Alzheimer's disease

- Prevalence of Mild Cognitive Impairment and Alzheimer's Disease and Related Dementias Among Older Residents of Publicly Subsidized Housing in the United States: Systematic-Review and Meta-Analysis
- 3-Hydroxyquinolin-2-Ones Act as Dual Inhibitors of Ferroptosis and Monoamine Oxidase B: Reducing Alzheimer's Disease-Related Amyloid Precursor Protein and Hyperphosphorylated Tau In Vivo
- Evaluating the therapeutic efficacy of a Benzofuran-Enaminone derivative for the management of Alzheimer's disease (AD)-like pathology in rats through regulating the expression of apoptosis and AD-related genes
- Lactoferrin-Anchored Carboxymethyl Pullulan-MgO Nanocomposites for Targeted Delivery of Trans-Ferulic Acid: Physicochemical Characterization, In vitro and Ex vivo Studies
- Computational mechanistic insight of fungal metabolites for novel acetylcholinesterase inhibitors
- The future of biomarkers for vascular contributions to cognitive impairment and dementia (VCID): proceedings of the 2025 annual workshop of the Albert research institute for white matter and cognition
- Cost Efficiency of fMRI Studies Using Resting-State Vs. Task-Based Functional Connectivity
- Proteomics-Based Trapping to Study Substrates of Histone Deacetylase 6 Catalytic Domain 1

Classification

Functional connectivity of the human brain, representing statistical dependence of information flow between cortical regions, significantly contributes to the study of the intrinsic brain network and its functional mechanism. To fully explore its potential in the early diagnosis of Alzheimer's disease (AD) using electroencephalogram (EEG) recordings, Shan et al. in an article introduce a novel dynamical spatial-temporal graph convolutional neural network (ST-GCN) for better classification performance. Different from existing studies that are based on either topological brain function characteristics or temporal features of EEG, the proposed ST-GCN considers both the adjacency matrix of functional connectivity from multiple EEG channels and corresponding dynamics of signal EEG channels simultaneously. Different from the traditional graph convolutional neural networks, the proposed ST-GCN makes full use of the constrained spatial topology of functional connectivity and the discriminative dynamic temporal information represented by the 1D convolution. We conducted extensive experiments on the clinical EEG data set of AD patients and Healthy Controls. The results demonstrate that the proposed method achieves better classification performance (92.3%) than the state-of-the-art methods. This approach can not only help diagnose AD but also better understand the effect of normal aging on brain network characteristics before we can accurately diagnose the condition based on resting-state EEG [1)].

Staging

Amyloid-β plaques and neurofibrillary tangles (NFTs) are the 2 histopathologic hallmarks of Alzheimer

disease (AD). On the basis of the pattern of NFT distribution in the brain, Braak and Braak proposed a histopathologic staging system for AD. Braak staging provides a compelling framework for staging and monitoring of NFT progression in vivo using PET imaging. Because AD staging remains based on clinical features, there is an unmet need to translate neuropathologic staging to a biologic clinical staging system. Such a biomarker staging system might play a role in staging preclinical AD or in improving recruitment strategies for clinical trials. Macedo et al. reviewed the literature regarding AD staging with the Braak framework using tau PET imaging, here called PET-based Braak staging. The aim is to summarize the efforts of implementing Braak staging using PET and assess correspondence with the Braak histopathologic descriptions and with AD biomarkers.

They conducted a systematic literature search in May 2022 on PubMed and Scopus combining the terms “Alzheimer” AND “Braak” AND (“positron emission tomography” OR “PET”).

The database search returned 262 results, and after assessment for eligibility, 21 studies were selected. Overall, most studies indicate that PET-based Braak staging may be an efficient method to stage AD since it presents an adequate ability to discriminate between phases of the AD continuum and correlates with clinical, fluid, and imaging biomarkers of AD. However, the translation of the original Braak descriptions to tau PET was done taking into account the limitations of this imaging technique. This led to important interstudy variability in the anatomic definitions of Braak stage regions of interest. Refinements in this staging system are necessary to incorporate atypical variants and Braak-nonconformant cases. Further studies are needed to understand the possible applications of PET-based Braak staging to clinical practice and research. Furthermore, there is a need for standardization in the topographic definitions of Braak stage regions of interest to guarantee reproducibility and methodologic homogeneity across studies [2)].

Risk Factors

Alzheimer's disease risk factors.

Pathogenesis

Alzheimer's disease pathogenesis.

Clinical features

Alzheimer's disease clinical features.

