

[3P]Alzheimer's Disease and Dementia

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Videos are available throughout the meeting period.*[3P-210]Assessment of reactive astrogliosis in patients with Alzheimer's disease using novel PET tracer ¹⁸F-SMBT-1**

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Reactive astrocytes contribute to neurodegeneration throughout the course of Alzheimer's diseases (AD) and other neurodegenerative diseases. Reactive astrocytes overexpress monoamine oxidase-B (MAO-B) in the outer mitochondrial membrane. Elevation of MAO-B density in autopsy-confirmed AD brains has been observed in in vitro binding studies with selective MAO-B radioligands. For in vivo assessment of reactive astrogliosis in the human brain, we have recently developed a novel MAO-B PET tracer named ¹⁸F-SMBT-1. SMBT-1 showed high binding affinity to MAO-B (K_d = 3.7 nM), and low binding affinity to other enzymes, receptors and misfolded proteins such as amyloid- β and tau. The amount of ¹⁸F-SMBT-1 binding was greater in AD brains than in control brains and consistent with MAO-B density. We performed a first-in-human study of ¹⁸F-SMBT-1 in Austin Health. Nine participants including 5 healthy elderly controls and 4 AD patients underwent ¹⁸F-SMBT-1 PET, amyloid PET with ¹⁸F-NAV4694 and tau PET with either ¹⁸F-MK6240 or ¹⁸F-PI2620. ¹⁸F-SMBT-1 retention were expressed as SUV or as tissue ratios using the cerebellar white matter as reference region. ¹⁸F-SMBT-1 yielded high contrast images at 60-90 min post injection. The spatial pattern of ¹⁸F-SMBT-1 binding was consistent with MAO-B density in postmortem brains. In AD patients, ¹⁸F-SMBT-1 retention was significantly elevated in parahippocampal, fusiform and inferior temporal gyrus and overlapped with amyloid- β and tau depositions. To confirm the selective binding ability of ¹⁸F-SMBT-1 to MAO-B, participants underwent a second ¹⁸F-SMBT-1 scan after treatment with selegiline. The result showed that ¹⁸F-SMBT-1 binding was completely displaced after treatment with selegiline, indicating high binding selectivity for MAO-B. From these results, we conclude that ¹⁸F-SMBT-1 is a highly selective MAO-B PET tracer, which will enable the assessment of reactive astrogliosis in human brain. Future longitudinal studies will clarify the time course of astrogliosis and its association with misfolded proteins in AD.