Evaluating Alzheimer Disease With Flortaucipir and Florbetapir PET

A Clinical Case Series

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Abstract: Early, accurate diagnosis of Alzheimer disease (AD) is essential but remains challenging. Neuropathological hallmarks of AD are β-amyloid neuritic plaques and tau protein neurofibrillary tangles. ^{18}F-Florbetapir is one of several available PET tracers for imaging cortical fibrillary β-amyloid plaques. ^{18}F-Flortaucipir PET was recently approved for evaluating the distribution and density of aggregated neurofibrillary tangles. We present cases of mild cognitive impairment or suspected AD to depict the nuances of flortaucipir distribution and scan interpretation as well as how combined information from amyloid and tau PET may help with differential diagnosis and prognosis.

Key Words: Alzheimer disease, mild cognitive impairment, biomarkers, tau protein, PET imaging

(*Clin Nucl Med* 2021;46: 605–608)

Received for publication October 29, 2020; revision accepted November 13, 2020.

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Conflicts of interest and sources of funding: none declared.

Subjects in this study were enrolled and scanned, after written informed consent, as part of a longitudinal study funded by Avid. P.M.D. and T.Z.W. have served as an advisor and received research grants from Avid as well as several other companies. T.Z.W. served on the advisory board for Eli Lilly (Amyvid). P.M.D. owns shares in several companies whose products are not discussed here, is a coinventor on several patents that are not discussed here, and serves on the boards of several organizations.

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ISSN: 0363-9762/21/4607–0605
DOI: 10.1097/RLU.0000000000003493

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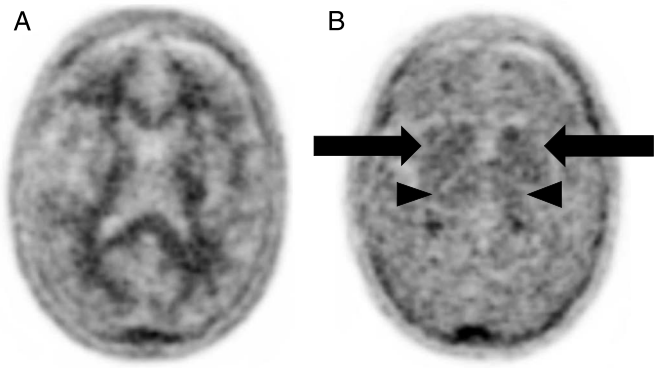

FIGURE 1. Negative amyloid and tau scans. This 68-year-old woman had normal cognition over 5 years follow-up. Florbetapir-PET (**A**) showed normal gray/white matter differentiation. Flortaucipir-PET (**B**) demonstrates physiologic basal ganglia (arrows) and thalami uptake (arrowheads), without cortical accumulation. Twenty percent to 40% of cognitively normal elderly with an apolipoprotein E4 genotype may have positive amyloid or tau scans.[1–5] Individuals with preclinical AD[5] may have a greater risk for future cognitive decline.[2,6]

