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

Elizabeth A. Boots[1], Stephanie A. Schultz[1], Jennifer M. Oh[1], Ryan J. Dougherty[2], Dorothy Farrar Edwards[1,2,3], Jean A. Einerson[4], Claudia E. Korcarz[4], Howard A. Rowley[4], Barbara B. Bendlin[3,5,6], Sanjay Asthana[3,4,6], Mark A. Sager[3,5], Bruce P. Hermann[1,3], Sterling C. Johnson[3,5,6], James H. Stein[4], Dane B. Cook[2], Ozioma C. Okonkwo[1,3,6], *[1]Wisconsin Alzheimer's Disease Research Center, University of Wisconsin School of Medicine and Public Health, Madison, WI, USA; [2]University of Wisconsin-Madison, Madison, WI, USA; [3]Wisconsin Alzheimer's Institute, University of Wisconsin School of Medicine and Public Health, Madison, WI, USA; [4]University of Wisconsin School of Medicine and Public Health, Madison, WI, USA; [5]Alzheimer's Disease Research Center, University of Wisconsin School of Medicine and Public Health, Madison, WI, USA; [6]Geriatric Research Education and Clinical Center, Wm. S. Middleton Veterans Hospital, Madison, WI, USA. Contact e-mail: eaboots@medicine.wisc.edu*

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.

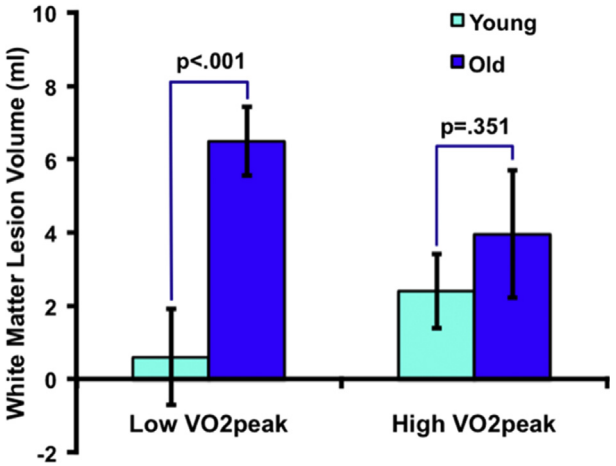

Figure. High cardiorespiratory capacity modifies the detrimental effects of age on white matter lesion burden.
Adjusted means and standard errors are displayed from the analysis modeling total white matter lesion volume as a function of age, sex, peak effort attainment, intracranial volume, VO2peak, 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

Nelly Joseph-Mathurin[1], Yi Su[1], Andrei Vlassenko[1], Mateusz S. Jasielec[1], Tyler Blazey[1], Karl A. Friedrichsen[1], Christopher J. Owen[1], Russ C. Hornbeck[1], Trish A. Stevenson[1], Lisa Cash[1], Chengjie Xiong[1], John M. Ringman[2], Adam M. Brickman[3], Robert A. Koeppe[4], Beau Ances[1], Marcus E. Raichle[1], John C. Morris[1], Randall Bateman[1], Tammie L.S. Benzinger[1], *[1]Washington University School of Medicine, St. Louis, MO, USA; [2]UCLA, Los Angeles, CA, USA; [3]Columbia University Medical Center, New York, NY, USA; [4]University of Michigan, Ann Arbor, MI, USA. Contact e-mail: mathurinn@npg.wustl.edu*

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

sporadic AD, studies have shown that early perfusion frames of amyloid imaging with [11C]-Pittsburgh Compound B PiB (ePiB) correlate well with glucose metabolism (Rostomian et al., 2011). Here, we evaluated whether ePiB is a reasonable surrogate marker for synaptic dysfunction, in comparison to glucose metabolism hypometabolism, and how ePiB changes with the disease progression. **Methods:** DIAN participants (n=110), including 65 asymptomatic and symptomatic mutation carriers (MC), underwent full dynamic PiB-PET and also had [18F]-fluorodeoxyglucose (FDG) PET and volumetric brain MRI. The MRI was used to register the PET images. A standardized uptake value ratio (SUVR) from MR segmented PiB and FDG regions. An ePiB image with 1-9 min time frames was selected. Voxel-wise spatial correlation between FDG and ePiB was performed for each participant. The mutation and cognitive status were taken into account in the analyses. For each imaging modality, relationship with EYO was evaluated with linear mixed models on specific regions such as inferior parietal and precuneus cortices. **Results:** FDG and ePiB were visually similar and showed high spatial correlation with an average of 0.8 ± 0.04 regardless of the mutation or cognitive status. As we have previously found, the association between FDG and EYO significantly differs between MC and non-carrier groups (p-value<0.001 and p-value<0.01 for inferior parietal and precuneus, respectively). However, these associations were not significant between ePiB and EYO. **Conclusions:** Our findings show that ePiB is strongly correlated with FDG within the same individual. However, ePiB does not display the same sensitivity as FDG to reflect disease progression in this population. Further studies are needed to fully determine the utility of ePiB measurements in clinic.

