



The Saga of Late-Onset Unexplained Epilepsy

R. A. Sarkis, MD, MSc¹ , E. L. Johnson, MD, MPH² , and A. D. Lam, MD, PhD¹

¹ Department of Neurology, Mass General Brigham, Harvard Medical School, Boston, MA, USA

² Department of Neurology, Johns Hopkins School of Medicine, Baltimore, MA, USA

*Correspondence: R. A. Sarkis, Department of Neurology, Mass General Brigham, Harvard Medical School, 60 Fenwood Road, Boston, MA, 02115, USA.

Email: rsarkis@bwh.harvard.edu

Abstract

Late-onset epilepsy is increasingly recognized as a major and growing neurological condition in older adults, driven by population aging and rising incidence rates, yet approximately one-third of cases remain unexplained (late-onset unexplained epilepsy, LoUE). LoUE is diagnostically challenging, as seizures are often subtle and nonconvulsive, routine EEG has limited sensitivity. Converging evidence from animal models and clinical studies suggests that aging-related reductions in seizure threshold, vascular dysfunction, neurodegenerative processes, and immune dysregulation (“inflammaging”) all contribute to epileptogenesis, often through interacting and cumulative pathways. Clinically, while many patients respond to antiseizure medications, a subset experience refractory disease. Importantly, LoUE should not be viewed as a single entity but rather as a heterogeneous syndrome arising within diverse biological contexts shaped by lifetime exposures, comorbidities, and underlying pathology. Advancing the field will require prospective, multimodal studies integrating neuroimaging, fluid biomarkers, and detailed phenotyping to define mechanistic subtypes and enable a transition toward precision medicine approaches aimed at reducing the burden of seizures and their downstream consequences in older adults.

Keywords

older adults, late-onset unexplained epilepsy, neurodegeneration

The Silver Epilepsy Tsunami

The public perception of epilepsy as a disease of childhood has been refuted for several decades. Epidemiologic studies from the United States, Iceland, and Sweden (among others) demonstrate a classic bimodal distribution of incident epilepsy by age, with rates rising in the older adult years after a period of low incidence in middle age.^{1–3} Combined with the well-described aging of the populations in the United States and Western Europe, the number of older adults diagnosed with epilepsy is rapidly increasing.

Strikingly, the incidence of epilepsy has risen not just with age, but over time as well. Population studies show that over the past decades, the rate of epilepsy in older adults is increasing (along with the overall population numbers of older adults).^{4,5} The incidence of epilepsy cases in adults 65 and older in the United States in 2019 was 3.9 per 1000,⁵ a growth from 0.6

to 1 per 1000 in the 1970s,⁶ which is projected to continue growing rapidly with time.

The increasing rates of epilepsy in older adults stand in contrast to other neurologic diseases. Despite an aging population, the rates of incident stroke in the United States fell between 1990 and 2020,⁷ buoyed by improving screening, public health campaigns for healthier lifestyles, and treatment of vascular disease. Similarly, age-adjusted dementia rates have declined in the past 25 years overall, helped by increasing education, and treatment of vascular risk factors.⁸ Stroke and dementia are 2 of the top causes of incident epilepsy in older adults.⁹ As these rates decline but overall epilepsy increases, the question of what other factors contribute to epilepsy in this age group is of increasing importance. The increased 2- to 3-fold risks of subsequent stroke and subsequent dementia following late-onset epilepsy^{10–12} make this topic even more critical.



Creative Commons Non Commercial CC BY-NC: This article is distributed under the terms of the Creative Commons Attribution-NonCommercial 4.0 License (<https://creativecommons.org/licenses/by-nc/4.0/>) which permits non-commercial use, reproduction and distribution of the work without further permission provided the original work is attributed as specified on the SAGE and Open Access page (<https://us.sagepub.com/en-us/nam/open-access-at-sage>).



