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Epilepsy in Elderly:

Clinical Features and Special Considerations

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Definition of “Epilepsy in Elderly”

- Age > 65 years old
- 2 groups
  1. New late-onset epilepsy (LOE)
  2. Young-onset patients with long history of epilepsy

SPECIAL REPORT

Epilepsia®

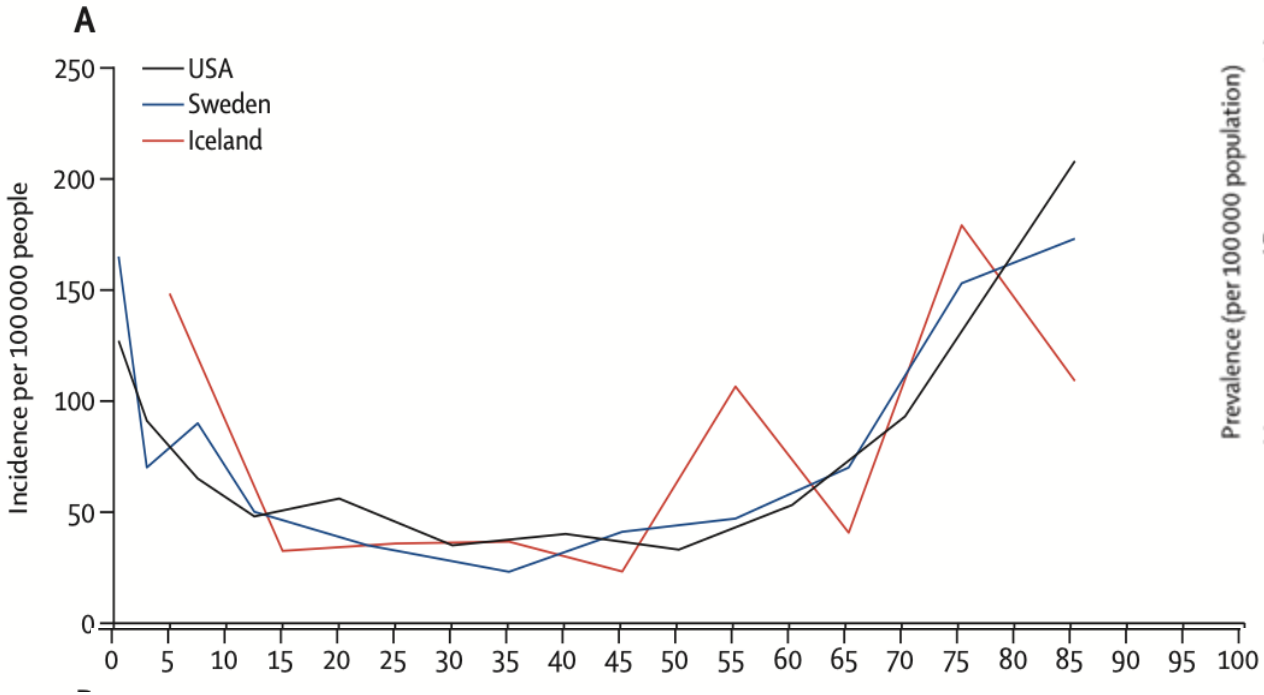
The epidemiology of epilepsy in older adults: A narrative review by the ILAE Task Force on Epilepsy in the Elderly

- The incidence of epilepsy is very high among adults older than 60 years.
- Reported rates vary widely around the world because of etiological and demographic factors.
- More data are needed from low-income region.

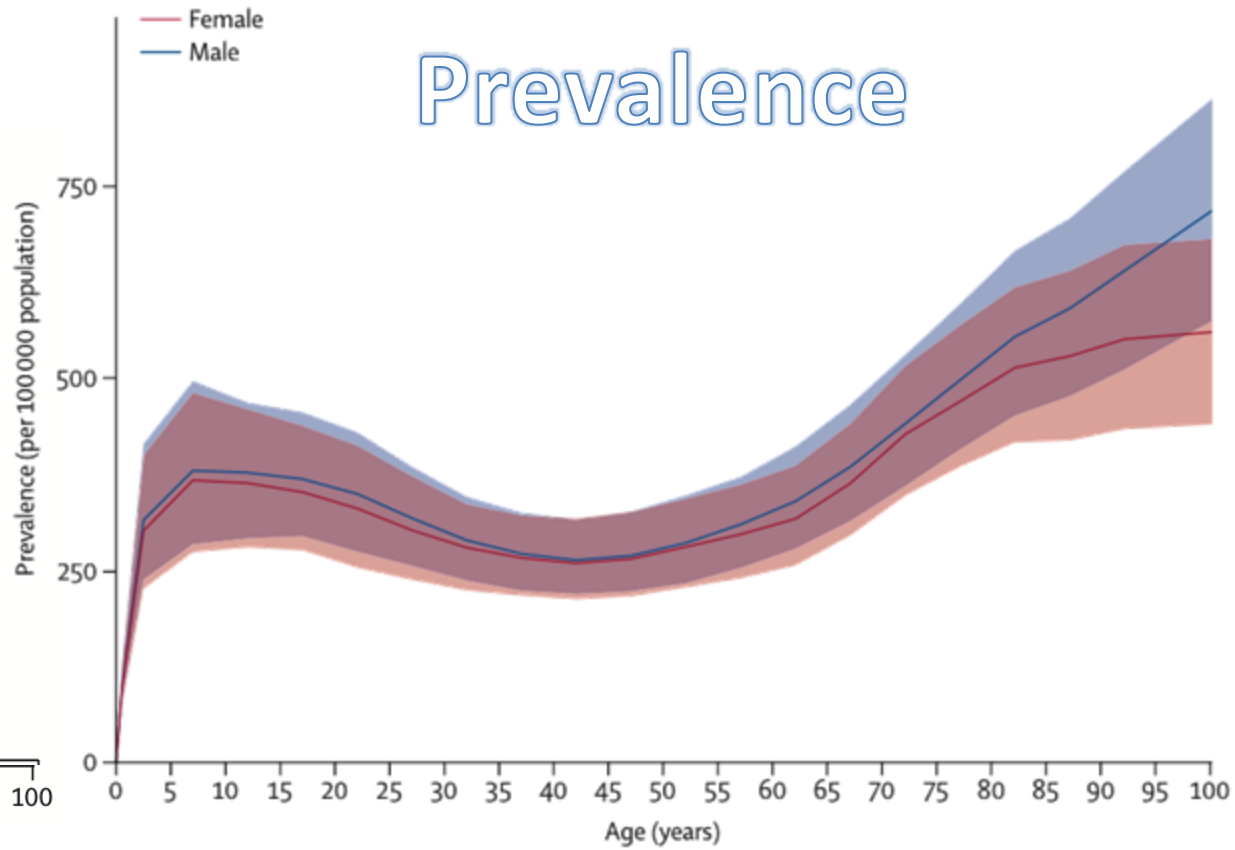
Beghi E, et al. Epilepsia. 2023;64:586–601.

Incidence and Prevalence

Incidence



Prevalence



"Bimodal Peak"