IC-03-03 AN EARLY ALZHEIMER'S DISEASE FUNCTIONAL IMAGING MARKER: OLFACTORY DEFICITS IN ALZHEIMER'S DISEASE AND MCI REFLECT DEGENERATION OF CENTRAL OLFACTORY SYSTEM

Megha Vasavada[1], Brittany Martinez[2], Prasanna Karunanayaka[3], Jianli Wang[4], Paul J. Eslinger[4], David Gill[5], **Qing X. Yang**[4], *[1]UCLA, Los Angeles, CA, USA; [2]The Pennsylvania State College of Medicine, Hershey, PA, USA; [3]The Pennsylvania State University, College of Medicine, Hershey, PA, USA; [4]The Pennsylvania State University - College of Medicine, Hershey, PA, USA; [5]Unity Rehabilitation and Neurology at Ridgeway, Rochester, NY, USA. Contact e-mail: qyang@hmc.psu.edu*

Background: Olfactory deficits are present in early AD and MCI (1-4). It is critical, however, to determine whether these deficits are due to degeneration of the central or peripheral olfactory system. We investigated involvement of the central olfactory system in AD and MCI with an implicit olfactory associative learning paradigm. **Methods:** Sixty-three subjects (15 AD, 21 MCI and 27 age-matched CN) were studied with cognitive tests, the University of Pennsylvania Smell Identification Test (UPSIT) and fMRI. The olfactory associative learning paradigm (Fig. 1) consisted of visual cues paired with lavender odor (visual+odor) followed by the same visual cue without an odor (visual-only). **Results:** Visual-only cue activated in the primary olfactory cortex (POC) and hippocampus as did the preceded visual+odor cue for each group ($p<0.05$), suggesting a rapid implicit olfactory associative learning under this paradigm (Fig. 2). The CN subjects had greater activated volume in hippocampus and POC during both visual+odor and visual-only conditions than either the MCI or AD subjects ($P < 0.05$). Both conditions correlated with the cognitive and olfactory tests. **Conclusions:** The activation by visual-only cue in POC and hippocampus is likely a result of implicit learning/memory since it occurs only when preceded by the visual cue paired with odor. The significant decline in brain activation under this condition suggests that the central olfactory processing contributed the olfactory dysfunction in AD and MCI patients, which could lead a sensitive functional imaging marker for AD.

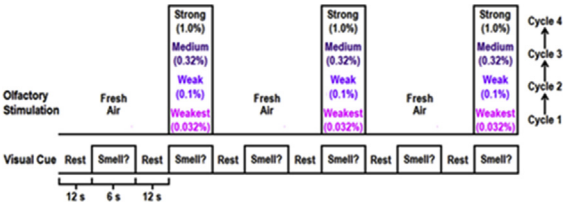

Figure. 1. The fMRI paradigm. The visual cue, the words "Smell?", was paired with lavender odor and then odorless air with a "Rest" in between. When "Smell?" is given, the subject responses with left hand button press if no smell and right hand if they smelled the stimulus. Four odorant concentrations were presented incrementally to offset the olfactory habituation.

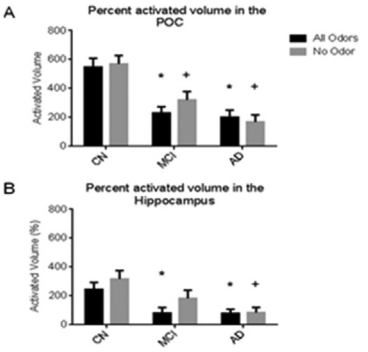

Figure. 2. Activated volume in POC and hippocampus (mean ± standard error) during visual + odor and visual- only conditions. The activated volume in the POC (A) and hippocampus (B) in MCI and AD) was decreased by more than 50 percent than that of the cognitively normal controls (CN) during odor presentation. Notes: * $P \leq 0.05$, ANOVAwhen compared to CN-AII Odors
$^{+}$ $P < 0.05$, ANOVAwhen compared to CN-No Odor.

JULY 18, 2015
ALZHEIMER'S IMAGING CONSORTIUM (IC)
IC-04
NOVEL APPROACHES

IC-04-01 CORTICAL CAPILLARY DYSFUNCTION IN PATIENTS SUSPECTED OF ALZHEIMER'S DISEASE

Simon Fristed Eskildsen[1], Louise Gyldensted[2], Kartheeban Nagenthiraja[1], Mikkel Bo Hansen[1], Rikke Beese Dalby[2], Jesper Frandsen[1], Anders Rodell[2], Carsten Gyldensted[2], Sune Nørhøj Jespersen[1], Kim Mouridsen[1], Hans Brændgaard[2], Leif Østergaard[2], *[1]Aarhus University, Aarhus, Denmark; [2]Aarhus University Hospital, Aarhus, Denmark. Contact e-mail: seskildsen@cfin.au.dk*