Neuroimaging: Understanding tau progression

Predicting future rates of tau accumulation on PET

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Abstract

**Background:** Our objective was to identify variables available in a research setting that predict future rates of tau PET accumulation separately among individuals who were either cognitively unimpaired or cognitively impaired.

**Method:** All 337 participants in this study were enrolled in one of the three longitudinal cohort studies at the Mayo Clinic that include serial tau PET scanning. For inclusion a person must have had a baseline study visit with MRI, amyloid PET, and tau PET exams, had at least one follow-up tau PET exam, and have met clinical criteria for membership in one of two clinical diagnostic groups - cognitively unimpaired (n=203) or cognitively impaired (n=134, a combined group of participants with either mild cognitive impairment or dementia with Alzheimer clinical syndrome). A temporal lobe tau PET meta-region of interest (ROI) was used in our primary analysis but we also examined four additional tau PET ROIs. Linear mixed effects models where used to estimate associations between age, sex, education, APOE genotype, amyloid and tau PET SUVR, cognitive performance, cortical thickness, and white matter hyperintensity volume at baseline, and the rate of subsequent tau PET accumulation. Log-transformed tau PET SUVR was used as the response and rates were summarized as annual percent change.

**Result:** In the cognitively unimpaired group only higher baseline amyloid PET was a significant independent predictor (i.e. in a multivariable model) of higher tau accumulation rates in the temporal meta-ROI (p<0.001). In the cognitively impaired group, younger age (p=0.02), higher baseline amyloid PET (p=0.05), APOE ε4 (p=0.05), and better cognitive performance (p=0.05) were significant independent predictors of higher tau accumulation rates in the temporal meta-ROI.

**Conclusion:** While we examined many possible predictor variables, the main independent predictor of high tau PET accumulation rates in cognitively unimpaired persons was amyloidosis. In contrast, in cognitively impaired individuals imaging and clinical variables that are consistent with early onset Alzheimer’s disease phenotype (younger age, amyloidosis, higher tau, APOE, less severe cognitive impairment) were associated with higher rates of tau PET accumulation suggesting this may be a highly advantageous group in which to conduct clinical trials that target tau-related mechanisms.