Sen A, et al. Lancet 2020; 395: 735–48

Causes & Risk Factors in LOE

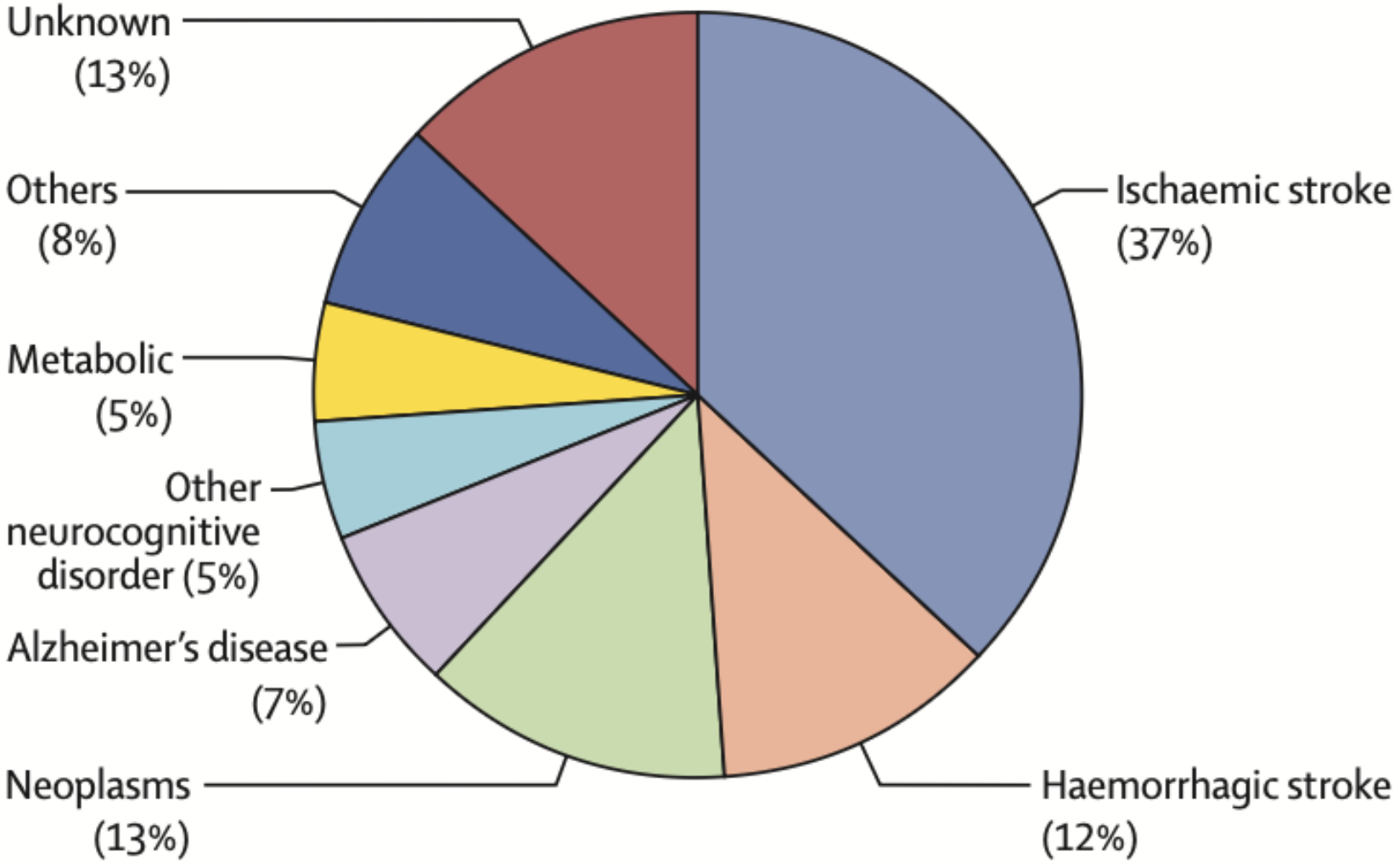
Common

- Acute symptomatic seizures
- Provoked seizures
- CNS infections
- Toxic, metabolics
- Traumatic brain injuries
- Vascular
- Tumor
- Dementia: Alzheimer's disease

Rare

New-onset Genetic-generalized epilepsy (GGE)

Causes of new-onset epilepsy in elderly



Sen A, et al. Lancet 2020; 395: 735–48

Population-based study of seizure disorders after cerebral infarction

E.L. So, MD; J.F. Annegers, PhD; W.A. Hauser, MD; P.C. O'Brien, PhD; and J.P. Whisnant, MD

***Table 2** SMR of developing initial late seizure and epilepsy in the whole cohort by time period after cerebral infarction*

Time after cerebral infarction	Observed cases	Expected cases*	SMR	95% CI
Less than 1 yr				
Initial late seizure	11	0.5	22.9	11.5–41.0
Epilepsy	6	0.3	17.5	6.4–38.0
1–4 yr				
Initial late seizure	12	1.1	11.1	5.8–19.5
Epilepsy	6	0.8	7.7	2.8–16.6
After 4 yr				
Initial late seizure	4	1.9	2.1	0.6–5.3
Epilepsy	6	1.4	4.2	1.5–9.1
Overall				
Initial late seizure	27	4.2	6.4	4.2–9.3
Epilepsy	18	3.0	5.9	3.5–9.4

* Number of expected cases rounded to nearest tenths.

SMR = Standardized morbidity ratio.

Compared with the population in the community, the risk during the first year

- 23 times higher for initial late seizures
- 17 times higher for epilepsy

So E L, et al. NEUROLOGY 1996;46:350-355

JAMA Neurology | Original Investigation

Association Between Midlife Risk Factors and Late-Onset Epilepsy
Results From the Atherosclerosis Risk in Communities Study

Emily L. Johnson, MD; Gregory L. Krauss, MD; Alexandra K. Lee, PhD, MSPH; Andrea L. C. Schneider, MD, PhD; Jennifer L. Dearborn, MD, MPH; Anna M. Kucharska-Newton, PhD, MPH; Juebin Huang, MD; Alvaro Alonso, MD, PhD; Rebecca F. Gottesman, MD, PhD

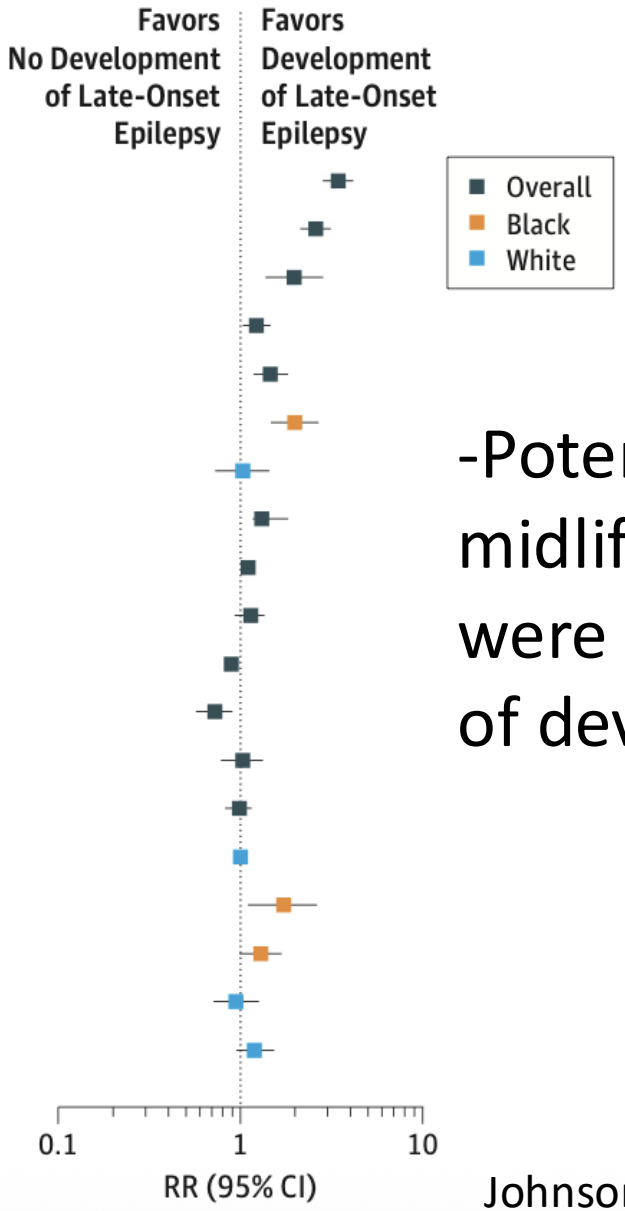
The Atherosclerosis Risk in Communities (ARIC) study is a prospective cohort study of 15792 participants followed up since 1987 to 1989.
Data were analyzed between April 2017 and May 2018.

Johnson E L, et al. JAMA Neurol.2018;75(11):1375-1382

Midlife Risk Factors for LOE

Risk Factor	Race/ Ethnicity	HR (95% CI)
Stroke	All	3.47 (2.85-4.23)
Dementia	All	2.68 (2.19-3.28)
APOE ε4: 2 alleles	All	1.93 (1.32-2.81)
1 allele	All	1.22 (1.02-1.46)
Diabetes[a]	All	1.43 (1.14-1.80)
	Black	2.04 (1.47-2.84)
	White	1.04 (0.74-1.45)
Hypertension	All	1.26 (1.05-1.51)
Smoking	All	1.09 (1.01-1.17)
Education (≥HS)	All	1.11 (0.91-1.36)
Exercise	All	0.89 (0.81-0.97)
Alcohol use: 1 drink/d	All	0.70 (0.56-0.88)
≥2/d	All	1.00 (0.76-1.31)
Male	All	0.96 (0.81-1.15)
Field center-race	NC-white	1 [Reference]
	NC-black	1.75 (1.12-2.75)
	MS-white	1.41 (1.07-1.85)
	MN-black	1.07 (0.81-1.41)
	MD-white	1.33 (1.04-1.70)

[a] Interaction with race, $P < .05$



-Potentially modifiable risk factors in midlife and the APOEε4 genotype were positively associated with risk of developing LOE.

