Medical Center, Brooklyn, NY, USA. