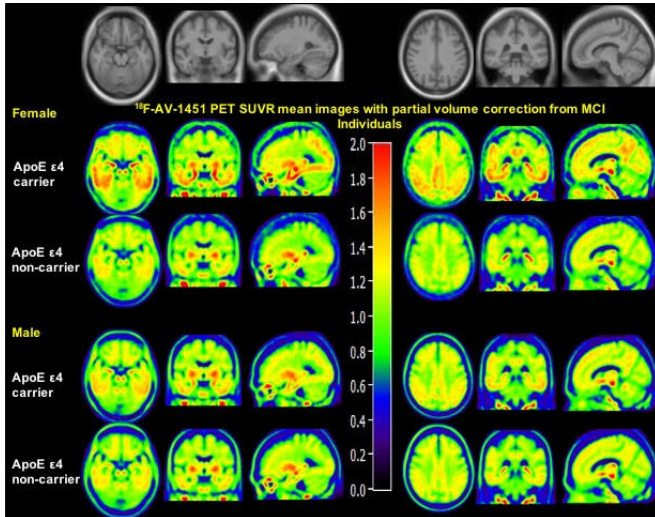


# Alzheimer's disease: Sex affects tau accumulation in the brain

24 June 2019



Sex Modulates the ApoE  $\epsilon$ 4 Effect on 18F-AV-1451 Tau PET. Credit: Paranjpe M, Liu M, Paranjpe I, et al.

The strongest genetic risk factor for Alzheimer's disease is the apolipoprotein E type 4 allele (ApoE  $\epsilon$ 4). Research presented by Manish Paranjpe at the 2019 Annual Meeting of the Society of Nuclear Medicine and Molecular Imaging (SNMMI) used positron emission tomography (PET) to show that women who are ApoE  $\epsilon$ 4 carriers and already experiencing mild cognitive impairment are more susceptible than men to tau accumulation in the brain.

"Sex plays an important role in Alzheimer's [disease risk](#), with females having a higher lifetime risk of developing the disease and an increased vulnerability to genetic risk factors," points out Yun Zhou, who led the project at the Mallinckrodt Institute of Radiology, Washington University in St. Louis School of Medicine. He explains, "This is the first study to demonstrate that sex modulates the effect of ApoE  $\epsilon$ 4 on brain tau depositing, measured using 18F-AV-1451-PET imaging, in the [entorhinal cortex](#), amygdala, parahippocampal

gyrus, and posterior cingulate of the brains of patients with [mild cognitive impairment](#) (MCI). Strikingly, females experience greater ApoE  $\epsilon$ 4-associated increases in brain tau deposition in these regions compared to their [male counterparts](#)."

This cross-sectional study involved 131 cognitively normal (CN) elderly controls (66 women) and 97 MCI subjects (39 women) from the Alzheimer's Disease Neuroimaging Initiative (ADNI) database. The mean age of all was 77. Preprocessed 18F-AV-1451 PET images, T1-weighted structural MRI scans and demographic information were included. After downloading pre-processed images from ADNI, a partial volume correction method was applied on all PET images (improving spatial resolution and contrast), and structural MRIs were used for PET spatial normalization. All [statistical analyses](#) were performed after controlling for baseline age and education.

In addition to finding women with the ApoE  $\epsilon$ 4 mutation more susceptible than men to tau accumulation, Zhou notes: "Our study also confirmed that sex does not modulate the ApoE  $\epsilon$ 4-associated tau deposition in the brains of cognitively normal elderly individuals, and it extends our understanding of how sex modulates the ApoE  $\epsilon$ 4 effect on tau deposition in the brains of individuals at the early stage of Alzheimer's disease."

Paranjpe adds, "Our results have implications for [clinical trials](#), biomarkers, and therapeutic development in Alzheimer's. In designing clinical trials aimed at an MCI cohort, potentially our study suggests that the dosage of anti-tau antibodies should be modified by ApoE  $\epsilon$ 4-sex group. Moreover, we hope that insights from our work will shed light on potential treatments for Alzheimer's disease, including sex-specific tau-targeted and ApoE-targeted drug development."

**More information:** Abstract 253: "Sex Modulates the ApoE  $\epsilon$ 4 Effect on Tau 18F-AV-1451 PET Imaging in Individuals with Normal Aging and Mild Cognitive Impairment"

Provided by Society of Nuclear Medicine and  
Molecular Imaging

APA citation: Alzheimer's disease: Sex affects tau accumulation in the brain (2019, June 24) retrieved 29 November 2020 from <https://medicalxpress.com/news/2019-06-alzheimer-disease-sex-affects-tau.html>

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