The Diagnostic Odyssey

Seizures in older adults are usually nonconvulsive, often non-motor, and may be subtle, going unrecognized and undiagnosed for several years.¹ Initial misdiagnosis as stroke, transient ischemic attack, cardiac arrhythmia, transient global amnesia, or syncope is common.¹³

When present, identification of an epileptogenic lesion (eg, tumor, cortical stroke, or prior trauma) on brain imaging helps with diagnosis in up to 2/3 of cases.¹⁴ Other MRI findings associated with seizures in older adults are often nonspecific and indicative of vascular risk factors, providing no aid in distinguishing epilepsy from its mimics.^{15,16} The limited sensitivity of routine EEG may further delay diagnosis: in one study, a standard routine (20-min) EEG detected epileptiform activity in only ~ 7% of patients with suspected seizures, a yield that increased 4-fold with prolonged (>3 h) monitoring.¹⁷

Even after a diagnosis of epilepsy and thorough history and investigation for structural and other etiologies is carried out, the cause remains unknown in about 30% of cases (late-onset unexplained epilepsy, LoUE).^{9,18}

Surveying the Unknown and Identifying Suspects

Why does epilepsy risk increase with age? Animal models provide insight as to why aging increases seizure susceptibility. Aged animal models exhibit increased spontaneous epileptiform activity and heightened susceptibility to chemoconvulsant-induced status epilepticus and neuronal injury.^{19,20} These findings suggest that aging lowers the seizure threshold while simultaneously impairing resilience to excitotoxic injury. Vascular dysfunction also appears to contribute, as hypertensive rat models show increased susceptibility to epilepsy, which can be mitigated by antihypertensive treatment.^{21,22} Transgenic amyloid and tau models of Alzheimer's disease (AD) similarly demonstrate spontaneous epileptiform discharges, recurrent seizures, and progressive network hyperexcitability. Notably, neuronal hyperexcitability can further promote the release and propagation of amyloid and tau, creating a feed-forward cycle that amplifies network dysfunction.^{23,24} Proposed mechanisms include excitatory–inhibitory imbalance, interneuron dysfunction, and synaptic and metabolic alterations.²⁵

Who are the usual suspects in LoUE? Despite the absence of an obvious epileptogenic lesion, brain MRI may still provide some clues. LoUE has frequently been attributed to cerebral small vessel disease (CSVD), though the mechanisms by which CSVD lowers seizure threshold remain incompletely understood. Higher white matter hyperintensity burden has been associated with increased epilepsy risk,²⁶ and emerging data suggest that juxtacortical and cortical–subcortical interface lesions can be particularly epileptogenic.²⁷ Hemorrhagic CSVD markers, such as superficial siderosis, have also been linked to seizures.²⁸ Regional atrophy patterns may suggest an underlying neurodegenerative process, with seizures representing an early manifestation. T2/FLAIR images, when combined with clinical tools such as the Antibody Prevalence in Epilepsy

and Encephalopathy score, facilitate early identification of antibody-mediated epilepsy, where prompt immunotherapy improves outcomes.²⁹

Cognitive testing, in conjunction with MRI and clinical history, may raise suspicion for underlying neurodegeneration and guide biomarker testing. Neurophysiologic testing with EEG, while useful for confirming the diagnosis and characterizing seizure type, is less informative regarding etiology. Polysomnography may identify comorbid obstructive sleep apnea (OSA), which can further lower seizure threshold.³⁰ The concept of “inflammaging” has also gained increasing attention in the context of late-life epileptogenesis. Age-related shifts in both central and peripheral immune function contribute to seizure susceptibility and modulate the downstream consequences of seizures.^{31,32} At present, clinical assessment of immune status is limited to antibody panels and nonspecific markers, with more detailed phenotyping remaining primarily a research tool. Finally, identified pathologies may not represent a single causal mechanism but rather an additional “hit” within a multifactorial epileptogenic cascade. For example, prior insults such as central nervous system infections, or head injury may only culminate in seizures when aging-related processes further lower seizure threshold.

Diagnosis and initial testing do not end the odyssey. Increasing evidence from large-scale studies finds that many (but not most) individuals with LoUE embark on a course of accelerated cognitive decline even if cognitively normal at the time of the first seizure.^{10,33} As a result, serial cognitive screening, optimizing vascular risk factors, and individualizing prognosis are ongoing efforts.

Charting the Management Landscape

The management of LoUE should not only prioritize seizure control but also include assessment of cognition and cerebrovascular risk. While there are well-tolerated antiseizure medications (ASMs) (lamotrigine, levetiracetam), enzyme-inducing drugs should be avoided due to negative vascular outcomes. Slow titration is key, given older adults' sensitivity to psychotropic agents, especially in those who are frail.³⁴ Most patients respond to ASMs, but a subset remain medically refractory and face higher risks of cognitive decline and mortality. In selected cases, surgical intervention may be curative, although potential benefits must be weighed against the risk of postoperative cognitive decline, to which older adults are particularly vulnerable.³⁵ When resective or ablative approaches are not feasible, neuromodulation therapies provide meaningful benefit by reducing seizure frequency and severity, even if not curative.³⁶

Comorbidities such as depression are common and should be routinely screened for, as they can affect quality of life and medication tolerability. Older adults are more likely to present with somatic and vegetative symptoms compared to their younger counterparts.³⁷ Driving restrictions further exacerbate mood symptoms and social isolation; therefore, providing appropriate social support is essential. Substance use should also be assessed; alcohol, in particular, lowers the seizure threshold and can serve as a trigger, with older adults more vulnerable to its effects. Clinical

history, collateral information, and screening questionnaires can help identify individuals who would benefit from polysomnography to evaluate for OSA, which is common in this age group and can trigger or exacerbate seizures and cognitive impairment. Polysomnography can also identify other disturbances, such as periodic limb movements, that further disrupt sleep.

Stroke and dementia risk reduction requires prioritizing control of vascular risk factors such as hypertension, hyperlipidemia, and diabetes, given their links to seizures, cognitive decline, and stroke. Keeping in mind that up to 45% of dementia cases are preventable or delayable,³⁸ targeting modifiable risk factors which may be overlooked is also essential. Lifestyle factors such as physical activity, stress reduction, and social engagement are associated with better brain health and can enhance resilience to the cognitive and neurological consequences of seizures. Tools such as the Brain Care Score may help identify modifiable risk factors and guide interventions.³⁹

Finally, when a specific etiology is identified, management should be tailored accordingly. In cases of autoimmune epilepsy, early initiation of immunomodulatory therapy is critical. For neurodegenerative conditions such as AD, anti-amyloid therapies may be considered in carefully selected patients.

Embracing Heterogeneity in LoUE Research and Navigating With Precision

As described above, LoUE is a highly heterogeneous entity that encompasses multiple epileptogenic mechanisms occurring across a wide range of biological contexts. These contexts are shaped by genetics, developmental factors, sociodemographic influences, lifestyle habits, medical problems and their treatments (eg, chemotherapy, immunotherapy), as well as untreated conditions (eg, OSA). The physiologic consequences of some factors may accumulate over decades, while others may have emerged more proximally to epilepsy onset. Identifying critical aspects of this “biological milieu” that contribute to LoUE, or that interact with epilepsy to increase dementia or stroke risk, is an urgent priority. Prospective studies that capture the biological contexts in which LoUE arises, together with associated clinical trajectories, will be essential for characterizing this heterogeneity with sufficient granularity to inform clinical care.