Diagnosis

Alzheimer's disease diagnosis.

Pathology

1. Key Pathological Features A. Amyloid-beta (Aβ) Plaques (Extracellular) Formed by abnormal cleavage of amyloid precursor protein (APP). Aggregates into oligomers and fibrils, leading to plaques. Found in the extracellular space, particularly in the neocortex. Neurotoxic effects: Induces inflammation via microglial activation. Disrupts synaptic function. Leads to oxidative stress and mitochondrial dysfunction. B. Tau Neurofibrillary Tangles (NFTs) (Intracellular) Tau hyperphosphorylation causes detachment from microtubules. Misfolded tau aggregates into paired helical filaments (PHFs). Intracellular accumulation leads to neuronal dysfunction and death. Spread follows a predictable pattern (Braak Staging): Starts in the entorhinal cortex. Progresses to the hippocampus. Spreads to the neocortex in advanced stages. C. Synaptic and Neuronal Loss Major cause of cognitive decline. Driven by both Aβ toxicity and tau pathology. Early synaptic dysfunction precedes large-scale neuronal death. D. Neuroinflammation Microglia and astrocytes become reactive in response to Aβ plaques and tau pathology. Chronic inflammation contributes to neuronal damage. Activation of inflammasomes (e.g., NLRP3) has been implicated.

Sánchez-Aced describes the combination of array tomography (AT) with two-colour direct stochastic optical reconstruction microscopy (dSTORM) to enhance lateral resolution for resolving synaptic terminals in a human postmortem brain.

They applied this combination to study synapses in brain samples (from biopsy and postmortem) from healthy subjects and pathological synaptic tau (aggregates and oligomers) in samples from AD patients.

AT combined with dSTORM allowed the orientation and shape of the synaptic terminals and the synaptic cleft to be characterised. In addition, this combination confirmed the presence of oligomeric tau in synaptic terminals in AD.

Overall, they found that the combination of AT and two-colour dSTORM provides optimal resolution to detect pathological synaptic tau and its spatial relationship with presynaptic and postsynaptic terminals [3)].

The study by Sánchez-Aced et al. (2025) represents a significant advancement in Alzheimer’s disease research by enhancing the spatial resolution of synaptic tau imaging. The combination of AT and two-colour dSTORM provides valuable insights into synaptic-level tau pathology, reinforcing the role of synaptic tau in AD progression. While the study excels in methodological innovation and structural characterization, future work should integrate functional, biochemical, and therapeutic perspectives to fully elucidate the role of synaptic tau aggregates in neurodegeneration.

Overall, this study serves as a valuable contribution to the field of neuropathology, offering a new imaging framework that could be applied to other neurodegenerative diseases characterized by synaptic dysfunction.

Differential diagnosis

Alzheimer's disease differential diagnosis.

Treatment

Alzheimer's disease treatment.

Case series

Alzheimer's disease case series

1)
Shan X, Cao J, Huo S, Chen L, Sarrigiannis PG, Zhao Y. Spatial-temporal graph convolutional network for Alzheimer classification based on brain functional connectivity imaging of electroencephalogram. Hum Brain Mapp. 2022 Jun 25. doi: 10.1002/hbm.25994. Epub ahead of print. PMID: 35751844.
2)
Macedo AC, Tissot C, Therriault J, Servaes S, Wang YT, Fernandez-Arias J, Rahmouni N, Lussier FZ, Vermeiren M, Bezgin G, Vitali P, Ng KP, Zimmer ER, Guiot MC, Pascoal TA, Gauthier S, Rosa-Neto P. The Use of Tau PET to Stage Alzheimer Disease According to the Braak Staging Framework. J Nucl Med. 2023 Jun 15:jnumed.122.265200. doi: 10.2967/jnumed.122.265200. Epub ahead of print. PMID: 37321820.
3)
Sánchez-Aced É, Moya-Llamas B, Aumatell Escabias J, Torres S, Colom-Cadena M, Pegueroles J, de Quintana-Schmidt C, Bayés À, Molina-Porcel L, Aldecoa I, Belbin O, Fortea J, Spires-Jones T, Pujals S, Sirisi S, Lleó A. Enhancing Lateral Resolution Using Two-Colour Direct Stochastic Optical Reconstruction Microscopy to Unravel Synaptic Tau Pathology in Alzheimer's Disease. Neuropathol Appl Neurobiol. 2025 Apr;51(2):e70010. doi: 10.1111/nan.70010. PMID: 40025904.