Johnson E L, et al. JAMA Neurol.2018;75(11):1375-1382

Challenges in DIAGNOSIS

- History is THE MOST IMPORTANT.
- 30% of epilepsy in elderly are MISDIAGNOSED at first evaluation
- History-taking from patient can be difficult
  - Language, cognitive impairment.
- History from reliable caregiver/ witness is crucial.
  - Initial symptoms, pallor, cyanosis, abnormal movements, tongue biting, urinary incontinence, and impaired conscious level.
  - Postictal state: confusion, headache, weakness

Seizure types in elderly

Seizure type	%
Focal aware motor	5.3
Focal impaired awareness non-motor	25.7
Focal impaired awareness motor	26.5
Bilateral tonic-clonic seizures	38.1
Absence	4.4

Referral sourse	%
Emergency department	18.6
General practitioner	41.6
Internal (hospital)	30.1
other	9.7

Green S F, et al. Journal of the Neurological Sciences 429 (2021) 118065

Diagnosis

- Diagnosis of epilepsy in elderly is more challenging.
  - Atypical presentation
  - More extraTLE, diverse semiology, less convulsion

Presentation

- Less specific esp in <u>complex partial seizure</u> **without** secondary GTC
  - Memory lapse
  - Episodes of confusion
  - Periods of inattention
  - Apparent syncope

Misdiagnosis are **common**.

Atypical presentation

- Aura: are not common and may have nonspecific symptom e.g. dizziness
- Postictal symptoms:
  - Can stay longer
  - Todd's paresis → days
  - Disorientation, hyperactivity, wandering, and incontinence might up to 1 week

Seizure characters	Young adults	Elderly
Aura	66-76%	**33-54%**
Ictal: subtle, brief confusion	0%	**18%**
Multiple phases to evolution	67%	**24%**
GTC	80%	**56%**
Postictal sleepiness or unresponsiveness	45%	**67%**

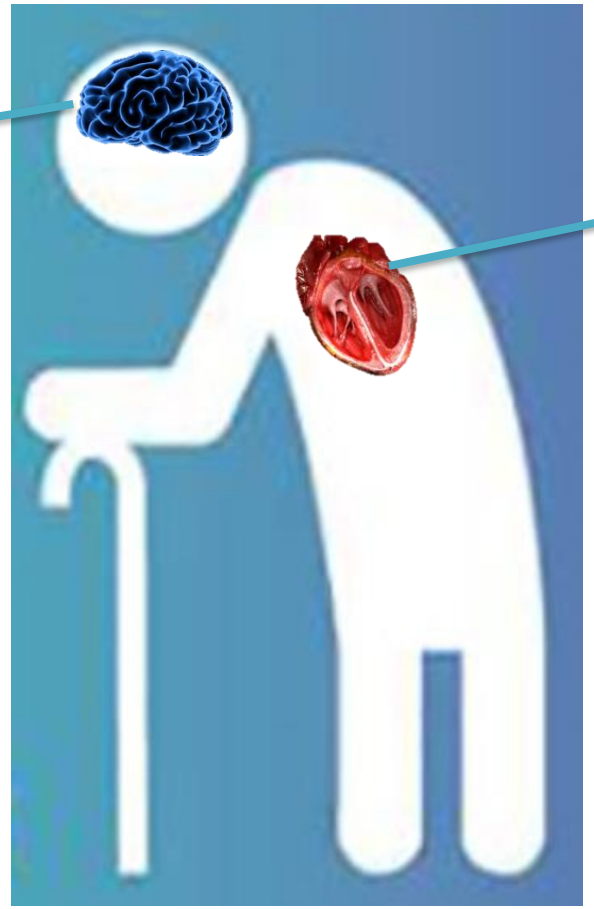
Clinical clues for seizure

- Confusion, behavioral change
- Unresponsiveness not associated with loss of postural control
- Loss of awareness
- Twitching, involuntary movement
- Sensory disturbance of a limb w/o LOC
- Recurrent sleep disorder episodes
- Frequent falls with no recollection

Seizure mimics in elderly

Neurological

- Transient global amnesia
- Transient ischemic attack
- Migraine
- Narcolepsy



Cardiovascular

- Vasovagal syncope
- Orthostatic hypotension
- Cardiac arrhythmia

Historical Criteria That Distinguish Syncope From Seizures

Question	Points (If Yes)
At times do you wake with a cut tongue after your spells?	2
At times do you have a sense of deja vu or jamais vu before your spells?	1
At times is emotional stress associated with losing consciousness?	1
Has anyone ever noted your head turning during a spell?	1
Has anyone ever noted that you are unresponsive, have unusual posturing or have jerking limbs during your spells or have no memory of your spells afterwards? *(Score as yes for any positive response)*	1
Has anyone ever noted that you are confused after a spell?	1
Have you ever had lightheaded spells?	−2
At times do you sweat before your spells?	−2
Is prolonged sitting or standing associated with your spells?	−2

The patient has seizures if the point score is ≥1, and syncope if the point score is <1.

