

Cerebellar gray matter atrophy associates with tau phosphorylation and multi-domain cognitive decline in Alzheimer’s disease continuum

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INTRODUCTION	METHODS	RESULTS	CONCLUSIONS	REFERENCES
Cerebellum is increasingly recognized as contributing to cognitive decline in Alzheimer’s disease (AD), yet the precise pattern of its structural vulnerability along the AD continuum and its relationship with tau pathology and multi-domain cognitive decline remain underexplored.	A total of 130 participants enrolled from Beijing Tiantan Hospital were precisely classified based on clinical symptoms and amyloid-beta (Aβ) - positron emission tomography (PET) into three groups: cognitively normal (NC, n=30), mild cognitive impairment due to AD (AD-MCI, n=52) and dementia due to AD (AD-D, n=48). All participants underwent comprehensive neuropsychological assessments, Aβ-PET, measurements of plasma AD biomarkers [including Aβ42, Aβ40, Aβ42/40, phosphorylated tau (P-tau)181, P-tau217], and structural brain 3.0T magnetic resonance imaging. Cerebellar gray matter volume was quantified using a voxel-based approach. Statistical analyses included one-way analysis of variance to assess between-group differences and Spearman partial correlation analysis to evaluate associations.	(1) Plasma levels of Aβ42/40 (NC: 0.100±0.027, AD-MCI: 0.090±0.015, AD-D: 0.078±0.019), P-tau181 (NC: 1.287±0.652, AD-MCI: 2.892±1.288, AD-D: 2.574±0.777) and P-tau217 (NC: 0.078±0.061, AD-MCI: 0.724±0.487, AD-D: 0.842±0.499) were progressively increased with AD progressed. (2) From NC gradually progressing to the AD-D stage, cerebellar gray matter exhibited a "bilateral-heavy, midline-sparing" atrophy pattern, predominantly affecting most bilateral cerebellar hemispheres (excluding bilateral lobules VIII-X) and the lobules I-II of vermis (all p<0.05). (3) In AD patients, gray matter atrophy in bilateral cerebellar hemispheric lobules I-VI showed a significant positive correlation with plasma P-tau217 level, with the strongest association observed in AD-D group (all p<0.05). (4) The reduced gray matter volumes in multiple cerebellar regions were significantly correlated with the decreased score of Mini-Mental State Examination scale, Stroop Color-Word Test and Trail Making Test (all p<0.05).	Cerebellar atrophy increases as AD progresses, with a significant link to plasma P-tau217 level, particularly in advanced stages. This atrophy correlates with memory, executive function, and attention, suggesting cerebellar damage may reflect AD pathology and contribute to cognitive decline. These findings support the cerebellum's role in AD staging and as a potential imaging biomarker.	Van Rossem D, Allemeersch GJ, Barros N, et al. Assessing the link between cerebellar volume and cognitive function in Alzheimer's disease: a pilot study. Sci Rep. 2025;15(1):32943. Munoz-Musat E, Le Prince G, Delmaire C, Paquet C. Cerebellar atrophy in biologically confirmed Alzheimer's disease: Associations with amyloidopathy measured by cerebrospinal fluid biomarkers. J Alzheimers Dis. 2025;108(3):1204-1211.
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