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[^{18}F]FEOBV PET imaging of the cholinergic neurotransmission system: An early biomarker of Alzheimer's risk

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In collaboration with the VUMC Radiochemistry core, we have developed a complete path to the production of a novel PET radiotracer, known as [^{18}F]FEOBV, which exhibits high binding affinity and specificity for presynaptic vesicular acetylcholine transporters. [^{18}F]FEOBV enables the in-vivo assessment of the brain cholinergic integrity. As part of a pilot study, we conducted [^{18}F]FEOBV scans on 6 postmenopausal women (age: 58 $\pm$ 6) who had completed baseline Alzheimer's disease (AD) biomarker assessments, including Aβ PET (with [^{18}F]florbetapir). The global [^{18}F]FEOBV uptake declined with aging, and was also lower in two participants who were Aβ+. We found a significant association between [^{18}F]FEOBV uptake and the volume of the nucleus basalis of Meynert on subjects' structural MRI (β=2.37, p-value = 0.042*). Throughout the progression of AD, the most consistent neuronal losses are seen in cholinergic neurons, where these losses negatively affect attention, learning, and memory formation. In the past, a lack of direct/specific biomarker of cholinergic integrity has posed a barrier to the in-vivo assessment of this key brain process. [^{18}F]FEOBV may be used an early in-vivo biomarker of Alzheimer's risk and identify individuals who may benefit the most from standard and novel pro-cholinergic treatments.

Acknowledgment: This study was funded by the TIPS Award from Vanderbilt Brain Institute.