Addressing this heterogeneity will also require greater rigor in defining study populations and outcomes. In particular, LoUE should not be conflated with general “late-onset epilepsy.” The latter includes many epilepsy etiologies such as stroke, neoplastic, or neurodegenerative disease, which are often associated with structural brain pathology that has produced physical or cognitive impairment even before the development of epilepsy. In contrast, patients with LoUE typically have nonlesional brain MRI findings, without an obvious structural basis for physical or cognitive impairment. Grouping these distinct entities under the single category of “late-onset epilepsy” based solely on age of seizure onset obscures this critical heterogeneity. Historically, this lack of granularity was a necessary compromise for studies that leveraged large population-based cohorts to examine outcomes in older

adults with epilepsy. Because these cohorts were not designed specifically to study epilepsy, they lacked detailed information on epilepsy etiology, severity, and treatment. However, as findings from those studies now motivate targeted prospective studies focused on epilepsy in older adults, it is essential to capture these etiologic details to avoid *unnecessary* heterogeneity and to move toward a precision medicine framework. In this context, “late-onset epilepsy” may be better contextualized as a group of distinct syndromes defined by the underlying cause of epilepsy (eg, poststroke, tumor-related, or epilepsy associated with a specific neurodegenerative disease).

Greater rigor is also needed in describing cognitive outcomes in LoUE. Foremost, the terms “dementia” and “AD” should not be used interchangeably. Dementia refers to a progressive decline in cognitive function that is severe enough to impair daily functioning and can arise from many underlying causes. AD is the leading cause of dementia, but is just one of multiple etiologies. Although epidemiologic studies have demonstrated bidirectional associations between epilepsy and dementia,^{10,11,40,41} these studies have not established whether the dementia observed in this context is specifically due to AD. Moreover, while many studies have shown that individuals with AD have a higher risk of developing epilepsy compared to cognitively normal older adults, this association is not unique to AD; other neurodegenerative diseases including frontotemporal dementia, dementia with Lewy bodies, and vascular dementia are also associated with an increased risk of epilepsy.^{42–46}

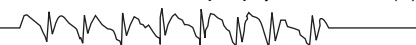
The future of LoUE research will depend on large-scale, multimodal biomarker studies capable of defining distinct disease subtypes, identifying the pathologic mechanisms that link epilepsy to dementia and stroke, and guiding targeted strategies to reduce these risks. Because noninvasive biomarkers are not yet available for many neurodegenerative diseases, it is critical to bank plasma samples for future biomarker discovery, as well as to establish brain banks. Notably, most pathological studies in epilepsy have relied on surgical brain tissue obtained from younger patients with refractory epilepsy. While these studies have made important contributions to the field,^{47–50} their relevance to older adults with well-controlled epilepsy who later develop dementia is uncertain. Compared to the fields of aging and neurodegenerative disease, epilepsy research has lagged in defining the associated pathology related to dementia and developing biomarkers to study this pathology in vivo. Building the infrastructure needed to close this gap—including prospective biomarker cohorts and brain banks—will be essential for advancing the field, and transforming the “unexplained” to “explained.”

Declaration of Conflicting Interests

The authors declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Funding

The authors received no financial support for the research, authorship, and/or publication of this article.



ORCID iDs

R. A. Sarkis  <https://orcid.org/0000-0001-8291-7864>
 E. L. Johnson  <https://orcid.org/0000-0001-6457-938X>
 A. D. Lam  <https://orcid.org/0000-0001-7754-4637>

