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Examining the effects of sex and age on tau PET binding in the absence of beta-amyloid pathology

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Abstract

Background: Tau PET imaging is an established tool for studying Alzheimer Disease but its sensitivity to primary age-related tauopathy (PART) as well as sex effects in individuals without abnormal levels of amyloid are unknown.

Methods: Cross-sectional data were collected from 2014 to 2019 in 144 cognitively normal younger, middle-aged, and older adults free from amyloid pathology as quantified using PET. Regional values of tau PET binding were measured using flortaucipir. Statistical models examined the main effects of increasing age, sex, race, and sub-threshold levels of amyloid. Secondary analyses also examined the relationship between tau PET binding and iron as measured using T2* weighted imaging and calcification as measured using CT.

Results: There were significant positive associations between tau binding and age in 19 regions, with the largest effects seen in the inferior temporal cortex (t=4.59), caudate (t=9.58), and putamen (t=12.57). Iron as measured using T2* imaging mediated only a modest (11.9%) amount of the association between age and tau binding. Elevated tracer uptake in females was present in 23 regions in frontal, lateral parietal, and temporal regions including, most prominently the rostral middle frontal gyrus (t=7.48), superior temporal gyrus (t=5.12) and the inferior temporal gyrus (t=4.22). There were no significant effects of race or sub-threshold levels of amyloid.

Conclusions: Tau PET is sensitive to primary effects of age in regions consistent with the neuropathological definition of PART although strong age effects in regions of off-target binding were also present. There was a robust effect of sex, suggesting prior observations of elevated binding in women is not solely a potentiation of Alzheimer pathology but instead represents an ubiquitous phenomenon. Understand how both sex and age impact tracer binding is critical to understanding the utility of PET tracers as well as interpreting tracer values in the context of disease.

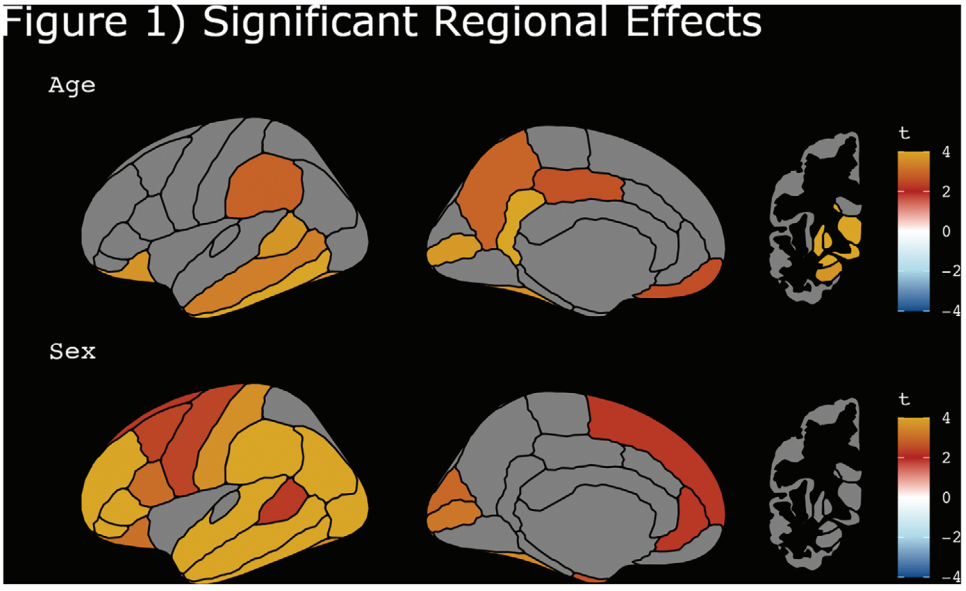

Figure 2) Regional Effects of Sex