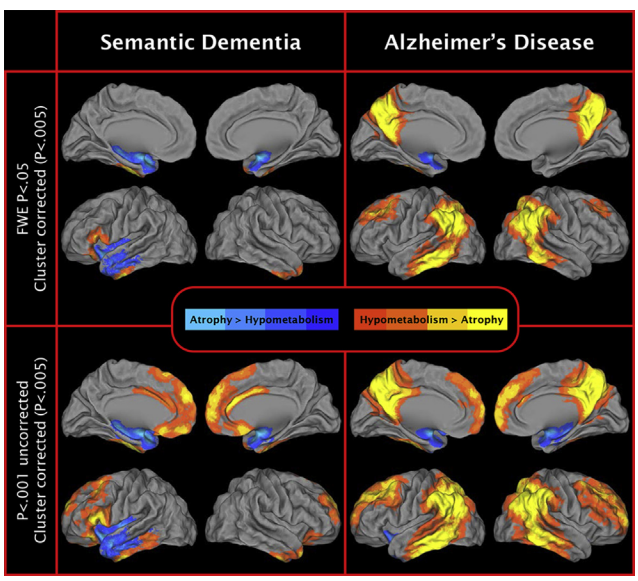
topographic discrepancies that pointed to specific pathological processes. To date, this has never been assessed in semantic dementia (SD) although atrophy and hypometabolism appear more similar than in AD as they both concern the anterior temporal lobe. Therefore, the aim of the present study was to compare atrophy *versus* hypometabolism discrepancies in SD to that observed in AD in order to highlight similarities and differences in the pathological processes between both diseases. **Methods:** Sixteen patients with SD, 24 patients with AD and 39 healthy controls matched for age, sex and years of education underwent both structural MRI and 18F-fluorodeoxyglucose PET scans. Images were spatially normalized using dartel in SPM. Age-adjusted Z-score maps were then computed for each patient and each imaging modality using the healthy controls group as a reference. Direct between-modality voxel-wise comparisons were then performed within each patient group. **Results:** Between-modality analyses highlighted more atrophy than hypometabolism in the medial temporal lobe in both SD and AD (FWE p<.05). By contrast, more hypometabolism than atrophy was found in extended medial and lateral parietal regions, temporo-parietal and frontal areas in AD, and in much more restricted brain regions in SD, i.e. mainly in the prefrontal regions when using a more liberal threshold (p<.001 uncorrected). **Conclusions:** Interestingly, both neurodegenerative disorders were found to be characterized by stronger atrophy than hypometabolism in the medial temporal lobe. However, unlike in AD, the pattern of hypometabolism only slightly differed from the pattern of atrophy in SD. This likely reflects distinct neuropathological processes in both diseases with much less distant effect of neuronal damage in the hippocampal formation in SD. Yet, the excessive prefrontal hypometabolism in SD might as well reflect diaschisis, or the higher sensitivity of 18F-fluorodeoxyglucose PET than structural MRI to detect the underlying neuropathology. Altogether, these findings suggest that the pathological mechanisms affecting the brain might be more homogeneous in SD than in AD.



IC-02-05 **HIPPOCAMPAL VOLUMES PREDICT RISK OF DEMENTIA WITH LEWY BODIES IN MILD COGNITIVE IMPAIRMENT**

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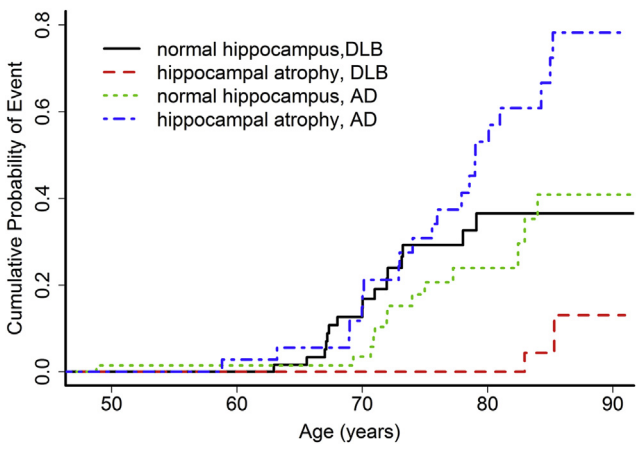
Background: Amnestic mild cognitive impairment (MCI) has been established on clinical grounds in order to identify individuals with prodromal Alzheimer's disease (AD) dementia. However, patients with MCI, who have impairments non-amnestic cognitive domains, may be at an increased risk of dementia with Lewy bodies (DLB). We investigated whether the risk of AD dementia versus DLB can be predicted by hippocampal volume (HV) in patients with MCI, broadly defined with impairments in amnestic and/or non-amnestic cognitive domains. **Methods:** Consecutive patients with MCI (n=108) from the Mayo Clinic Alzheimer's Disease Research Center, who participated in the MRI study during years 2005 through 2013 were included and followed with approximately annual clinical evaluations. Patients with neurologic diseases other than cognitive impairment were excluded. MRIs were performed at 3Tesla and 3D MPRAGE scans were acquired at baseline. HVs were analyzed using FreeSurfer (5.3), and adjusted for TIV. Hippocampal atrophy was determined from the 10th percentile of the measurement distributions in clinically diagnosed AD patients in a previous study. The hazard ratios for progression to AD dementia versus DLB were estimated by taking into account the competing risks. **Results:** After a median (range) follow-up of 1.97 (0.78-8.10) years, 18 (16%) patients with MCI progressed to probable DLB and 34 (32%) progressed to AD dementia. Taking into account the competing risks, the estimated hazard ratio (95% confidence interval) for hippocampal atrophy (relative to normal HV) for progression to AD dementia was 4.58 (2.28-9.19) (p<0.001). The estimated hazard ratio for hippocampal atrophy (relative to normal HV) for progression to DLB was 0.213 (0.050-0.912), corresponding to an estimated hazard ratio for normal HV (relative to hippocampal atrophy) for progression to DLB of 4.71 (1.1-20.2) (p=0.037). (Figure) **Conclusions:** Patients with MCI who progress to DLB tend to have normal HV. Whereas hippocampal atrophy increases the risk of progression to AD demen-



tia, preserved hippocampal volumes increases the risk of DLB in MCI. Preservation of HV may be a supportive feature of prodromal DLB in patients with MCI.

