Background and Objectives

The role of early cortical tau accumulation in the pre-symptomatic stages of Alzheimer’s disease (AD) remains unclear. In a cohort of cognitively normal, late-middle-aged individuals at increased risk of developing AD, we used Positron Emission Topography (PET) imaging to investigate the relationships between cortical tau and cortical beta-amyloid (Aβ), cerebrospinal fluid phosphorylated tau (p-tau), and cognitive performance.

Methods

Participants

- One hundred and nineteen (119) cognitively normal older adults with a familial history of AD

PET Imaging

Siemens HRRT PET scanner

- Standardized uptake value ratios (SUVRs) were calculated from 35 non-atrophic Desikan regions using the cerebellum grey matter (tau-PET) and inferior cerebellum grey matter (Aβ-PET) as the reference region.

Biomarker Positivity

Cerebrospinal Fluid P-tau

- Subsample of 59 subjects also underwent a lumbar puncture
- Immunoassay (Fujirebio, Ghent, Belgium) used to assess phosphorylated tau levels

Cognitive Assessment

- Repeatable Battery for the Assessment of Neurocognitive Status (RBANS)

Statistics

- ROI-based analyses of AV-1451 binding
- Lasso regressions adjusted for age and sex
- P-values corrected with use of 1000 permutations

Results

1) There is higher AV-1451 binding in AD-typical regions in Aβ-positive individuals.

2) Higher AV-1451 binding in AD-typical regions is associated with higher CSF p-tau levels.

3) Higher AV-1451 binding in AD-typical regions is associated with worse cognitive performance.

Conclusions

These findings indicate that, even in cognitively normal adults with relatively low AV-1451 SUVRs, AV-1451 binding in AD signature regions is significantly increased among Aβ-positive individuals. Higher tau binding is also associated with higher CSF p-tau and lower cognition. Except for the association with cognition, these findings were still present when removing the seven individuals with the highest levels of tau (classified as tau-positive individuals), supporting the idea that very early elevation in tau-PET signal is clinically meaningful.

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