Background: Cerebral white matter hyperintensities (WMH), detected in vivo with magnetic resonance imaging (MRI), are commonly used to assess cerebrovascular burden in cognitive impairment. However, the association between WMH and cognition is not consistent across the literature. We hypothesized that some determinants including cognitive reserve (CR) and age could modulate the effects of WMH on the risk of Mild Cognitive Impairment (MCI) or dementia. **Methods:** We followed 500 healthy subjects from a cohort of community-dwelling persons aged 65 years and over (ESPRIT Project). At baseline, WMH volume was measured using a semi-automatic method on T2-weighted MRI. Standardized cognitive and neurological evaluations were repeated after 2, 4 7, and 10 years. Stratified Cox proportional hazards models were run to predict incident dementia and Mild Cognitive impairment. **Results:** After adjustment for potential confounders, we found that CR and age have an impact on the relationship between WML and progression to dementia and MCI. 1) the association between severe WMH and increased MCI/dementia risk was significant in the low CR group (education $\leq$8 years) (p=0.02, HR= 3.77 [1.29-10.99]), but not in the high CR group (education >8 years) (p=0.82, HR=1.07 [0.61-1.87]). 2) the association between WMH volume and the risk of developing severe cognitive deterioration was significant in the younger group ($\leq$73 years) (p<0.01, HR= 1.03 [1.02-1.05]), but not in the older group (>73 years) (p=0.70, HR=1.01 [0.98-1.04]). **Conclusions:** These findings suggest that 1) the association between increasing WMH volume and cognitive deterioration becomes weaker with advancing age. These results have implications in clinical trials using WML as surrogate marker, in raising the question of relevance of such a marker in the old-old. 2) Subjects with higher CR level were seen to be more likely to be resilient to the deleterious effects of severe WMH. The CR hypothesis suggests several avenues for dementia prevention.

DT-01-06 BASELINE FDG-PET AND VOLUMETRIC MRI PREDICTS ALZHEIMER'S DISEASE CONVERSION FROM MILD COGNITIVE IMPAIRMENT: AN ADNI STUDY

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Background: The feasibility of using imaging based biomarker data in the early stage of the AD (or preclinical phase of AD) such as Mild Cognitive Impairment (MCI) due to AD has been investigated in multiple studies recently. In this study, using data from Alzheimer's disease neuroimaging initiative (ADNI), we examine baseline measurement of FDG-PET, structural MRI each alone and in combination with cognitive tests in distinguishing individuals with MCI who converted to AD and those who did not aiming to establish their usefulness in as predictors for progression to AD. **Methods:** Total of 139 ADNI participants who were diagnosed as MCI were included in this study. Among them, 78 (75.8$\pm$7.0 years old) developed incident AD during the subsequent 36 months, and the remaining (75.3$\pm$8.0) did not during the same period. All subjects had baseline FDG-PET and MRI data. In addition to voxel-wise analysis for each of the two imaging modalities, FDG-PET hypometabolic convergence index (HCI) and MRI hippocampal (HCV) volume were used each separately or in combination together also with Alzheimer's Dementia Assessment Scale-modified (ADAS-mod) to examine the statistical power in distinguishing the two groups using Receiver Operating Curve (ROC). **Results:** The two group did not differ in mean age, education and gender ratio. However, they differed significantly in APOE4 ratio (p=0.03) and cognitive tests (ADAS-MOD p=1.1e-9, AVLT-LTM p=3.7e-7, MMSE p=0.001). Voxel-based analysis for both baseline FDG PET and MRI VBM demonstrated reduced glucose uptake and regional gray matter volumes in converters compared to non-converters in the anterior cingulate, medial prefrontal cortex, posterior cingulate and precuneus regions. HCI, HCV and ADAS-mod each separately distinguished converters from non-converters (sensitivity/specificity =80%/64%, 78%/71% and 70%/64% for HCI, HCV and ADAS-mod). When combining these 3 indices together, the sensitivity and specificity were both increased and more balanced (sensitivity=82%, and specificity=80%). **Conclusions:** FDG PET measured glucose uptake, MRI measured hippocampal volume and ADAS-mod at baseline can all distinguish MCI converters from non-converters and with increased statistical power when combined. Our findings validate several previous studies that demonstrated imaging based biomarkers as predictors of future clinical decline.

WEDNESDAY, JULY 17, 2013
DEVELOPING TOPICS
ORAL SESSIONS: DT-O2

DT-02-01 FIRST CASE REPORT: IMAGE TO AUTOPSY CORRELATION FOR TAU IMAGING WITH [18F]-T808 (AV-680)

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Background: [F-18]-T808 has been shown to have high affinity and selectivity for tau pathology in brain tissue sections from Alzheimer's disease (AD) patients (Zhang et al., 2012) and has recently been tested in 11 human subjects with promising results. Due to the death of one subject, an opportunity arose for an exploratory post mortem pathological analysis of brain tissue and comparison to the PET images. **Methods:** The male subject (aged approximately 85 years) had been diagnosed with AD 5 years prior to this study and had a Mini-Mental State Exam score of 21 at the time of the PET study. The PET session consisted of a dynamic 0-50 min PET scan after injection of 10 mCi (370 MBq) iv of [18F]-T808. Static PET images (30-50 minutes post injection) were used for analysis. Cerebellum uptake was used as a reference area. Approximately 2 weeks after imaging the patient died (unrelated to the procedure), allowing brain tissue sample collection and pathological evaluation for PHF-tau. **Results:** The [18F]-T808 PET images revealed pronounced signal in the frontal, parietal, temporal lobes, and hippocampus. Less pronounced tracer retention was observed in the posterior cingulate and the putamen. The cerebellum had low tracer retention. Post mortem staining for PHF-tau to date has been done with the fluorescent tau ligand T557 and was largely in agreement with the observed in vivo tracer distribution. Thus, tissue sections obtained from frontal, parietal and temporal lobe areas, and the hippocampus, appeared strongly positive for PHF-tau. The posterior cingulate and putamen displayed fewer tau tangles, and the cerebellum was negative. **Conclusions:** The observed pattern of regional in vivo [F-18]-T808 uptake in the test subject is consistent with post mortem PHF-Tau staining. The considerable spread of tau pathology, observed in vivo and ex vivo, suggests an advanced Braak stage, and is consistent with the dementia that the subject experienced. These results support [F-18]-T808 as a PET tracer for identification of PHF-tau in human brain. Additional work is planned to evaluate tau and