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

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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 19% and in thalamus none.

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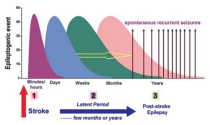
Early post-stroke seizures

- 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



Reddy DS, et al. J or Neurosci Res 2017;95:1000-16

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Late post-stroke seizures

- Persistent changes in neuronal excitability
- 90% of patients with ischemic stroke and late onset seizures may develop epilepsy as 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

Lin et al, 2021; Pitkanen et al, 2017; Zollner et al, 2021

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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.

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Therapy post-stroke seizures

Review | Open Access | Published: 06 December 2021

Seizures and epilepsy in patients with ischaemic stroke

Johann Philipp Zöllner, Friedhelm C. Schmitt, Felix Rosenow, Konstantin Kohlhase, Alexander Seiler, Adam Strzelczyk & Hermann Stefan

Neurological Research and Practice 3, Article number: 63 (2021) | Cite this article

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

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Therapy post-stroke seizures

Author	Study design	Participants (n)	Age (years)	Medication (mg)	Period	Seizure recurrence	Tolerability	Limitations
Alvarez-Sabin et al. [38]	Prospective Observational	48 ischaemic 23 haemorrhagic	63.9	GBP 900–1800 mg	30 months	18%	Adverse events 38%; discontinued 3%	SN, NR, NP
Gilad et al. [28]	Prospective Randomised	64 ischaemic	LTG 67.2 CBZ 67.7	LTG 25–200 mg CBZ 100–600 mg	12 months	LTG 28% CBZ 56%	Discontinued LTG 3%, CBZ 31%	SN, NP, NDB
Kutlu et al. [116]	Prospective Observational	34 ischaemic	69.8	LEV 1000–2000 mg	17.7 months	18%	Discontinued 21%; stopped 3%	SN, NR, NP
Belcastro et al. [30]	Prospective Observational	35 ischaemic	71.9	LEV 1000–2000 mg	18 months	9%	Discontinued 11%	SN, NR, NP
Consoli et al. [32]	Prospective Randomised	79 ischaemic 27 haemorrhagic	LEV 74.1 CBZ 54	LEV 52 CBZ 54	13,5 months	LEV 6% CBZ 15%	Discontinued LEV 33%, CBZ 39%	SN, NP, NDB
Tanaka and Ihara [117]	Retrospective Observational	69 ischaemic 43 haemorrhagic	72.3	23 VPA, 22 PHT 15 CBZ	12 months	VPA 48% PHT 18% CBZ 13%	–	SN, mono- and polytherapy
Huang et al. [118]	Retrospective Observational	1729 ischaemic 1893 haemorrhagic	60.3	PHT 2507 VPA 712 CBZ 157 Newer ASM 246	100 person - months	PHT 1.05% (ER visits) VPA 0.7% CBZ 0.4% Newer ASM 0.38%	–	Seizure in first 3 months excluded
Sales et al. [39]	Retrospective Observational	76 PSE 1590 EPI*	PSE 63 EPI 61.4	ESL/PSE 887 ESL/EPI 983	12 months	51.4% 68.3%	Adverse events 36% versus 35.8%	Multicentric, differences between cohorts

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Therapy post-stroke seizures

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- 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!

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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.

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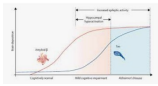
Seizures in Alzheimer's disease

- 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

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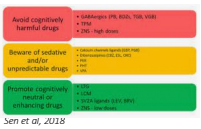
Seizures in Alzheimer's disease

- 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.



Sen et al, 2018

JOURNAL ARTICLE
Cognition and dementia in older patients with epilepsy
Arjune Sen, Valentina Capelli, Masud Husain · Author Notes
Brain, Volume 141, Issue 6, June 2018, Pages 1592–1608,
https://doi.org/10.1093/brain/awy022
Published: 28 February 2018 **Article history**

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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!"

Vossel et al, 2017

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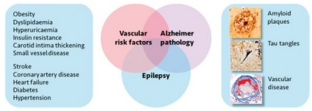
Interaction between AD, stroke and epilepsy



The intersections of Alzheimer's disease, epilepsy and vascular disease. Several overlapping pathologies (*right*) can contribute to development of late-onset epilepsy as well as the development of dementia. In particular, vascular risk factors (*left*) are common in people with epilepsy. These may represent modifiable risk factors for both the development of dementia and of epileptogenesis.

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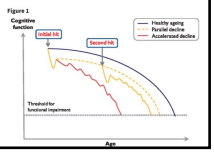
Do seizures cause dementia?

- Elderly patients (55-70y) with chronic epilepsy (>20y) screened for cognitive deterioration compared to expected pre-morbid ID 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"

Breuer, Boon & Aldenkamp, 2018



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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.

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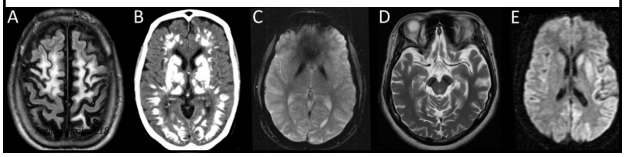
Seizures and movement disorders (MD)

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



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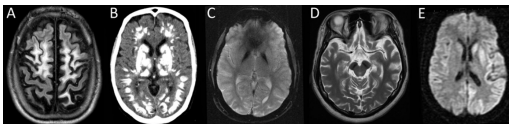
Seizures and movement disorders (MD)



- **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 nuclei

Freitas et al, 2018

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Seizures and MD

- Overlap of clincial 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

Freitas et al, 2018

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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 movements disorders.
- Antipsychotic drugs diminish dopaminergic transmission and increase likelihood of seizures.
- Further research ongoing…

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