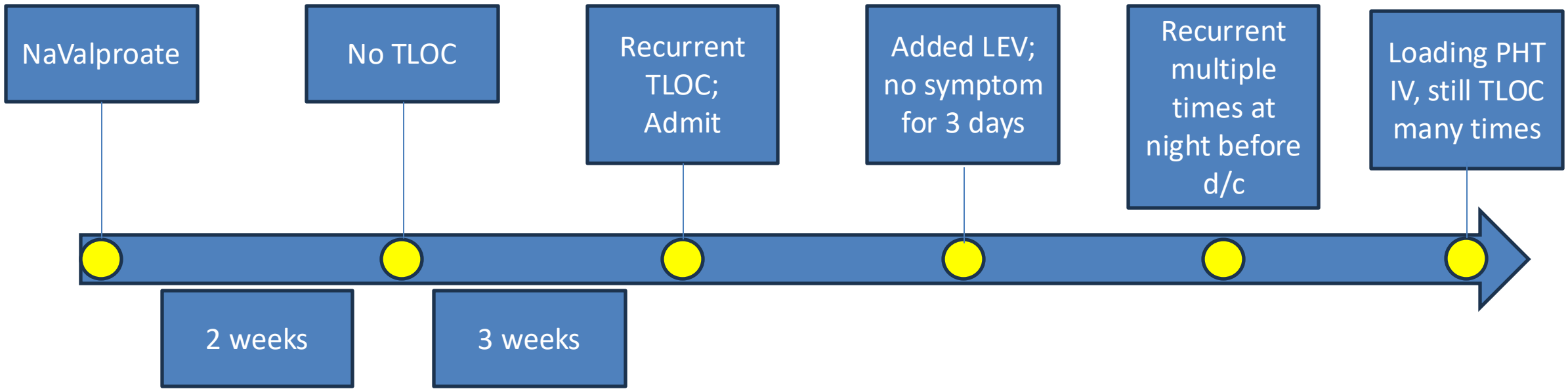
Sens 94%
Spec 94%

Sheldon R, et al. J Am Coll Cardiol 2002;40:142–8

A 72-year-old female

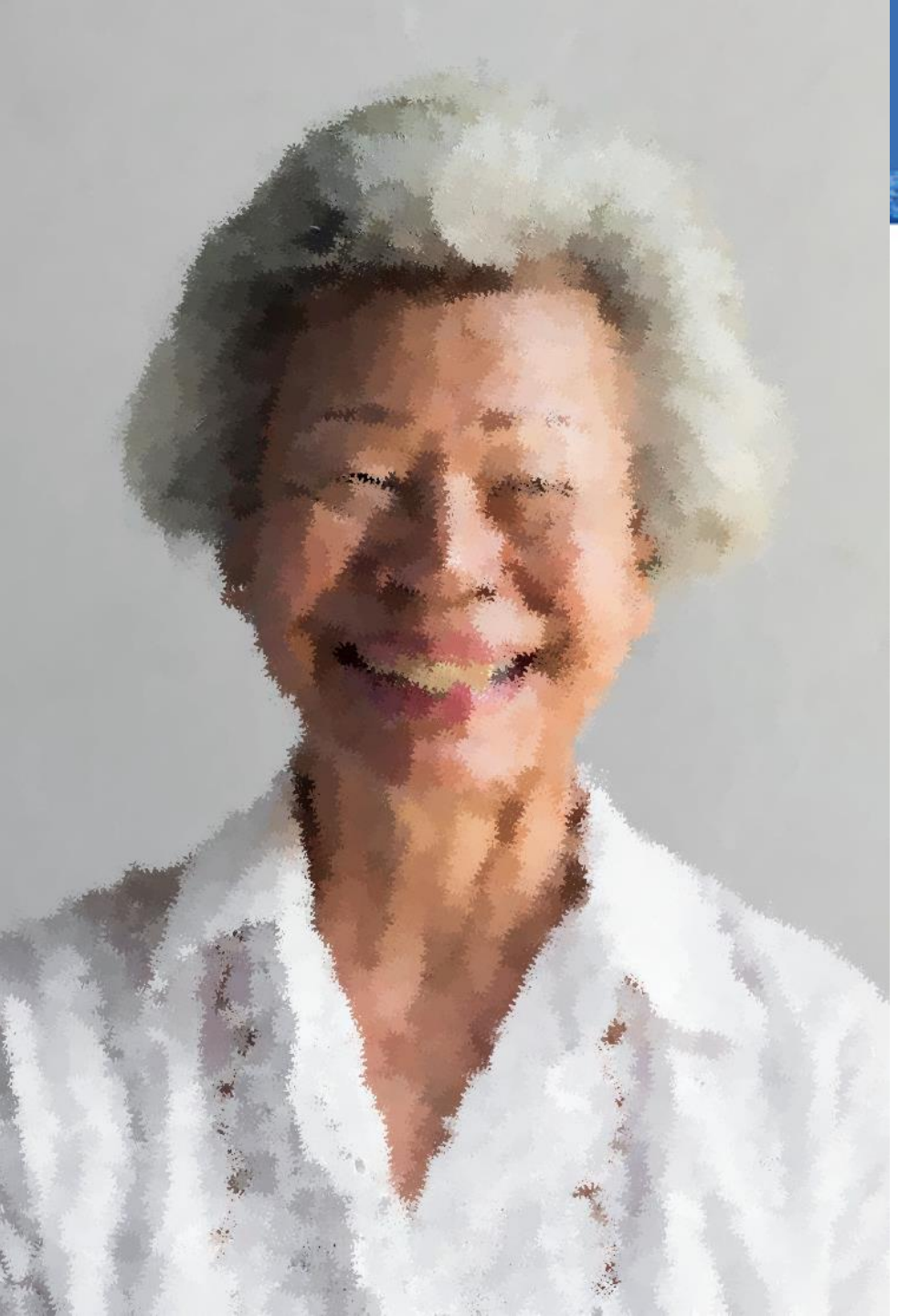
- Recurrent transient loss of consciousness for >10 times in 4 months
- Description
  - ตาลอย นิ่งไม่ตอบสนอง แล้วค่อยๆเอนตัวล้มลง มักเป็นตอนนั่งอยู่ หน้าซีดๆ
  - หมดสติ 1 นาที/ครั้ง
  - มีวิดีโอคลิปหลายคลิป
- Seen by cardiologist; work up Echo, Holter → negative for cardiac syncope

- CT brain; unremarkable
- EEG; intermittent theta slowing right temporal
- Dx: possible focal impaired consciousness with observable manifestation



- V/S: HR 30-40 bpm by pulse oximeter
- Monitor EKG; HR 30-40 bpm with pause → 3rd degree AV block

- Dx: Likely syncope
- **Phenytoin can unmask or exacerbate underlying cardiac issues, potentially leading to syncope (fainting).**



A 76-year-old female

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- UD: CAD, HT, DLP, AF, old ischemic stroke mRS=0
- On dabigatran 110 mg bid
- Presented with blank staring, unresponsive for few minutes
- PE at ER showed mild right sided weakness and fully recovery within 30 min → Dx: TIA
- Admit stroke unit

A 76-year-old right-handed female

- Dx: r/o TIA
- Rx: ↑ Dabigatran 150 mg bid
- After discharge, still having the similar events for few times within 2 weeks
- Per phone video recorded:
  - Sitting, eye opening but did not respond, looking around.
  - No stiffening, no jerky movement.

- Final Dx: post-stroke epilepsy

Investigation

- History, witness, video clips
- Basic blood work
- Brain imaging
- CSF; infection, inflammation, malignancy
- Autoimmune:
  - LGI-1, CASPR-2, paraneoplastic Ab
  - New-onset frequent seizures, cognitive impairment, psychiatric manifestations
- Repeat investigations if diagnosis uncertainty

EEG & MRI finding

- EEG; routine, ambulatory, long-term
- Epileptiform discharges → 29.2%
- Treatment was changed in only small number of patients.

MRI finding	n
Infarct	27
Small vessel disease	37
Mild	23
Moderate	13
Severe	1
White matter hyperintensities	4
Microhaemorrhage	2
Global atrophy	14
Mild	7
Moderate	6
Severe	1
Regional atrophy	9
Cystic changes	5
Tumour	10
Gliosis	4
Arteriovenous malformation	3
Other	5
Normal scan	5

Green S F, et al. Journal of the Neurological Sciences 429 (2021) 118065

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Contents lists available at ScienceDirect

Seizure: European Journal of Epilepsy

journal homepage: www.elsevier.com/locate/seizure

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Review

EEG and semiology in the elderly: A systematic review☆

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[b] Department of Clinical Neurophysiology, Aarhus University Hospital*, and Department of Clinical Medicine, Aarhus University, Palle Juul-Jensens Boulevard 165, 8200 Aarhus N, Denmark

EEG

- Normal EEG; 1-52%
- Slow Focal; 4-85%
- Slow Generalized; 11-89%
- IED Focal; 7-93%
- IED Generalized; 1-14%

Semiology

- Less motor symptom
- Non-motor
  - Unresponsiveness
  - Confusion
  - Language problem

M.L. Pirgit and S. Beniczky. Seizure: European Journal of Epilepsy 128 (2025) 90–121

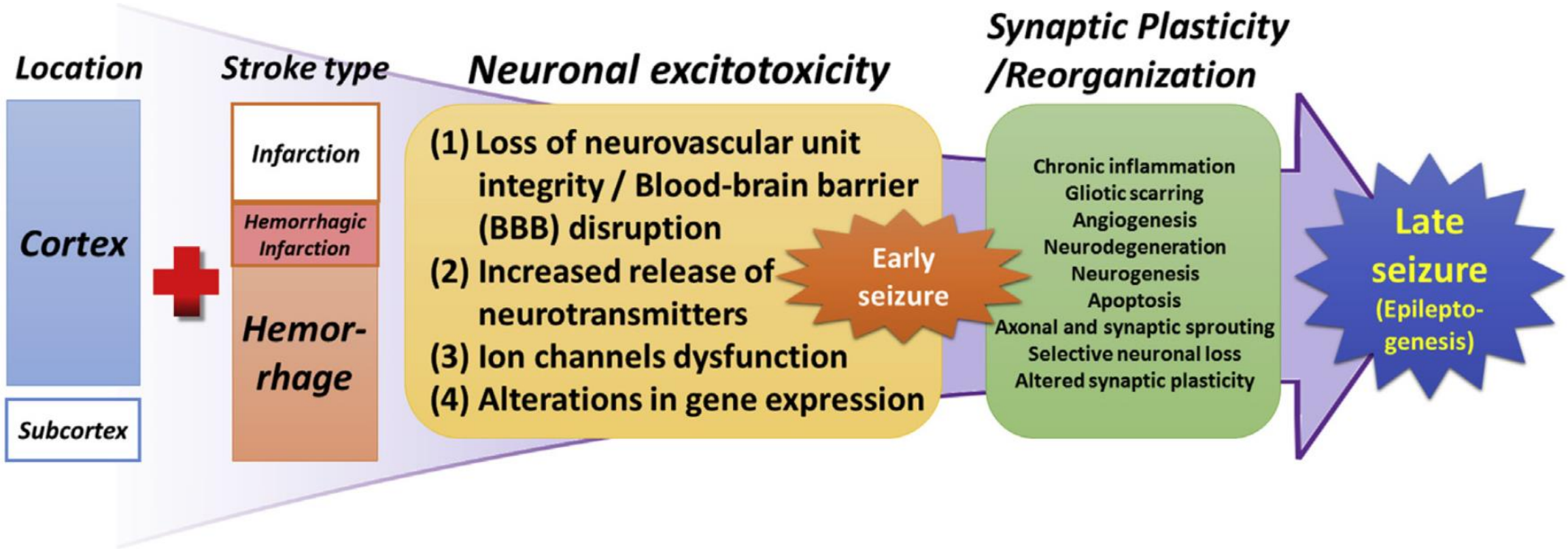
Specific epilepsy syndrome in elderly

- Poststroke epilepsy
- Dementia-associated epilepsy
- Transient epileptic amnesia
- Antibody-mediated epilepsy

