to calculate white matter hyperintensity volume and total brain parenchyma volume by a blinded observer. Additionally, a subjective categorization of the distribution of white matter hyperintensity was assigned to each case by a blinded observer into one of three categories (central, peripheral, or mixed). Statistical analysis was performed to identify correlation between patterns of distribution, volume of hyperintensity, and presence/absence of disease and disease progression. Results: There was significant differences of the volume of hyperintensity with respect to distribution of disease within the normal (p = 0.002) and MCI (p = 0.046) subjects. There was a significant interaction (P = 0.020) between the assigned pattern of white matter disease distribution and the subject’s disease burden. There was no association (p = 0.221) between the disease status (normal controls, MCI with and without progression) and total volume of white matter hyperintensity, although this strengthened after adjusting for total parenchymal volume (p = 0.131).

Conclusions: The correlation between the pattern of brain white matter changes distribution and the disease status may help in determining which patients with MCI will be more likely to progress to dementia, therefore allowing directed therapy or better targeting of therapeutic trials. Additional characterization with a larger cohort including volumetric analysis of the white matter hyperintensity pattern and correlating with clinical diagnosis of metabolic syndrome could yield more specific resolution as to whether or not this can predict progression of MCI to dementia.

**P3-378 FIRST-IN-HUMAN PET STUDY WITH 18F-AM-PBB3 AND 18F-PM-PBB3**

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**Background:** Recent advancements of novel tau positron emission tomography (PET) ligands are shedding light on the nature of diverse tauopathies, such as Alzheimer's disease (AD), primary age-related tauopathy (PART), progressive nuclear palsy (PSP), corticobasal degeneration (CBD). Affinity and selectivity for distinct tau pathologies vary among diverse ligands. Our previous studies demonstrated that 11C-pyridinylbutadienyl-benzothiazole 3 (11C-PBB3) can detect a broad range of tau inclusions. However, there are several technical issue on the use of 11C-PBB3, including a relatively short half-life of 11C, limited dynamic range, metabolic instability and off-target binding in the basal ganglia and thalamus, hampering wider use and application to early detection of tau pathologies especially in PSP and CBD. To overcome these drawbacks of 11C-PBB3, we developed novel PBB3 derivatives, 18F-AM-PBB3 and 18F-PM-PBB3. The present study aims to investigate characteristics of in vivo PET imaging of these fluorinated tau radioligands.

**Methods:** A small-scale clinical PET study with 18F-AM-PBB3 or 18F-PM-PBB3 was performed for AD and age-matched cognitive healthy control (HC) subjects. Arterial blood sampling and free fraction measurements were performed after injection of 18F-AM-PBB3 and 18F-PM-PBB3. 11C-PiB and 18F-PET scans were also performed within one month. Parametric images of standardized uptake value ratio (SUVR) to the cerebellar cortex were generated for all radioligands on a voxel-by-voxel basis.

**Results:** Dynamic ranges of 18F-AM-PBB3 and 18F-PM-PBB3 for detection of AD tau lesions were about 1.5- and 2-fold higher, respectively, than that of 11C-PBB3. Regional distribution of specific binding was similar among these three ligands. Off-target binding of 11C-PBB3 was noticeable in the basal ganglia and thalamus, while 18F-AM-PBB3 and 18F-PM-PBB3 showed no prominent off-target signals in these regions. Binding to choroid plexus was conspicuous in 18F-PM-PBB3 and slightly noticeable in 18F-AM-PBB3, while 11C-PBB showed little off-target binding in this structure.

**Conclusions:** This study demonstrated that fluorinated PBB3 derivatives showed regional distribution of specific binding similar to 11C-PBB3, and broader dynamic range and less off-target binding to the basal ganglia and thalamus than 11C-PBB3. These findings support the potential utility of fluorinated PBB3 derivatives in non-AD tauopathies, which is currently being examined.

**P3-379 ALTERED FUNCTIONAL CONNECTIVITY OF THE BASAL NUCLEUS OF MEYNERT IN MILD COGNITIVE IMPAIRMENT: A RESTING-STATE FMRI STUDY**

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**Background:** Cholinergic dysfunction plays an important role in mild cognitive impairment (MCI). The basal nucleus of Meynert (BNM) provides the main source of cortical cholinergic innervation. Previous studies have characterized structural changes of the cholinergic basal forebrain in individuals at risk of developing Alzheimer’s disease. However, whether and how functional connectivity of the BNM (BNM-FC) is altered in MCI remains unknown.

