Associations of Stages of Objective Memory Impairment With Amyloid PET and Structural MRI

The A4 Study

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Study Question
Is there an association between the Stages of Objective Memory Impairment (SOMI) system and neuroimaging biomarkers of Alzheimer Disease (AD)?

What Is Known and What This Paper Adds
The SOMI system distinguishes retrieval impairment (SOMI 0–2) observed in preclinical AD from memory storage impairment that occurs later in the AD continuum (SOMI 3–4). SOMI is highly associated with likelihood of AD neuropathologic change and neurofibrillary tangle pathology. This study provides Class I evidence that, in normal elderly, higher stages of memory impairment assessed using FCSRT were associated with higher amyloid imaging burden and lower volume of hippocampus, entorhinal cortex, and inferior temporal lobes.

Methods
Cross-sectional data from 4,484 cognitively unimpaired participants from the Anti-Amyloid Treatment in Asymptomatic Alzheimer’s (A4) study were used. A4 is a multicenter, secondary prevention clinical trial being conducted in the US, Canada, Australia, and Japan. Cognitively normal participants, defined by CDR = 0, MMSE score of 25–30 and delayed story recall of 6–18 were eligible to proceed to screening. All participants had amyloid PET imaging at screening and a subset of 1,262 β-amyloid positive (Aβ+) individuals had structural MRI scans. Volumetric measures of different cortical and subcortical regions were calculated automatically using FreeSurfer 6.0. SOMI stage was determined by free recall (FR) and total recall (TR) scores on the picture version of the Free and Cued Selective Reminding Test with Immediate Recall. We used analysis of covariance to compare biomarker values of SOMI groups accounting for age, sex, education, and APOE4 status. Post-hoc pairwise comparisons with Sidak correction were performed to assess differences between groups defined by SOMI.

Results and Study Limitations
Participants had a mean age of 71.3 (SD = 4.6) years, were 40.6% male, and 32.3% were Aβ+. Individuals in higher SOMI stages had higher global amyloid SUVR (p < 0.001), reflecting concurrent storage and retrieval deficits. Those with higher SOMI stages had smaller hippocampal volumes (p = 0.003), entorhinal cortices (p < 0.05), and inferior temporal lobes (p < 0.05), but there were no differences in volumes between parahippocampal gyri.

Study limitations were that 3.4% of participants could not be classified into a SOMI stage, the high educational level of the participants, and the likelihood that the relationship between SOMI stage and MRI volumetrics would be weaker in a sample not screened for amyloid positivity.

Study Funding and Competing Interests
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