OBJECTIVES

Aβ accumulation starts almost two decades before the onset of the symptoms of Alzheimer’s Disease (AD). Given increasing evidence suggesting that sub threshold Aβ accumulation in older adults is biologically relevant, we sought to investigate different markers of AD in relation with varying amount and spread of Aβ burden in asymptomatic individuals at risk of AD.

PARTICIPANTS

One hundred and twenty-nine cognitively unimpaired individuals with a family history of AD (PREVENT-AD cohort) underwent Aβ (11C)Nav4694 and tau (18F)(AV1451) PET scans. We assessed the cognition with the RBANS (both cross-sectionally and longitudinally) and Subjective Cognitive Decline Score.

We used Gaussian-mixture models to create region-specific thresholds of Aβ positivity in seven regions identified previously to be sensitive to early Aβ accumulation (Villeneuve et al, Brain, 2015). Individuals who were Aβ-positive in all regions were classified as the Regional Aβ group, while others were considered Aβ-negative. The Regional Aβ group had elevated tau-PET binding in the entorhinal cortex and middle temporal gyrus when compared with the Aβ-negative group. The Widespread Aβ group had elevated tau PET signal compared with the two other groups across all seven regions investigated. (p<0.05; **p<0.01; ***p<0.001)

PATTERN OF 18F(AV1451 BINDING ACROSS INDIVIDUALS

These figures represent the vowel-wise correlations between Tau-PET signal binding and local Aβ-PET for our 3 groups. Regardless of the Aβ region, associations for the Aβ negative and Regional Aβ groups occur in non-tau regions suggesting unspecific binding. When the Widespread Aβ group is included, vowel-wise analyses show a consistent pattern across the 7 regions of interest.

CONCLUSIONS

Elevated tau-PET signal outside of the entorhinal cortex and measurable cognitive decline are detected when Aβ deposition is widespread across the cortex. It is hard to detect any change in the Regional Aβ group because the Prevent-AD cohort is quite young and longitudinal follow-up is required in order to investigate whether they will progress to the Widespread Aβ group and show cognitive decline over time.