Post-stroke seizure (PSS) vs Epilepsy (PSE)

- Post-stroke seizure
- Seizures that occur after having stroke without previous history of epilepsy
- Classification by time of onset → 1-2 weeks
  - Early (<1-2wks) vs late (>1-2wks) seizures

- Not all post-stroke seizures → post-stroke epilepsy (PSE)
  - Early onset → thought to be provoked



T. Tanaka, M. Ihara / Neurochemistry International 107 (2017) 219-228

Stroke
Journal of the American Heart Association
American Heart Association | American Stroke Association

The CAVE Score for Predicting Late Seizures After Intracerebral Hemorrhage

Elena Haapaniemi, Daniel Strbian, Costanza Rossi, Jukka Putaala, Tuulia Sipi, Satu Mustanoja, Tiina Sairanen, Sami Curtze, Jarno Satopää, Reina Roivainen, Markku Kaste, Charlotte Cordonnier, Turgut Tatlisumak and Atte Meretoja

Stroke. 2014;45:1971-1976; originally published online May 29, 2014;
doi: 10.1161/STROKEAHA.114.004686
Stroke is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231

Print ISSN: 0039-2499. Online ISSN: 1524-4628

C: cortical
A: age < 65
V: vol > 10ml
E: sz in 7d

Late onset SZ (9.2%)

- At 1-5 yrs →
- 7.1%, 10.0%, 10.2%, 11.0%, and 11.8%

CAVE	Risk of LS
C: cortical involvement (1 point)	0 point: 0.6%
A: age <65 years (1 point)	1 point: 3.6%
V: volume >10 mL (1 point)	2 points: 9.8%
E: early seizure (1 point)	3 points: 34.8%
	4 points: 46.2%

Haapaniemi E, et al. Stroke. 2014;45:1971-1976

Prediction of late seizures after ischaemic stroke with a novel prognostic model (the SeLECT score): a multivariable prediction model development and validation study

Marian Galovic, Nico Döhler, Barbara Erdélyi-Canavese, Ansgar Felbecker, Philip Siebel, Julian Conrad, Stefan Evers, Michael Winklehner, Tim J von Oertzen, Hans-Peter Haring, Anna Serafini, Giorgia Gregoraci, Mariarosaria Valente, Francesco Janes, Gian Luigi Gigli, Mark R Keezer, John S Duncan, Josemir W Sander, Matthias J Koepp, Barbara Tettenborn

	SeLECT score (points)
(Se) Severity of stroke	
NIHSS ≤3	0
NIHSS 4–10	1
NIHSS ≥11	2
(L) Large-artery atherosclerosis	
No	0
Yes	1
(E) Early seizure (≤7 days)	
No	0
Yes	3
(C) Cortical involvement	
No	0
Yes	2
(T) Territory of MCA	
No	0
Yes	1

SeLECT	RISK AT 1YR	RISK AT 5YR
0	0.7%	1.3%
1	1%	2%
2	2%	4%
3	4%	6%
4	6%	11%
5	11%	18%
6	18%	29%
7	28%	45%
8	44%	65%
9	63%	83%

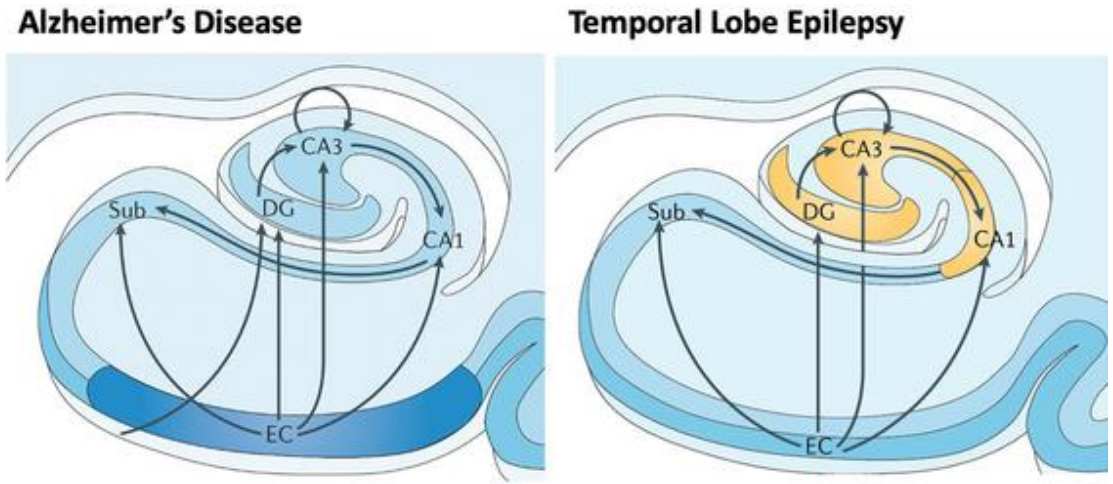
Galovic M, et al. Lancet Neurol 2018; 17: 143–52

Specific epilepsy syndrome in elderly

- Poststroke epilepsy
- Dementia-associated epilepsy
- Transient epileptic amnesia
- Antibody-mediated epilepsy

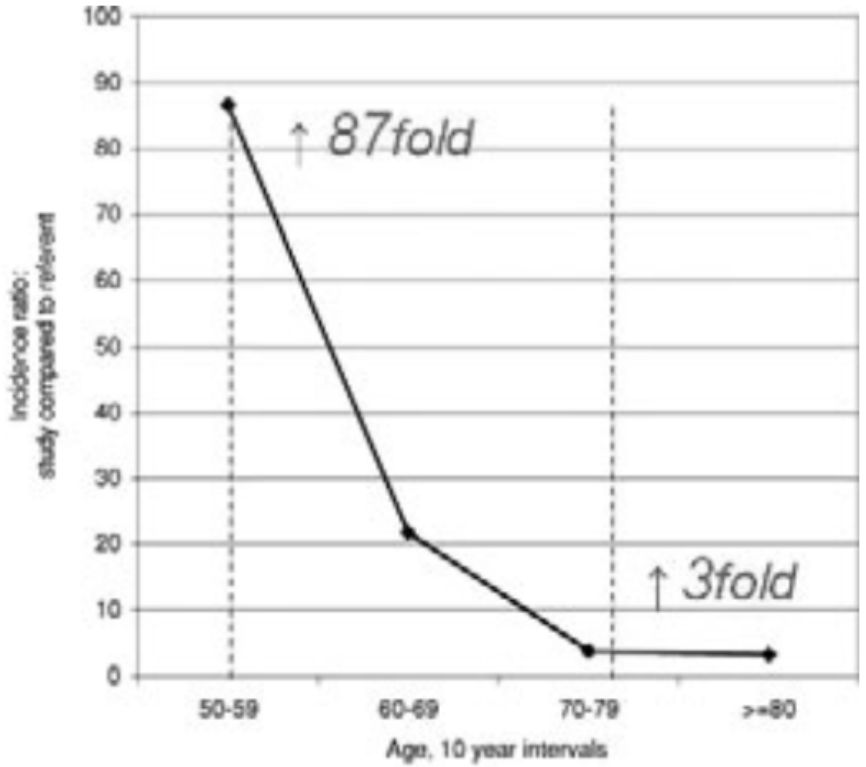
Dementia-associated epilepsy

- All dementia types, esp Alzheimer's disease → seizure



A perfect storm: Converging paths of epilepsy and Alzheimer's dementia intersect in the hippocampal formation