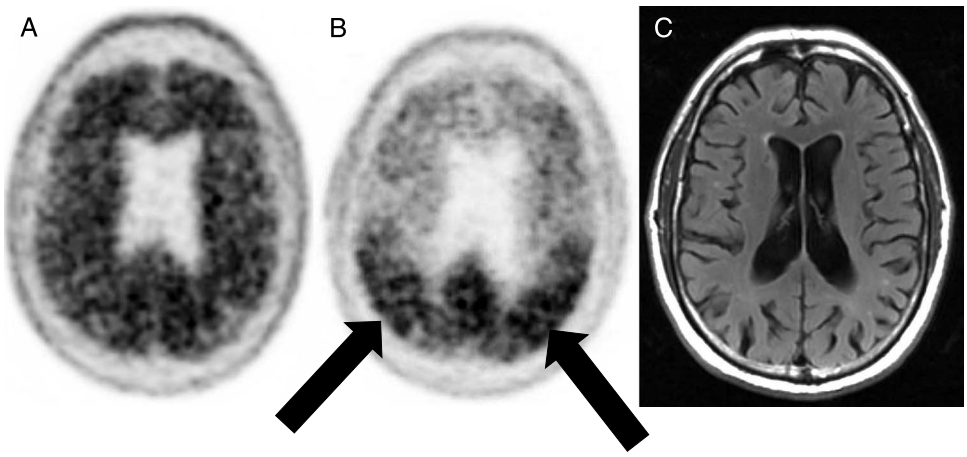

FIGURE 2. Positive amyloid and tau scans. This 70-year-old man has a 4-year history of memory impairment and a strong family history of Alzheimer disease (AD). Florbetapir-PET (**A**) shows loss of gray/white matter differentiation. His flortaucipir-PET (**B**) shows symmetric bilateral intense parietal lobe accumulation (arrows) typical for AD.[7] MRI (**C**) was normal for age. He received cholinesterase inhibitor therapy. He progressed over 4 years to advanced dementia. Flortaucipir-PET has a sensitivity of 89.9% and specificity of 90.6% for discriminating AD from other neurodegenerative diseases.[8]

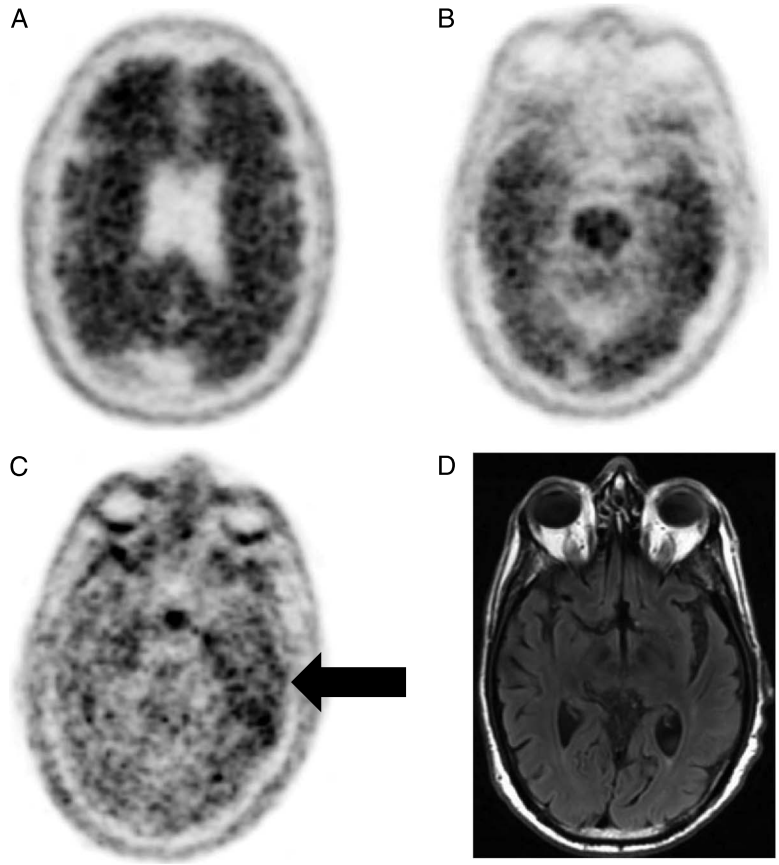

FIGURE 3. Slowly progressive dementia. A 71-year-old man with an apolipoprotein E4/4 genotype and mild memory loss over 3 years. Florbetapir-PET (**A** and **B**) demonstrates loss of gray/white matter differentiation.[9] His flortaucipir-PET (**C**) indicated left temporal lobe tau accumulation (arrow) without MRI abnormality (**D**). At 18-month follow-up, he showed very little decline but over 5 years, he progressed to moderate dementia due to AD.