SATURDAY, JULY 18, 2015
ALZHEIMER'S IMAGING CONSORTIUM (IC)
IC-03
SYMPOSIUM SESSION: HIGHLIGHTING EMERGING TOPICS

IC-03-01 CARDIORESPIRATORY CAPACITY CORRELATES WITH CEREBRAL BLOOD FLOW, WHITE MATTER HYPERINTENSITIES, AND COGNITION IN PRECLINICAL ALZHEIMER'S DISEASE

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Background: Cerebral hypoperfusion and white matter hyperintensities (WMHs), indicators of poor vascular health, are often observed in Alzheimer's disease (AD). Physical fitness improves vascular health and is protective against AD, yet little research has examined the influence of fitness on cerebral blood flow (CBF) and WMHs in individuals at-risk for AD. Therefore, the objective of this study was to determine whether cardiorespiratory capacity is associated with increased CBF in AD-related brain regions, decreased WMHs, and better cognitive performance in a middle-aged cohort at-risk for AD. **Methods:** 105 cognitively-healthy adults from the Wisconsin Registry for Alzheimer's Prevention (age=64.06±5.90 years) participated in this study. Participants performed graded treadmill exercise testing, and peak oxygen consumption (VO2peak, ml/kg/min) was used as the index for cardiorespiratory capacity. Participants underwent comprehensive cognitive testing, T1-weighted and T2 FLAIR structural MRI scanning, and CBF assessments using pseudocontinuous ASL. CBF values were sampled from regions implicated in AD using the Alzheimer's Disease Neuroimaging Initiative FDG Meta-ROI suite that includes the left and right angular and temporal gyri, posterior cingulate, and a composite ROI. Total WMHs were quantified using Lesion Segmentation Toolbox, and adjusted for intracranial volume in analyses. Linear regression, adjusted for relevant covariates, was used to examine relationships between VO2peak, CBF, WMHs, and cognition. **Results:** Higher VO2peak was associated with greater CBF in the left (p=.047) and right (p=.006) angular gyri, right temporal cortex (p=.019), and the composite ROI (p=.011). VO2peak was also associated with better cognitive performance in Speed & Flexibility (p=.020), a composite measure consisting of Trails A&B and the Stroop Color-Word Test Interference Trial. VO2peak was not associated with WMHs (p=.931), however VO2peak did modify the association between age and WMHs such that more fit individuals had fewer WMHs with increasing age compared to their less fit peers (p=.046; Figure). **Conclusions:** Higher cardiorespiratory capacity is associated with greater CBF in key AD brain regions, better executive function, and modifies the relationship between age and WMH burden in a cohort at-risk for AD. This suggests that participation in regular exercise may increase brain vascular health and cognitive function, thereby decreasing future risk for AD.

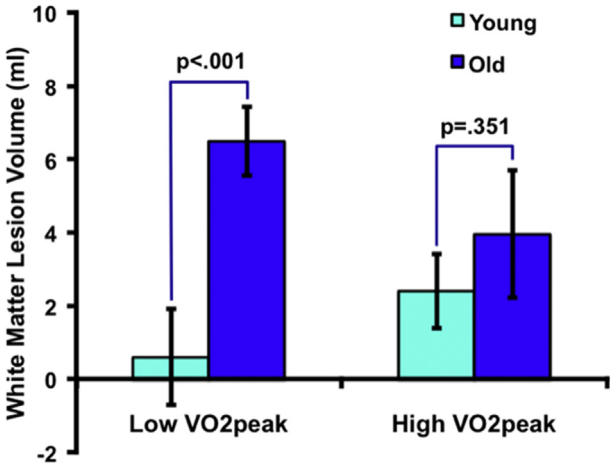

Figure. High cardiorespiratory capacity modifies the detrimental effects of age on white matter lesion burden.
Adjusted means and standard errors are displayed from the analysis modeling total white matter lesion volume as a function of age, sex, peak effort attainment, intracranial volume, VO2peak, and a VO2peak*age interaction. The V02peak*age interaction term was the effect of primary interest. VO2peak and age were included as continuous variables in the analysis, but for graphing purposes we chose two anchor points (i.e., ± 1 SD) to represent Low vs. High VO2peak and Young vs. Old age.
VO2peak = peak oxygen consumption (ml/kg/min).

IC-03-02 EARLY FRAME OF PIB AND FDG IN AUTOSOMAL DOMINANT ALZHEIMER'S DISEASE: SIMILARITY, DISCREPANCY, AND CLINICAL IMPLICATION

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Background: Alzheimer's disease (AD), the leading cause of dementia in the elderly, can affect individuals in their thirties in autosomal dominant form. The Imaging Core of the Dominantly Inherited Alzheimer Network (DIAN) aims to characterize transition from preclinical to symptomatic disease using imaging biomarkers. Decreases in cerebral glucose metabolism in the parietal lobe are detectable 10 years before the estimated year of symptom onset (EYO) (Benzinger, Blazey et al., 2013) and may represent synaptic dysfunction. In