Jeffrey Noebels

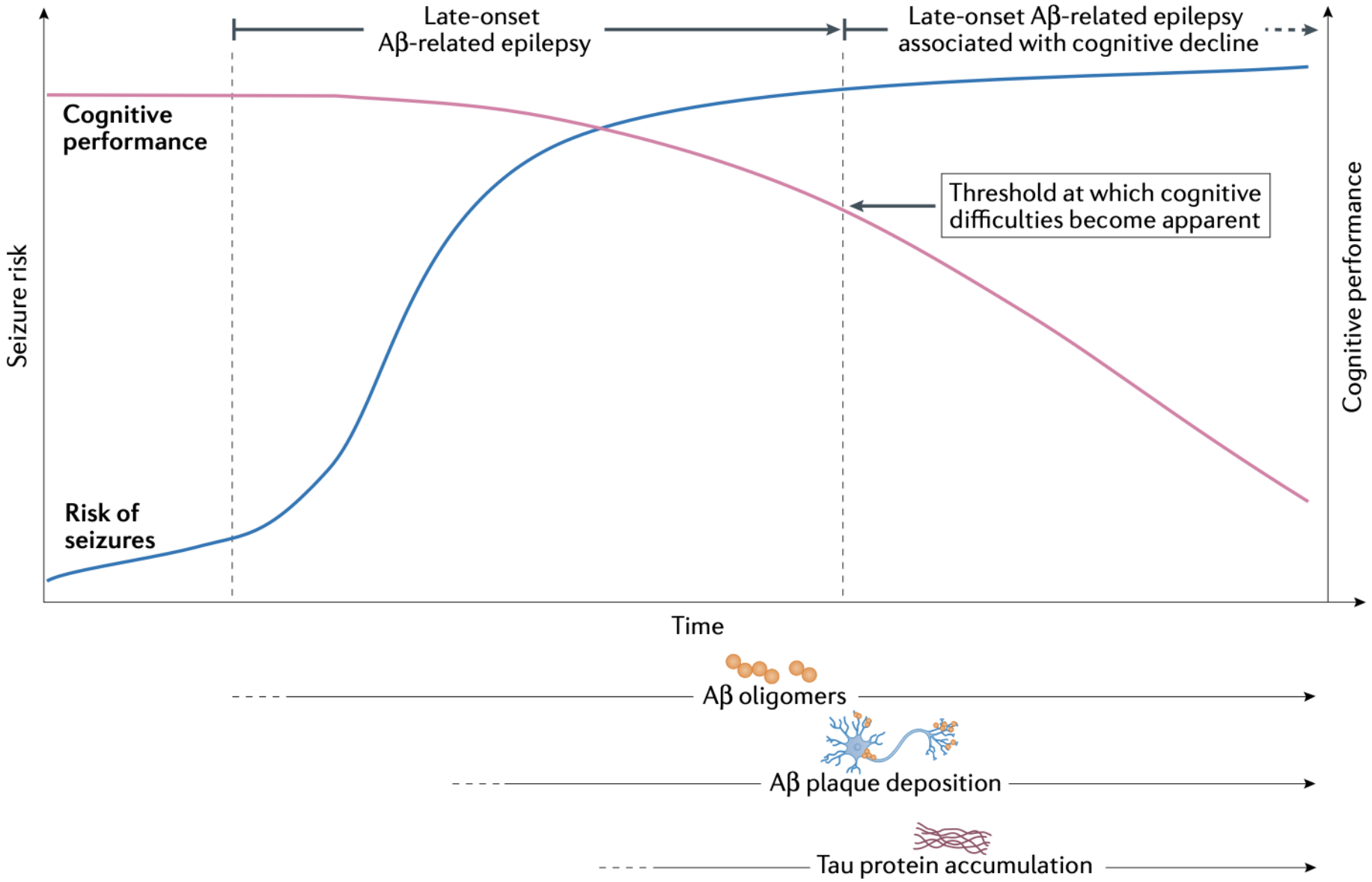


Amatniek et al, 2006

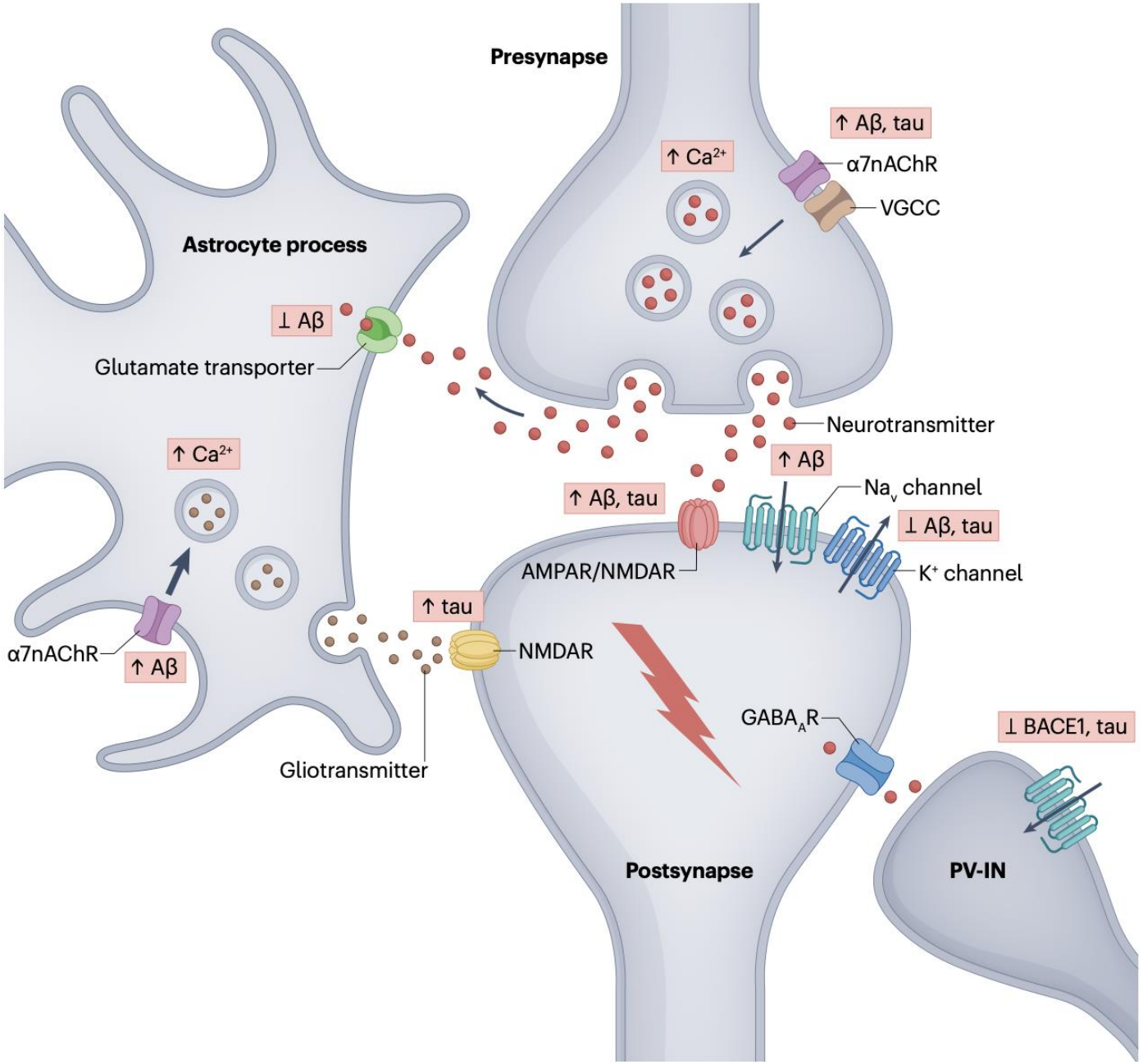
Late-onset epilepsy of unknown origin (LOEU)

- 1/3 of LOE
- CSF of LOEU: ↓ Aβ levels and ↑ p-tau levels in the
- 37.5% of people with LOEU without dementia had pathological Aβ CSF levels at baseline, → 3.4-times higher chance of developing AD over a 3-year follow-up
- The finding is consistent with that in people with AD → indicative of AD-specific neurodegenerative processes in LOEU.

Kamondi A., Grigg-Damberger M., Löscher W. et al. Nat Rev Neurol 20, 162–182 (2024).



Romoli M., Sen A., Parnetti L. et al. Nat. Rev. Neurol. 17, 469–485 (2021).



Amyloid-β and p-tau induce changes in cellular excitability.

Kamondi A., Grigg-Damberger M., Löscher W. et al. Nat Rev Neurol 20, 162–182 (2024).

Specific epilepsy syndrome in elderly

- Poststroke epilepsy
- Dementia-associated epilepsy
- Transient epileptic amnesia
- Antibody-mediated epilepsy

Transient Epileptic Amnesia: TEA

- Frequently lasts less than an hour.
- Specific characteristics

  : more frequent on awakening

  : repetitive questioning

  : residual incomplete amnesia of the event itself

- Olfactory hallucinations – 40%
- Recurrent nature of stereotypical events

Specific epilepsy syndrome in elderly

- Poststroke epilepsy
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- Transient epileptic amnesia
- Antibody-mediated epilepsy

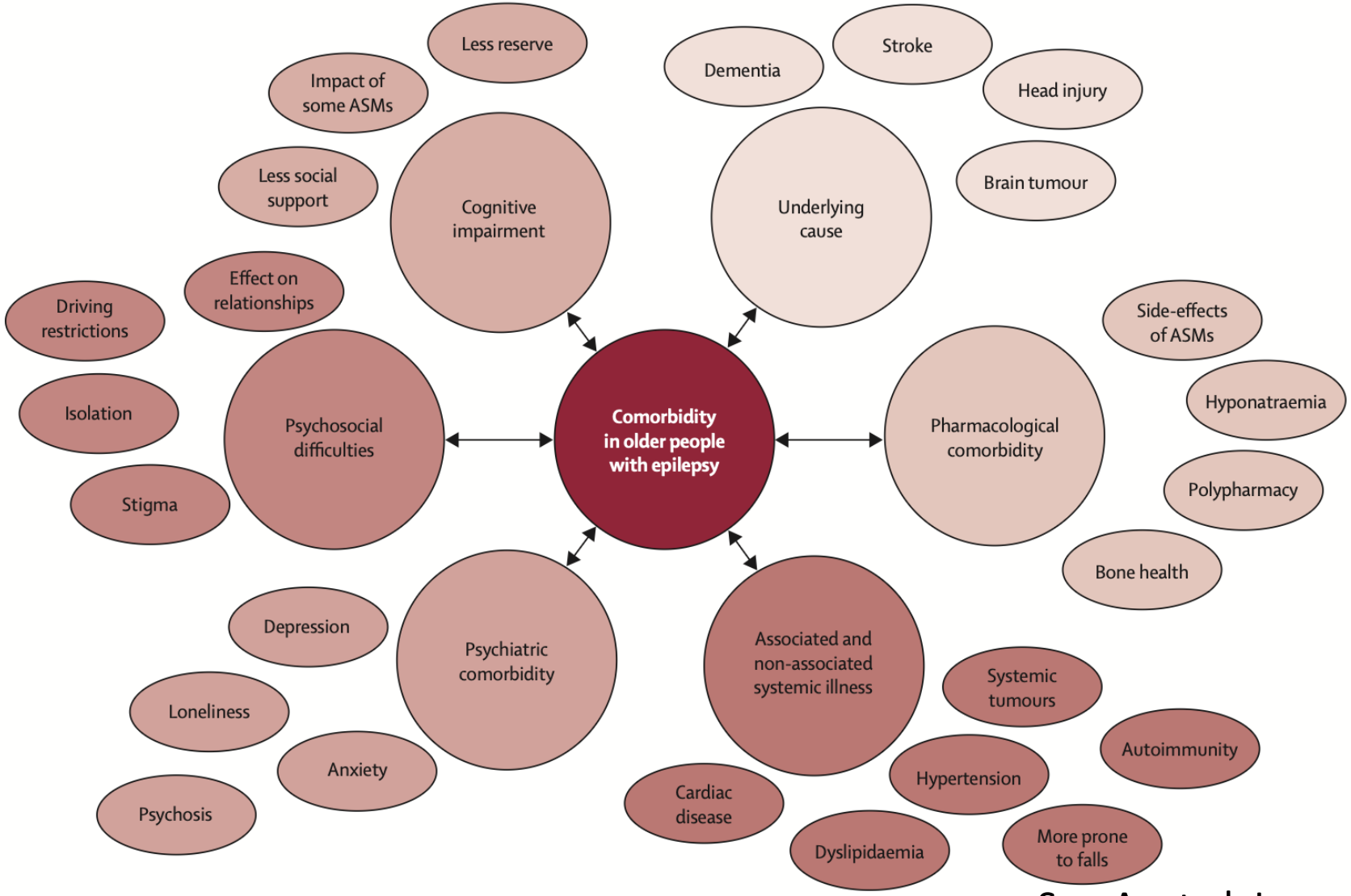
Antibody-mediated epilepsy

- Manifestations: seizures + cognitive & behavioral change
- Common in middle aged (>45 years) to older adults :anti-GABA-Br, anti-AMPAr, anti LGI1 and anti-CASPR2 antibodies
- Phenotypic features
  - Anti LGI1 antibodies: faciobrachial dystonic seizures
  - Delayed-onset dyskinesias are observed in anti-NMDA-R
  - Myoclonus in anti-glycine receptor antibody

Antibody-mediated epilepsy

- Autoimmune epilepsies respond poorly to conventional AEDs and instead should be treated with immunosuppression.
- The earlier diagnosed, the better outcome.
- Should investigate for occult malignancy.
- Treatment should also include tumor removal

Co-morbidity in elderly epilepsy

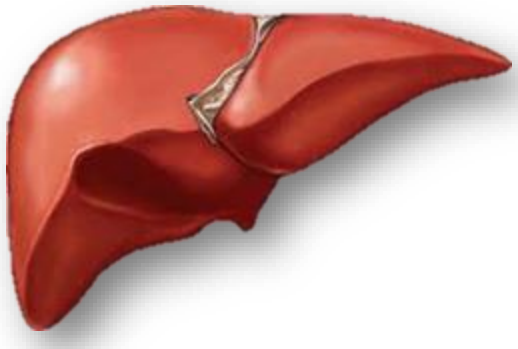


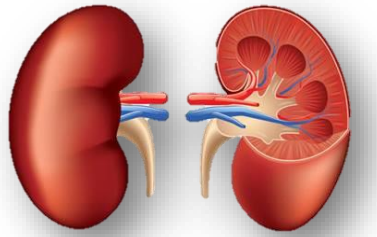
Sen A, et al. Lancet 2020; 395: 735–48

Pharmacology in old age

PK

- Absorption
- Protein binding
- Hepatic metabolism
- Enzyme inducibility
- Renal elimination





PD

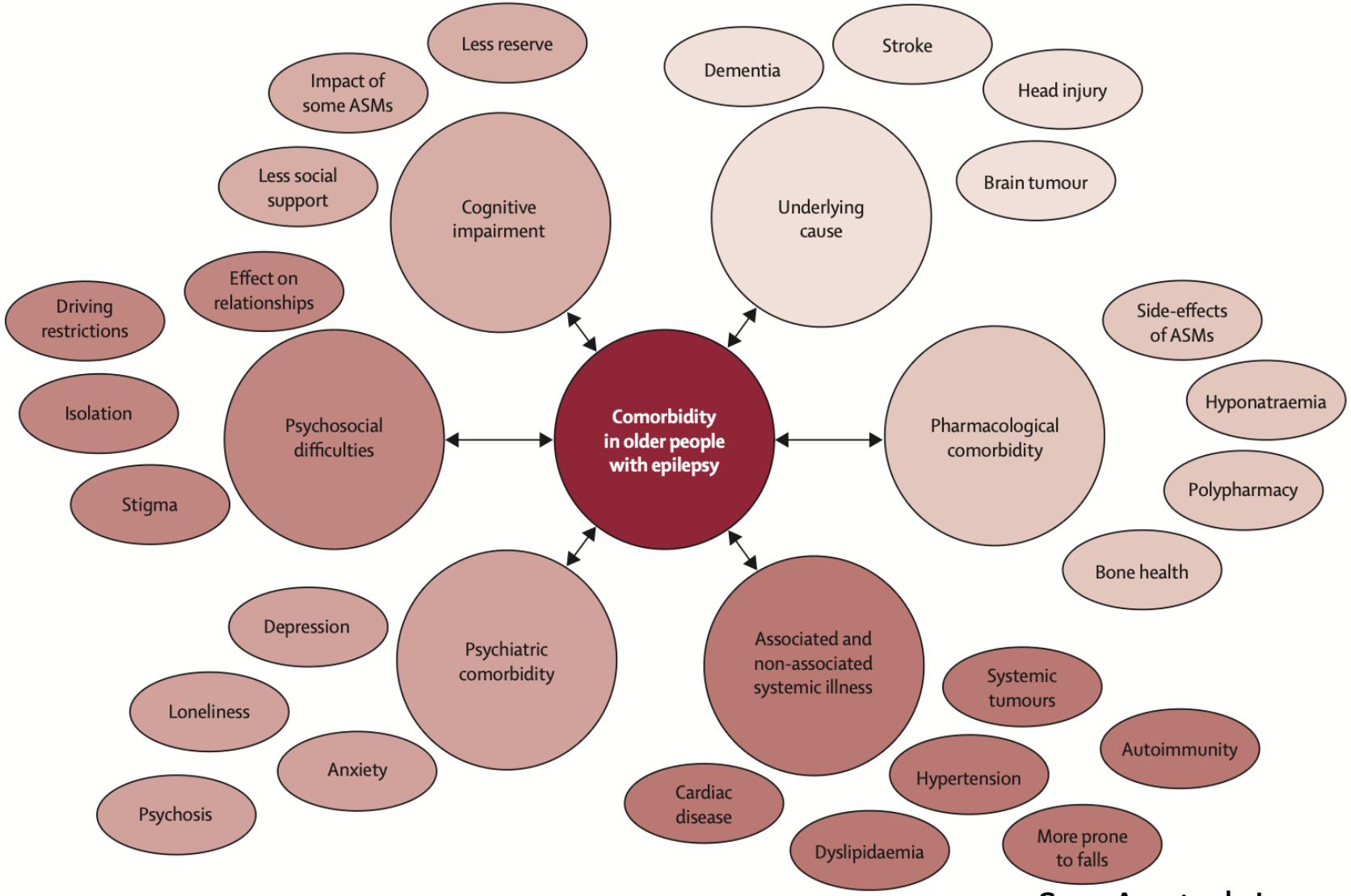
- Brain neurotransmitters
- Receptor function
- Autonomic pharmacology
- Homeostatic mechanisms