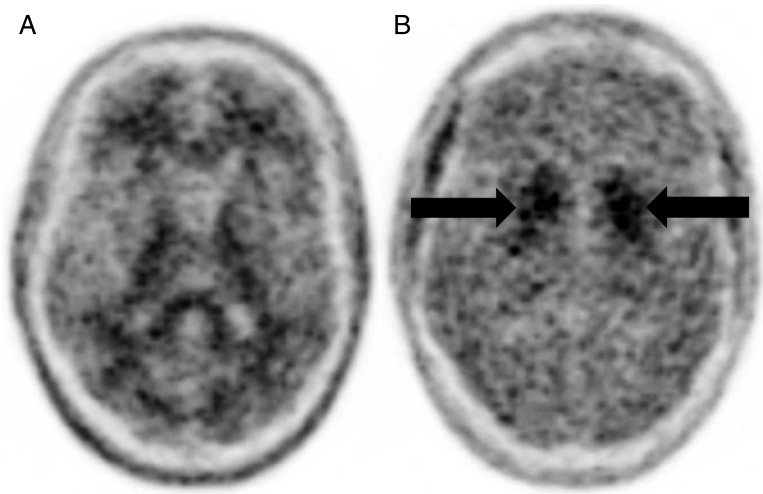

FIGURE 4. Nonprogressive memory loss. This 71-year-old man with a 6-year history of short-term forgetfulness was diagnosed 3 years ago with probable AD. Florbetapir-PET (**A**) demonstrated normal gray/white matter differentiation. Flortaucipir-PET (**B**) demonstrated incidental prominent bilateral basal ganglia uptake (arrows). At 3-year follow-up, there was no further decline. A prior study reported that negative amyloid PET had a 90% negative predictive value for 36-month cognitive decline.[6]

