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Memory decline accompanies subthreshold amyloid accumulation

By: Landau, SM (Landau, Susan M.)^[1]; Horng, A (Horng, Andy); Jagust, WJ (Jagust, William J.)

Group Author(s): Alzheimer's Dis Neuroimaging

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Abstract

Objective

Extensive cortical beta-amyloid (A beta positivity) has been linked to cognitive decline, but the clinical significance of elevations in A beta within the negative range is unknown.

Methods

We examined amyloid and cognitive trajectories (memory, executive function) in 142 cognitively normal older individuals enrolled in the Alzheimer's Disease Neuroimaging Initiative who were A beta-negative at baseline and who had at least 2 [F-18]-florbetapir PET scans over 3.9 +/- 1.4 years. We determined whether A beta accumulation was associated with longitudinal changes in memory or executive function.

Results

Among baseline-negative individuals, florbetapir slope (mean annual increase 0.002 +/- 0.008 standardized uptake value ratio units/y) was not related to age, sex, education, APOE4 status, baseline memory or executive function, temporoparietal glucose metabolism, baseline hippocampal volume, or hippocampal volume change; but it was related to higher baseline cortical florbetapir, indicating that A beta accumulation was ongoing at baseline in those who accumulated during the study. Over the course of follow-up, 13 individuals converted to florbetapir+ and 14 nearly nonoverlapping individuals converted to mild cognitive impairment or Alzheimer disease. Amyloid accumulation among baseline-negative individuals was associated with poorer longitudinal memory performance (p = 0.019), but it was not associated with changes in executive function. Reducing the sample to individuals with at least 3 timepoints to estimate the florbetapir slope strengthened the relationship further between florbetapir accumulation and memory decline (p = 0.007).

Conclusions

Memory decline accompanies A beta accumulation in otherwise healthy, A beta-negative older adults. Amyloid increases within the negative range may represent the earliest detectable indication of pathology with domain-specific cognitive consequences.

Keywords

KeyWords Plus: NEUROIMAGING INITIATIVE ADNI; MILD COGNITIVE IMPAIRMENT; WHITE-MATTER REFERENCE ALZHEIMER DISEASE COMPOSITE SCORE COMPOUND B PET NEURODEGENERATION

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