Easily get neurotoxicity

Easily get idiosyncratic reaction

“Start low, go slow”

Co-morbidity in elderly epilepsy



Sen A, et al. Lancet 2020; 395: 735–48

Acta Neurol Scand 2014: 130: 172–177 DOI: 10.1111/ane.12260

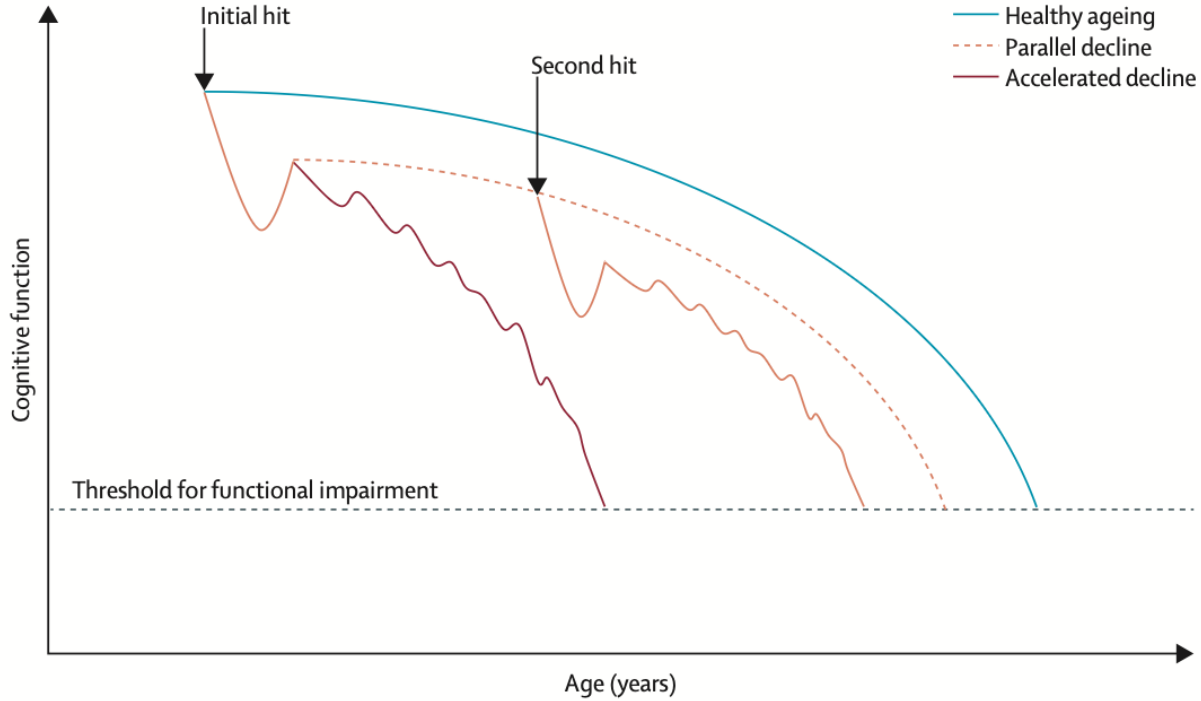
ACTA NEUROLOGICA
SCANDINAVICA

Cognitive-behavioral screening in elderly patients with new-onset epilepsy before treatment

- Assess new-onset elderly epilepsy with
  - objective assessment of executive function
  - subjective ratings of cognition
- 58% of patients deficits in executive function vs 27% with subjective rating
- Underline the importance of cognitive screening at baseline, to see what effect ASMs

Witt J A, et al. Acta Neurol Scand 2014: 130: 172–177

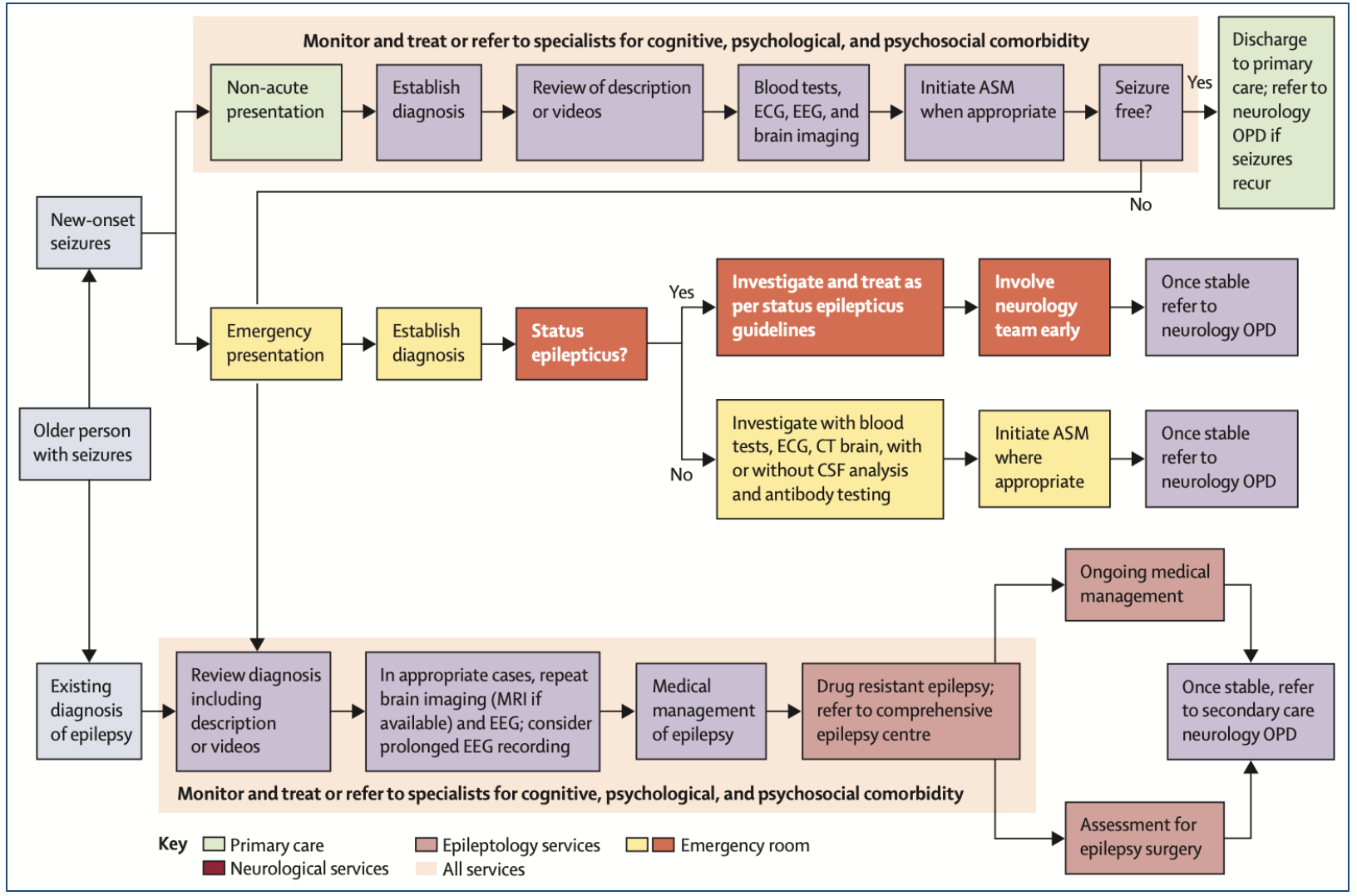
- Cognitive progression could be
  - Accelerated aging
  - Chronic accrual of pathology (eg, vascular)
  - Epilepsy itself (overt seizures or subclinical, abnormal cortical activity)



Initial hit, e.g; stroke TBI
Second hit, epilepsy itself, or accumalation of pathology

Sen A, et al. Lancet 2020; 395: 735–48

Care pathways for epilepsy in elderly



Sen A, et al. Lancet 2020; 395: 735–48

Care pathways for epilepsy in elderly