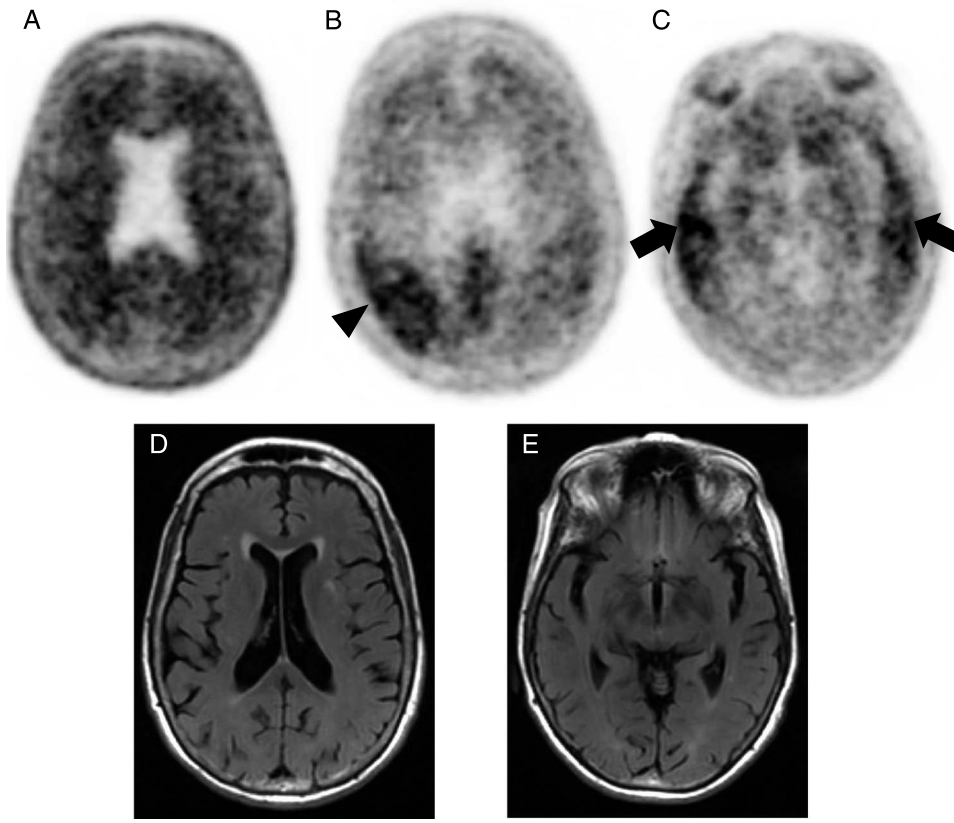

FIGURE 5. Prodromal AD. An 80-year-old woman with 1-year of memory loss was diagnosed with mild cognitive impairment (MCI). Florbetapir-PET (**A**), demonstrating loss of gray/white matter differentiation, was amyloid positive. Flortaucipir-PET (**B** and **C**) indicated abnormal distribution in the bilateral temporal (arrows) and right parietal lobes (arrowhead). This supports AD.[7,8] T2 FLAIR (**D** and **E**) demonstrate no significant temporal or parietal lobe abnormalities. Her cognition and functioning rapidly declined despite symptomatic therapy. Two years later, she entered a long-term memory care facility. MCI patients with positive PET examinations have a greater risk for future cognitive decline.[2,6]

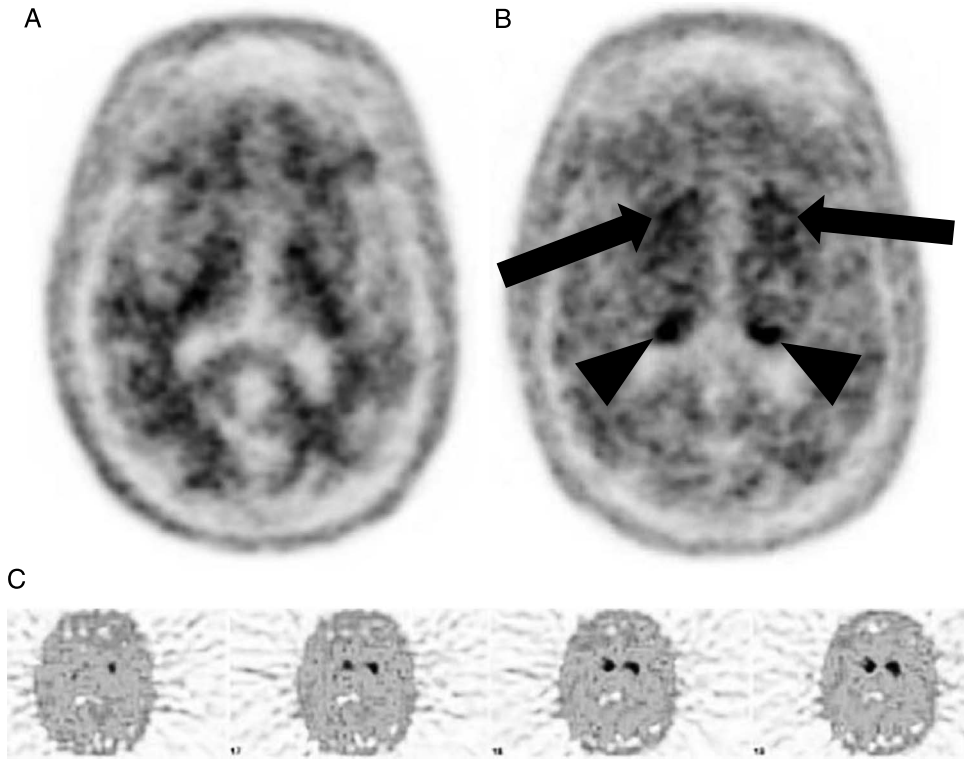

FIGURE 6. Nonprogressive memory loss. A 72-year-old man was diagnosed with MCI. Florbetapir-PET (**A**) shows normal gray/white matter differentiation. Flortaucipir-PET (**B**) showed nonspecific symmetric bilateral basic ganglia (arrows) and thalamic uptake (arrowheads). Tau accumulation was negative. Over the next 4 years, his cognition remained unchanged. He had also developed tremors, and ^{123}I DaTscan SPECT (**C**) revealed bilateral putamina decreased uptake, left greater than right, suggestive of Parkinson disease. Over the next 4 years, his cognition did not worsen, and carbidopa plus levodopa therapy greatly improved his symptoms. The utility of flortaucipir to image midbrain neuromelanin[10] and discriminate Parkinson disease from progressive supranuclear palsy is under investigation.[11]