**Methods:** One-hundred-and-eleven MCI patients and one hundred and seven HC’s underwent resting-state functional magnetic resonance imaging (rs-fMRI). Imaging data were processed with Statistical Parametric Mapping. BNM-FC was examined via correlation in low frequency fMRI signal fluctuations between the BNM and all other brain voxels. Group difference was tested by covariance analysis to control for age, gender, and years of education. Pearson regression was conducted to evaluate the relationship between the BNM-FC and clinical assessments.

**Results:** Compared with HCs, MCI group showed decreased BNM-FC in the right anterior cingulate cortex (ACC), right putamen, as well as left insula and dorsal striatum, including caudluma, putamen/pallidum and caudate. Further, greater decreases in BNM-FC to these regions were associated with more severe impairment in immediate and delayed recall in MCI patients.

**Conclusions:** MCI is associated with changes in BNM-FC to the ACC, putamen, insula and caudatum, in relation to cognitive impairments. These new findings may advance research of the cholinergic bases of cognitive dysfunction during...
health aging and in individuals at risk of developing Alzheimer’s disease.

P3-380 CHANGES IN WHITE MATTER INTEGRITY AND CEREBRAL BLOOD FLOW IN THE EPISODIC MEMORY NETWORK IN COGNITIVELY NORMAL OLDER ADULTS WITH β-AMYLOID PATHOLOGY

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Background: A large proportion of asymptomatic older adults present beta-amyloid (Aβ) deposition, a pathological hallmark of Alzheimer’s disease. Using multimodal neuroimaging measures, we assessed how Aβ deposition relates to resting-state cerebral blood flow (CBF) and white matter integrity (WMI) in brain regions critical for episodic memory among cognitively normal older adults.

Methods: We assessed cerebral blood flow and white matter integrity that were measured by arterial spin labeling and diffusion tensor imaging (DTI), respectively, in cognitively normal older adults who participated in the Alzheimer’s Disease Neuroimaging Initiative (ADNI). A level of Aβ deposition was quantified by 18F-Florbetapir positron emission tomography (PET). Forty and 47 cognitively normal older adults (mean age = 72.8, 25 females) were included for CBF and DTI results, respectively, and classified into either Aβ+ or Aβ− according to the criteria set by the ADNI processing pipeline. Effects of dichotomized and continuous Aβ measures on CBF and WMI in a priori regions of interest were assessed using analyses of covariance and multiple regression models. For behavioral measures, baseline scores and slopes representing longitudinal changes in the 11-item ADAS-cog and RAVLT immediate recall and percent forgetting were assessed and related to biomarker measures.

Results: Higher Aβ deposition was associated with lower CBF in entorhinal cortex but increased CBF in posterior cingulate cortex, the latter of which further predicted steeper longitudinal decline in RAVLT among Aβ+ older adults. Higher Aβ deposition was associated with significant reduction in white matter integrity in most association fibers including superior longitudinal fasciculus, inferior fronto-occipital fasciculus, cingulum, and body of corpus callosum. Conclusions: Despite cognitively normal status, clinically intact older adults undergo Aβ-related differences in both functional and structural brain measures. Cerebral blood flow and white matter tract integrity measures may serve as an early biomarker for amyloid pathology at the initial stage of Alzheimer’s disease. Longitudinal studies are warranted to address the directionality between these measures and amyloid pathology.

P3-381 FIRST EVALUATION OF THE NEUROFIBRILLARY TANGLES RADIOLIGAND [18F]MK-6240 IN ALZHEIMER’S DISEASE PATIENTS

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Background: Dementia correlates strongly with the extent of neurofibrillar tangles (NFT). We recently disclosed [18F]MK-6240, a potent and selective NFT radioligand designed to be more specific and sensitive than previously known NFT radioligands. Here, we present the clinical characterization of [18F]MK-6240 in Healthy Elderly subjects (HEs) and Alzheimer’s disease (AD) patients.

Methods: Enrollment consisted of 6 ADs (MMSE 11-28) and 4 HEs (MMSE 29). Participants were administered [18F]MK-6240 and dynamic PET scans were acquired for a minimum of 90 min and up to 150 min and standard uptake value (SUV) time-activity curves were generated. Arterial input functions were obtained for 3 HEs and 3 ADs and compartmental modelling allowed for measurement of regional volumes of distribution (Vr). Cerebellar cortex was used as the reference region for the assessment of SUV ratios (SUVRs) and distribution volume ratios (DVRs).

Results: In HEs, [18F]MK-6240 uptake in the brain was high (peak SUV ~ 5) and followed by a fast washout across all brain regions. In ADs, a similar high uptake occurred, however, a slower washout was observed in regions associated with the NFT deposits while a fast washout was observed in other brain regions. In ADs, Vr’s of NFT rich regions were ~ 2-3 fold higher than the rest of the brain or corresponding regions in healthy aging and in individuals at risk of developing Alzheimer’s disease.