Tau levels are higher in objective subtle cognitive decline, but not subjective memory complaint

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Abstract

Background: The 2018 NIA-AA Alzheimer’s disease (AD) Research Framework states that subtle cognitive decline in cognitively unimpaired individuals can be measured by subjective report or evidence of objective decline on neuropsychological measures. Both subjective memory complaint (SMC) and objective subtle cognitive decline (Obj-SCD) have been shown to be associated with future cognitive decline and AD biomarkers. We examined whether there are tau PET differences in a) SMC- vs. SMC+ participants, b) Obj-SCD- vs. Obj-SCD+ participants, and c) participants with overlapping/discrepant SMC and Obj-SCD classifications.

Method: Participants without MCI or dementia from the Alzheimer’s Disease Neuroimaging Initiative (ADNI; n = 236) were classified at baseline as positive or negative for SMC (SMC- n = 77; SMC+ n = 159) based on the first 12 items of the Cognitive Change Index and/or classified as positive or negative for Obj-SCD (Obj-SCD- n = 173; Obj-SCD+ n = 63) based on previously defined neuropsychological criteria. Analyses of covariance, adjusting for age, sex, APOE ε4 status, and pulse pressure, examined group differences in tau PET (AV-1451) using a composite SUVR for regions consistent with Braak stage III/IV. Chi-squared tests examined tau positivity rates across groups.

Result: Obj-SCD+ participants had higher tau levels (p = .035, ηp² = .019) and higher rates of tau positivity (15.8% Obj-SCD- vs. 30.2% Obj-SCD+) than Obj-SCD- participants. Neither tau levels (p = .381, ηp² = .003) nor tau positivity rates (18.2% SMC- and 20.1% SMC+) differed for SMC groups. There was little agreement between SMC and Obj-SCD (42%; η = 0.01, p = .811). Participants with only Obj-SCD had the highest tau PET levels and differed from participants with only SMC (p = .022). Tau levels in SMC+/Obj-SCD+ participants did not differ from those with only Obj-SCD (p = .216). Tau positivity rates across SMC-/Obj-SCD-, SMC+/Obj-SCD-, SMC-/Obj-SCD+, and SMC+/Obj-SCD+ groups were 10.5%, 18.1%, 40.0%, and 25.6%, respectively.

Conclusion: Participants with Obj-SCD had greater tau burden than those without Obj-SCD, but SMC was not associated with higher tau levels. The combination of SMC and Obj-SCD did not have higher tau levels than Obj-SCD alone. Findings add to the evidence that the Obj-SCD classification is associated with AD biomarkers and faster cognitive decline in ADNI participants, but further work is needed to validate this approach in more representative/diverse cohorts.
Figure 1. Residual Braak III/IV SUVR by a) SMC status and b) Obj-SCD status. Covariates included age, education, sex, APOE ε4 carrier status, and pulse pressure. *p<.05

Figure 2. Residual Braak III/IV SUVR by overlapping/discrepant SMC and Obj-SCD classifications. Covariates included age, sex, APOE ε4 carrier status, and pulse pressure. *p<.05