References

- Sen A, Jette N, Husain M, Sander JW. Epilepsy in older people. *Lancet*. 2020;395(10225):735-748. doi:10.1016/S0140-6736(19)33064-8
- Faught E, Richman J, Martin R, et al. Incidence and prevalence of epilepsy among older U.S. Medicare beneficiaries. *Neurology*. 2012;78(7):448-453.
- Olafsson E, Ludvigsson P, Hesdorffer D, Kjartansson O, Hauser WA, Gudmundsson G. Incidence of unprovoked seizures and epilepsy in Iceland and assessment of the epilepsy syndrome classification: a prospective study. *Lancet Neurol*. 2005;4(10):627-634. doi:10.1016/S1474-4422(05)70172-1
- Sillanpää M, Lastunen S, Helenius H, Schmidt D. Regional differences and secular trends in the incidence of epilepsy in Finland: a nationwide 23-year registry study. *Epilepsia*. 2011;52(10):1857-1867. doi:10.1111/j.1528-1167.2011.03186.x
- Warner DF, Fein HL, Schiltz NK, et al. Incident epilepsy among us medicare beneficiaries, 2019: differences by age, sex, and race/ethnicity. *Neurology*. 2024;103(7). doi:10.1212/WNL.0000000000209804
- Hauser WA, Annegers JF, Kurland LT. Incidence of epilepsy and unprovoked seizures in Rochester, Minnesota. *Epilepsia*. 1993;34(3):1935-1984. doi:10.1111/j.1528-1157.1993.tb02586.x
- Renedo D, Acosta JN, Leasure AC, et al. Burden of ischemic and hemorrhagic stroke across the US from 1990 to 2019. *JAMA Neurol*. 2024;81(4):394-404. doi:10.1001/jamaneurol.2024.0190
- Freedman VA, Comman JC. Dementia prevalence, incidence, and mortality trends among U.S. adults ages 72 and older, 2011–2021. *J Gerontol A Biol Sci Med Sci*. 2024;79(Supplement_1):S22-S31. doi:10.1093/geron/glae105
- Hauser WA, Annegers JF, Kurland LT. Incidence of epilepsy and unprovoked seizures in Rochester, Minnesota: 1935-1984. *Epilepsia*. 1993;34(3):453-468. doi:10.1111/j.1528-1157.1993.tb02586.x
- Keret O, Hoang TD, Xia F, Rosen HJ, Yaffe K. Association of late-onset unprovoked seizures of unknown etiology with the risk of developing dementia in older veterans. *JAMA Neurol*. 2020;77(6):710-715. doi:10.1001/jamaneurol.2020.0187
- Johnson EL, Krauss GL, Kucharska-Newton A, et al. Dementia in late-onset epilepsy: the atherosclerosis risk in communities study. *Neurology*. 2020;95(24):E3248-E3256. doi:10.1212/WNL.0000000000011080
- Wall J, Knight J, Emsley HCA. Late-onset epilepsy predicts stroke: systematic review and meta-analysis. *Epilepsy Behav*. 2021;115:107634. doi:10.1016/j.yebeh.2020.107634
- Pellinen J, Foster EC, Wilmschurst JM, Zuberi SM, French J. Improving epilepsy diagnosis across the lifespan: approaches and innovations. *Lancet Neurol*. 2024;23(5):511-521. doi:10.1016/S1474-4422(24)00079-6
- Arabi M, Dirani M, Hourani R, et al. Frequency and stratification of epileptogenic lesions in elderly with new onset seizures. *Front Neurol*. 2018;9:401410. doi:10.3389/fneur.2018.00995
- Hanby MF, Al-Bachari S, Makin F, Vidyasagar R, Parkes LM, Emsley HCA. Structural and physiological MRI correlates of occult cerebrovascular disease in late-onset epilepsy. *Neuroimage Clin*. 2015;9:128-133. doi:10.1016/j.nicl.2015.07.016
- Johnson EL, Krauss GL, Lee AK, et al. Association between white matter hyperintensities, cortical volumes, and late-onset epilepsy. *Neurology*. 2019;92(9):E988-E995. doi:10.1212/WNL.0000000000007010
