

PET Imaging with Pittsburgh Compound B and Subcortical Small Vessel Disease

Cerebrovascular disease is increasingly recognized as a cause of cognitive impairment in the elderly. The most prevalent form of vascular cognitive impairment is caused by subcortical small vessel disease. Manifestations of subcortical small vessel disease that can be quantified on MRI include white matter hyperintensities (WMH) and lacunar infarctions. There is accumulating evidence that these MRI lesions, once considered to be mostly “silent”, are in fact associated with cognitive impairment and cognitive decline. These lesions are common, potentially preventable with currently available therapeutic agents, and are therefore an ideal target for clinical trials aimed at preventing cognitive decline.

There are, however, many unresolved questions regarding the role of subcortical small vessel disease in cognitive decline. It is unclear whether subcortical small vessel disease is sufficient, on its own, to cause mild cognitive impairment (MCI) or dementia, or whether additional cofactors such as Alzheimer’s pathology must also be present. It is also unclear to what extent cerebral amyloid angiopathy (CAA), which may accompany Alzheimer’s disease (AD) and has been associated with large WMH volume, is a cause of WMH in the general population.

We propose to investigate the relationships between WMH and beta-amyloidoses (AD and CAA) using PET imaging with Pittsburgh Compound B (PET-PIB) as a marker of deposited beta-amyloid. Three study groups will be compared: mild cognitive impairment (MCI) subjects with extensive WMH, MCI subjects without extensive WMH, and probable CAA subjects. All subjects have had, or will undergo, PET-PIB imaging and advanced MRI with quantification of WMH. For the subjects with MCI and extensive white matter lesions, PET-PIB acquisition will be funded through this application. For the groups with 1) MCI without extensive WMH and 2) CAA, MRI and PET-PIB data will be used that is being collected by Co-Investigators as part of other funded studies. This multi-disciplinary cross-institutional grant brings together investigators from the MGH Dept of Neurology, MGH Dept of Radiology, MGH Dept of Psychiatry and Gerontology Research Unit, and the BWH Dept of Neurology.