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Medial Temporal Tau Predicts Memory Decline in Cognitively Unimpaired Elderly

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Abstract : Alzheimer's disease (AD) can be detected in living people using in vivo biomarkers of amyloid-β (Aβ) and tau, even in the absence of cognitive impairment during the preclinical phase. [^{18}F]-MK-6420 is a high affinity positron emission tomography (PET) tracer that quantifies tau neurofibrillary tangles, but its ability to predict cognitive changes associated with early AD symptoms, such as memory decline, is unclear. Here, we assess the prognostic accuracy of baseline [18F]-MK-6420 tau PET for predicting longitudinal memory decline in asymptomatic elderly individuals. In a longitudinal observational study, we evaluated a cohort of cognitively normal elderly participants (n = 111) from the Translational Biomarkers in Aging and Dementia (TRIAD) study (data collected between October 2017 and July 2020, with a follow-up period of 12 months). All participants underwent tau PET with [^{18}F]-MK-6420 and Aβ PET with [^{18}F]-AZD-4694. The exclusion criteria included the presence of head trauma, stroke, or other neurological disorders. There were 111 eligible participants who were chosen based on the availability of Aβ PET, tau PET, magnetic resonance imaging (MRI), and APOEε4 genotyping. Among these participants, the mean (SD) age was 70.1 (8.6) years; 20 (18%) were tau PET positive, and 71 of 111 (63.9%) were women. A significant association between baseline Braak I-II [^{18}F]-MK-6240 SUVR positivity and change in composite memory score was observed at the 12-month follow-up, after correcting for age, sex, and years of education (Logical Memory and RAVLT, standardized beta = -0.52 (-0.82-0.21), $p < 0.001$, for dichotomized tau PET and -1.22 (-1.84-(-0.61)), $p < 0.0001$, for continuous tau PET). Moderate cognitive decline was observed for A+T+ over the follow-up period, whereas no significant change was observed for A-T+, A+T-, and A-T-, though it should be noted that the A-T+ group was small.Our results indicate that baseline tau neurofibrillary tangle pathology is associated with longitudinal changes in memory function, supporting the use of [^{18}F]-MK-6420 PET to predict the likelihood of asymptomatic elderly individuals experiencing future memory decline. Overall, [^{18}F]-MK-6420 PET is a promising tool for predicting memory decline in older adults without cognitive impairment at baseline. This is of critical relevance as the field is shifting towards a biological model of AD defined by the aggregation of pathologic tau. Therefore, early detection of tau pathology using [^{18}F]-MK-6420 PET provides us with the hope that living patients with AD may be diagnosed during the preclinical phase before it is too late.

Keywords : alzheimer's disease, braak I-II, in vivo biomarkers, memory, PET, tau
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