

Regional amyloid accumulation and cognitive decline in initially amyloid-negative adults

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Study objective

To assess whether regional changes in amyloid burden over 4 years predict early episodic memory decline in initially amyloid-negative adults.

Summary results

Changes in amyloid burden in posterior cortical regions can predict early episodic memory decline in initially amyloid-negative adults.

What is known and what this paper adds

A recent longitudinal study detected an early synchrony between changes in global amyloid burden and memory decline in individuals who were initially assessed as being amyloid-negative. This study clarifies that these amyloid-related changes in memory are localized to posterior cortical regions, and that this relationship is apparent as early as middle age.

Participants and setting

This study examined 126 community-dwelling participants aged 30–89 years at baseline (58.7% female; mean baseline age, 63.16 ± 13.39 years) in the Dallas Lifespan Brain Study who were initially amyloid-negative and cognitively normal.

Design, size, and duration

The participants underwent baseline and 4-year follow-up assessments. At both assessments, episodic memory performance was assessed with the Hopkins Verbal Learning Test and the Cambridge Neuropsychological Test Automated Battery's Verbal Recognition Memory task, and amyloid burden was assessed with [^{18}F]-florbetapir PET. Standardized value uptake ratios (SUVRs) were calculated within 8 regions of interest (ROIs). General linear models (GLMs) were used to determine whether global and ROI-specific SUVR changes were associated with changes in z-transformed episodic memory scores.

Table GLM results for ROI-specific relationships between SUVR changes and episodic memory decline

| ROI | Whole cohort | Baseline ages of 30–59 y |
|----------------------------|------------------------|--------------------------|
| Posterior cingulate cortex | $F = 6.284; p = 0.014$ | $F = 8.613; p = 0.006$ |
| Precuneus | $F = 7.948; p = 0.006$ | $F = 9.665; p = 0.004$ |
| Lateral parietal cortex | $F = 6.211; p = 0.014$ | $F = 12.074; p = 0.001$ |

Main results and the role of chance

ROI-specific relationships between SUVR changes and episodic memory decline were detected in the posterior cingulate cortex, the precuneus, and the lateral parietal cortex in the whole cohort (aged 30–89 years), and remained when restricted to younger individuals aged 30–59 years.

Bias, confounding, and other reasons for caution

Declines in SUVR over time that contribute to the observed linear effects may reflect noise related to blood flow and nonspecific binding and having only 2 timepoints limited measurement reliability. Reverse causality cannot be ruled out. Older participants were more likely to be lost to follow-up, so effects might have been underestimated.

Generalizability to other populations

The reliance on data from community-dwelling volunteers with higher levels of education (mean 15.4 ± 2.14 years) may limit the generalizability of this study's results.

Study funding/potential competing interests

This study was funded by the NIH, the Alzheimer's Association, and Avid Radiopharmaceuticals. Avid also donated the tracer. The authors report no competing interests. Go to Neurology.org/N for full disclosures.

A draft of the short-form article was written by M. Dalefield, a writer with Editage, a division of Cactus Communications. The authors of the full-length article and the journal editors edited and approved the final version.

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