitive deterioration compared to expected pre-morbid IQ and co-morbid disorders (cardiovascular, cerebrovascular and post-traumatic)
• Decreased cognitive reserve due to older age, low premorbid IQ and education level and later age at seizure onset : “dual hit model”
• “Accelerated cognitive aging”

References: Unpublished data, Vossel et al, 2017

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Seizures and Parkinson’s disease and MD

- Prevalence of PD in population older than 65y >1%, fastest growing neurological condition.
- Classical teaching: Parkinson disease (PD) and epilepsy are mutually exclusive!
- More recent findings: PD patients have 1.7 higher risk of developing epilepsy, risk is higher in co-morbid dementia and stroke.
- The risk of developing PD is 3 times higher in patients with epilepsy after adolescence.
- Patients with PD are at higher risk of developing status epilepticus than age-matched controls with chronic epilepsy.

Seizures and movement disorders (MD)

- Involvement of basal ganglia, that may be functionally altered to sustain ongoing seizure activity.
- Different movement disorders can be accompanied by seizures.

Seizures and movement disorders (MD)

- Wilson disease: (sub)cortical WM hyperintense lesions
- Fahr’s disease: calcium deposition, hyperintense subcortex and basal ganglia
- Pantothenate kinase-associated neurodegeneration (PKAN) due to PANK2 mutation: “eye of the tiger” in GP
- Beta-propeller protein-associated neurodegeneration: hypointensities in substantia nigra
- Creutzfeld Jacob disease: hyperintense cortex and caudate and lentiform nucleus
Seizures and MD

• Overlap of clinical semiology
• Hypokinetic and hyperkinetic seizures versus movement disorders
• Nocturnal frontal seizures versus episodic dystonia
• Dystonic posturing during temporal lobe focal seizures versus dystonia in the context of movement disorders

Seizures and MD, therapeutic aspects

• High frequency DBS of the subthalamic nucleus suppresses experimental absence seizures.
• Dopaminergic drugs protect against seizures both in animals and men.
• Zonisamide (ASM with dopaminergic effects) decreases motor fluctuations in PD.
• ASM such as VPA and LTG may trigger movement disorders.
• Antipsychotic drugs diminish dopaminergic transmission and increase likelihood of seizures.
• Further research ongoing.