

Similar Cognitive Trajectories but Faster Functional and MRI Decline in Amyloid-positive Alzheimer’s Disease With Pathogenic Variants

Jialu Bao¹, Yuyue Qiu², Jing Gao¹, Liling Dong¹, Chenhui Mao¹, Yuhua Jiang², Yuanhong Li², Tianyi Wang¹, Yunfan You¹, Shanshan Chu¹, Wei Jin¹

¹Peking Union Medical College Hospital, Beijing, China ²Chinese Academy of Medical Sciences & Peking Union Medical College, Beijing, China

AAIC 2026

Poster 2026-A-6949-AAIC

PUNCH • Memory Clinic Cohort

Contact: 1710122524@pku.edu.cn

RESEARCH HIGHLIGHTS

1 Cognition

MMSE, MoCA, AVLT and executive-function slopes were broadly similar by carrier status.

2 Function

P/LP carriers showed faster decline in activities of daily living.

3 MRI

Carriers showed accelerated atrophy and ventricular expansion over time.

Background & Objective

Pathogenic/likely pathogenic (P/LP) variants are established causes of familial and early-onset AD. With increasing clinical sequencing, such variants are also identified in amyloid-positive patients who present as apparently sporadic AD.

Question: do P/LP variants add prognostic information beyond amyloid positivity and cognitive trajectories?

Aim: compare longitudinal cognition, ADL, and structural MRI progression between P/LP carriers and non-carriers.

Study Design

A+ clinical AD cohort → WES → ACMG P/LP vs non-carriers → Longitudinal LMM

- Population: amyloid-positive patients with a clinical phenotype consistent with AD.
- Variant classification: ACMG criteria; VUS excluded from the carrier/non-carrier comparison.
- Outcomes: MMSE, MoCA, AVLT, executive function, ADL, cortical atrophy, and ventricular expansion.
- Models: linear mixed-effects models; primary parameter was time-by-carrier interaction.
- Covariates: age or age at onset, sex, education, APOE ε4 status, and baseline disease severity.

Primary Readouts

Cognition Global cognition and episodic-memory slopes

Function ADL decline over follow-up

MRI Regional cortical atrophy and ventricular expansion

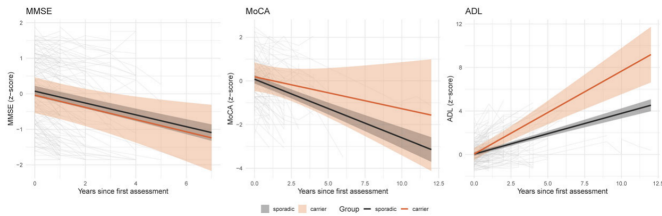
Notes

P/LP = pathogenic/likely pathogenic. A+ = amyloid-positive. WES = whole-exome sequencing. LMM = linear mixed-effects model.

Disclosure: J. Bao, none.

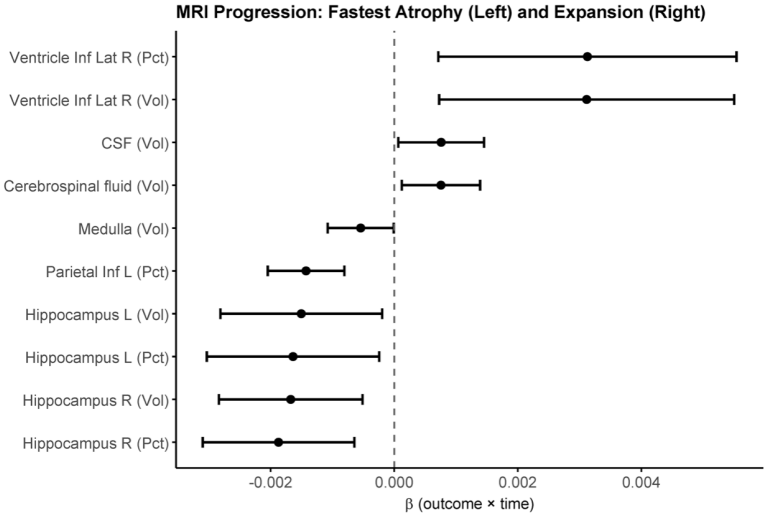
For final submission, replace figure panels with original high-resolution exports if available. Contact: 1710122524@pku.edu.cn

Result 1. Cognition appears similar; ADL separates



Key visual: the ADL panel shows the clearest carrier-related divergence, whereas global cognitive measures remain broadly similar.

Result 2. MRI progression is faster in P/LP carriers

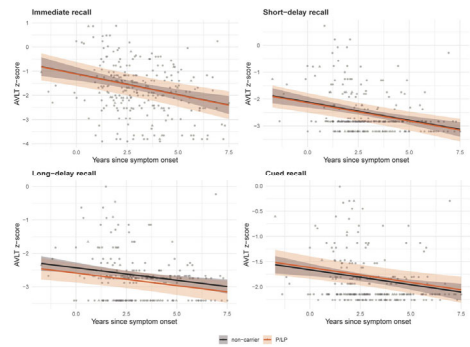


Interpretation: negative estimates indicate faster atrophy; positive estimates indicate faster ventricular/CSF expansion. The strongest signal is structural progression rather than global cognition.

Key Results

- No significant carrier-related difference in longitudinal MMSE, MoCA, AVLT episodic memory, or executive-function trajectories.
- P/LP carriers demonstrated faster functional decline on ADL over follow-up.
- Structural MRI showed accelerated neurodegeneration among carriers, including faster cortical atrophy and more rapid ventricular expansion.

Result 3. AVLT memory slopes remain broadly parallel



Memory subtests support the “similar cognition” part of the story.

Conclusion

Among amyloid-positive patients with clinically diagnosed AD, P/LP variant carriage was associated with faster functional decline and accelerated MRI-defined neurodegeneration, even when longitudinal cognitive trajectories appeared similar.

Genetic information may add prognostic value beyond amyloid status and cognitive measures.

- Use genotype to refine risk stratification.
- Monitor ADL and MRI progression when cognition alone is equivocal.
- Consider variant status when designing longitudinal studies.