- Chochoi M, Tyvaert L, Derambure P, Szurhaj W. Is long-term electroencephalogram more appropriate than standard electroencephalogram in the elderly? *Clin Neurophysiol*. 2017;128(1):270-274. doi:10.1016/j.clinph.2016.10.006
- Blank LJ, Johnson EL, Pellerin KR, et al. Late-onset seizures: etiology and demographics in US tertiary care epilepsy centers. *Neurology*. 2026;106(11):e214948. doi:10.1212/WNL.00000000000214948
- El-Hayek YH, Wu C, Ye H, Wang J, Carlen PL, Zhang L. Hippocampal excitability is increased in aged mice. *Exp Neurol*. 2013;247:710-719. doi:10.1016/j.expneurol.2013.03.012
- Liang LP, Beaudoin ME, Fritz MJ, Fulton R, Patel M. Kainate-induced seizures, oxidative stress and neuronal loss in aging rats. *Neuroscience*. 2007;147(4):1114-1118. doi:10.1016/j.neuroscience.2007.03.026
- Russo E, Leo A, Scicchitano F, et al. Cerebral small vessel disease predisposes to temporal lobe epilepsy in spontaneously hypertensive rats. *Brain Res Bull*. 2017;130:245-250. doi:10.1016/j.brainresbull.2017.02.003
- Friedman A, Kaufer D, Heinemann U. Blood-brain barrier breakdown-inducing astrocytic transformation: novel targets for the prevention of epilepsy. *Epilepsy Res*. 2009;85(2-3):142-149. doi:10.1016/j.eplepsyres.2009.03.005
- Palop JJ, Chin J, Roberson ED, et al. Aberrant excitatory neuronal activity and compensatory remodeling of inhibitory hippocampal circuits in mouse models of Alzheimer's disease. *Neuron*. 2007;55(5):697-711. doi:10.1016/j.neuron.2007.07.025
- Gomez-Murcia V, Sandau U, Ferry B, et al. Hyperexcitability and seizures in the THY-Tau22 mouse model of tauopathy. *Neurobiol Aging*. 2020;94:265-270. doi:10.1016/j.neurobiolaging.2020.06.004
- Vossel KA, Tartaglia MC, Nygaard HB, Zeman AZ, Miller BL. Epileptic activity in Alzheimer's disease: causes and clinical relevance. *Lancet Neurol*. 2017;16(4):311-322. doi:10.1016/S1474-4422(17)30044-3
- Johnson EL, Krauss GL, Lee AK, et al. Association between white matter hyperintensities, cortical volumes, and late-onset epilepsy. *Neurology*. 2019;92(9):E988-E995. doi:10.1212/WNL.0000000000007010
- Nasca A, Sokolović L, Koprda O, Haage P, Schmidt T, Kukolja J. Late-onset first epileptic seizure and cerebral small vessel disease: role of juxtacortical white matter lesions. *Front Neurol*. 2025;15:1508663. doi:10.3389/fneur.2024.1508663
- Freund BE, Sanchez-Boluarte SS, Blackmon K, et al. Incidence and risk factors associated with seizures in cerebral amyloid angiopathy. *Eur J Neurol*. 2023;30(12):3682-3691. doi:10.1111/ene.15903
- Dubey D, Singh J, Britton JW, et al. Predictive models in the diagnosis and treatment of autoimmune epilepsy. *Epilepsia*. 2017;58(7):1181-1189. doi:10.1111/epi.13797
- Chihorek AM, Abou-Khalil B, Malow BA. Obstructive sleep apnea is associated with seizure occurrence in older adults with epilepsy. *Neurology*. 2007;69(19):1823-1827. doi:10.1212/01.wnl.0000279334.78298.d5
- Hollis A, Lukens JR. Role of inflammasomes and neuroinflammation in epilepsy. *Immunol Rev*. 2025;329(1):e13421. doi:10.1111/imr.13421
- Di Benedetto S, Müller L, Wenger E, Düzel S, Pawelec G. Contribution of neuroinflammation and immunity to brain aging and the mitigating effects of physical and cognitive interventions. *Neurosci Biobehav Rev*. 2017;75:114-128. doi:10.1016/j.neubiorev.2017.01.044

