In vivo imaging of mouse models directed toward diagnosis and treatment of Alzheimer's disease

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Alzheimer’s disease (AD) is the most common neurodegenerative dementia afflicting a vast number of elderly people, and is neuropathologically characterized by formation of extracellular and intracellular amyloid lesions, termed senile plaques and neurofibrillary tangles, respectively, despite notable diversity of possible etiologies. Amyloid depositions emerge early in the pathogenesis of AD, and is mechanistically implicated in the neurodegenerative processes leading to neuronal death. Thus, neuroimaging technologies to visualize amyloid in living brains are conceived to make great contribution to diagnosis of AD at a prodromal stage, and evaluation of novel disease-modifying anti-amyloid treatments. In order to establish an experimental system allowing preclinical tests of diagnostic and therapeutic approaches to AD, we generated amyloid-binding radiotracer with high specific radioactivity, and applied it to high-resolution positron emission tomographic (PET) imaging of transgenic mice modeling senile plaques. Progressive amyloid accumulation during aging and elimination of amyloid following amyloid immunotherapy were successfully captured by longitudinal PET scans. It is also noteworthy that roles of neuroinflammatory response in the anti-amyloid treatment could be pursued by combined PET studies with radiotracers for amyloid and activated microglia. Meanwhile, our recent study on mouse models of neurofibrillary tangles has provided compelling evidence for critical involvement of microglial activation in neurodegeneration, indicating that dysregulated neuroinflammation may deteriorate neurofibrillary pathology. These observations collectively support the utility of in vivo imaging technology for animal models of AD in development of optimal imaging agents, which sensitively detect pathological hallmarks and/or provide measures of outcome and undesirable effects of potential therapies.