



PET method discriminates Alzheimer's from other brain disorders



New research finds that, among patients with established diagnoses at a memory disorder clinic, [18F]flortaucipir positron emission tomography (PET) was able to discriminate Alzheimer's disease from other neurodegenerative diseases. The accuracy and potential utility of this test in patient care require further research in clinically more representative populations, according to investigators.

"In this multicentre cross-sectional study that included 719 participants, the use of [18F]flortaucipir PET had an estimated sensitivity of 89.9% and specificity of 90.6% for Alzheimer's disease versus other neurodegenerative diseases, and outperformed established volumetric magnetic resonance imaging measures," says the study published in JAMA.

Distinguishing Alzheimer's disease (AD) dementia from other neurodegenerative disorders often poses a diagnostic challenge to clinicians due to substantial overlap in symptoms across etiological entities. Using biomarkers of amyloid- β ($A\beta$) and neurodegeneration has been proposed to support the clinical diagnosis. However, $A\beta$ pathology already starts accumulating 15 to 30 years before symptom onset. The prevalence of $A\beta$ pathology consequently rises steeply with advancing age, which results in high rates of (comorbid) $A\beta$ positivity in non-AD neurodegenerative disorders and cognitively normal elderly individuals, reducing the specificity of $A\beta$ biomarkers.

The PET tracer [18F]flortaucipir allows in vivo quantification of paired helical filament tau, a core neuropathological feature of AD, but its diagnostic utility is unclear. The JAMA study sought to determine the discriminative accuracy of [18F]flortaucipir PET for AD dementia versus other neurodegenerative disorders, compare [18F]flortaucipir with established MRI markers, and examine the diagnostic performance of [18F]flortaucipir at the prodromal (mild cognitive impairment [MCI]) stage of AD.

The study included 719 participants who were recruited from three dementia centres in South Korea, Sweden, and the U.S. between June 2014 and November 2017 (160 cognitively normal controls, 126 patients with MCI, of whom 65.9% were $A\beta$ positive, 179 patients with AD dementia, and 254 patients with various non-AD neurodegenerative disorders). The index test was the [18F]flortaucipir PET standardised uptake value ratio (SUVR) in five predefined regions of interest (ROIs). Cutoff points for tau positivity were determined using the mean +2 SDs observed in controls and Youden Index for the contrast AD dementia versus controls.

Among 719 participants, the overall mean (SD) age was 68.8 (9.2) years and 48.4% were male. The proportions of patients who were $A\beta$ positive were 26.3%, 65.9%, 100%, and 23.8% among cognitively normal controls, patients with MCI, patients with AD dementia, and patients with non-AD neurodegenerative disorders,

respectively.

[18F]flortaucipir uptake in the medial-basal and lateral temporal cortex showed 89.9% (95% CI, 84.6%-93.9%) sensitivity and 90.6% (95% CI, 86.3%-93.9%) specificity using the threshold based on controls (SUVR, 1.34), and 96.8% (95% CI, 92.0%-99.1%) sensitivity and 87.9% (95% CI, 81.9%-92.4%) specificity using the Youden Index–derived cutoff (SUVR, 1.27) for distinguishing AD dementia from all non-AD neurodegenerative disorders.

Additionally, the AUCs for all five [18F]flortaucipir ROIs were higher (AUC range, 0.92-0.95) compared with the three volumetric MRI measures (AUC range, 0.63-0.75; all ROIs $P < .001$). Diagnostic performance of the five [18F]flortaucipir ROIs were lower in MCI due to AD (AUC range, 0.75-0.84).

While MRI, A β PET, and cerebrospinal fluid (CSF) are increasingly used as add-ons to clinical examination in patients with cognitive impairment, the utility of [18F]flortaucipir PET as a diagnostic biomarker has yet to be defined. Due to the limited specificity, A β biomarkers are often used to rule out rather than rule in a diagnosis of AD. Notably, due to the tight temporal association of AD-like tau pathology with clinical manifestation of the disease, [18F]flortaucipir may have higher discriminative accuracy in older populations compared with A β biomarkers.

"This is supported by the current study showing higher specificity for [18F]flortaucipir in discriminating AD dementia from non-AD cases and controls compared with A β status," the authors say. "Accordingly, an intended clinical use of [18F]flortaucipir PET might be to improve the diagnostic workup as an add-on test to A β biomarkers in patients with early-onset dementia and possibly as a triage or even replacement test in patients with late-onset dementia in whom incidental A β pathology is common."

Source: [JAMA](#)

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