- 
33. Johnson EL, Krauss GL, Walker KA, et al. Late-onset epilepsy and 25-year cognitive change: the atherosclerosis risk in communities (ARIC) study. *Epilepsia*. 2020;61(8):1764-1773. doi:10.1111/epi.16616
 34. McCarthy LM, Boylan KA, Sarkis RA. Antiseizure medications in older adults with epilepsy: considerations in pharmacology, safety, tolerability, and effectiveness of newer agents. *Drugs Aging*. 2026;43(3):251-265. doi:10.1007/s40266-026-01283-z
 35. Punia V, Abdelkader A, Busch RM, et al. Time to push the age limit: epilepsy surgery in patients 60 years or older. *Epilepsia Open*. 2018;3(1):73-80. doi:10.1002/epi4.12099
 36. Zawar I, Krishnan B, Mackow M, Alexopoulos A, Nair D, Punia V. The efficacy, safety, and outcomes of brain-responsive neurostimulation (RNS® system) therapy in older adults. *Epilepsia Open*. 2021;6(4):781-787. doi:10.1002/epi4.12541
 37. Hegeman AJM, Kok RM, Van Der Mast RC, Giltay EJ. Phenomenology of depression in older compared with younger adults: meta-analysis. *Br J Psychiatry*. 2012;200(4):275-281. doi:10.1192/bjp.bp.111.095950
 38. Livingston G, Huntley J, Liu KY, et al. Dementia prevention, intervention, and care: 2024 report of the Lancet standing commission. *Lancet*. 2024;404(10452):572-628. doi:10.1016/S0140-6736(24)01296-0
 39. Singh SD, Oreskovic T, Carr S, et al. The predictive validity of a brain care score for dementia and stroke: data from the UK Biobank cohort. *Front Neurol*. 2023;14:1291020. doi:10.3389/fneur.2023.1291020
 40. Stefanidou M, Beiser AS, Himali JJ, et al. The bi-directional association between epilepsy and dementia. The Framingham Heart Study. *Neurology*. 2020;95(24):e3241-e3247. doi:10.1212/WNL.0000000000011077
 41. Ophir K, Ran B, Felix B, Amir G. Ten year cumulative incidence of dementia after late onset epilepsy of unknown etiology. *J Clin Neurosci*. 2021;86:247-251. doi:10.1016/j.jocn.2021.01.030
 42. Hesdorffer DC, Hauser WA, Annegers JF, et al. Dementia and adult-onset unprovoked seizures. *Neurology*. 1996;46(3):727-730. doi:10.1212/WNL.46.3.727
 43. Irizarry MC, He JS, Emond F, et al. Incidence of new-onset seizures in mild to moderate Alzheimer disease. *Arch Neurol*. 2012;69(3):368-372. doi:10.1001/archneurol.2011.830
 44. Beagle AJ, Darwish SM, Ranasinghe KG, La AL, Karageorgiou E, Vossel KA. Relative incidence of seizures and myoclonus in Alzheimer's disease, dementia with Lewy bodies, and frontotemporal dementia. *J Alzheimers Dis*. 2017;60(1):211-223. doi:10.3233/JAD-170031
 45. Imfeld P, Bodmer M, Schuerch M, Jick SS, Meier CR. Seizures in patients with Alzheimer's disease or vascular dementia: a population-based nested case-control analysis. *Epilepsia*. 2013;54(4):700-707. doi:10.1111/epi.12045
 46. Kilpeläinen A, Aaltonen M, Aho K, et al. Prevalence of epilepsy in frontotemporal dementia and timing of dementia diagnosis. *JAMA Neurol*. 2025;82(7):715-721. doi:10.1001/jamaneurol.2025.1358
 47. Hoffmann L, Blümcke I. Neuropathology and epilepsy surgery. *Curr Opin Neurol*. 2022;35(2):202-207. doi:10.1097/WCO.0000000000001030
 48. Tai XY, Koepp M, Duncan JS, et al. Hyperphosphorylated tau in patients with refractory epilepsy correlates with cognitive decline: a study of temporal lobe resections. *Brain*. 2016;139(9):2441-2455. doi:10.1093/brain/aww187
 49. Thom M, Liu JYW, Thompson P, et al. Neurofibrillary tangle pathology and Braak staging in chronic epilepsy in relation to traumatic brain injury and hippocampal sclerosis: a post-mortem study. *Brain*. 2011;134(10):2969-2981. doi:10.1093/brain/awr209
 50. Gourmaud S, Shou H, Irwin DJ, et al. Alzheimer-like amyloid and tau alterations associated with cognitive deficit in temporal lobe epilepsy. *Brain*. 2020;143(1):191-209.