Characterization of a novel monoamine oxidase-B tracer [^{18}F]SMBT-1 for imaging of reactive astrocytes

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Astrocytes support the health of the brain, but reactive astrocytes are strongly associated with various neurodegenerative diseases, including the neurotoxic A1 astrocyte and neuroprotective A2 astrocyte, and an increase in their density has been demonstrated in Alzheimer's disease brains. Positron-emission tomography (PET) is a nuclear imaging technique, making it possible to follow-up changes in astrocytic activation in vivo, thereby tracing disease progression. Monoamine oxidase B (MAO-B) is one of the markers for imaging astrocytes, whose activity is expressed in plaque-associated astrocytes. Recently, we developed a selective and reversible tracer for MAO-B called [^{18}F]SMBT-1. Besides, [^3H]BU99008 is a tracer designed for another astrocyte marker called imidazoline 2 binding sites (I2BS). Therefore, the aim of this study was to characterize which phenotype of astrocyte does MAO-B exist in and whether [^{18}F]SMBT-1 can be used for imaging astrocytes.

Double immunostaining of MAO-B and C3d/S100A10, which is A1/A2 astrocyte marker, indicated that MAO-B was expressed in both A1 and A2 astrocytes. In vitro autoradiography for amyloid β , tau, and MAO-B in the same sections demonstrated the existence of MAO-B expressing astrocytes vicinity of amyloid plaque. Competitive binding assays with [^{18}F]SMBT-1 or [^3H]BU-99008 showed strong affinity of both tracers for human postmortem brain homogenates but different binding sites. Regional binding distribution revealed a stronger correlation between [^{18}F]SMBT-1 and GFAP than [^3H]BU-99008 and GFAP.

In conclusion, MAO-B is expressed in both A1 and A2 astrocyte, and [^{18}F]SMBT-1 is a useful PET tracer for imaging reactive astrocytes.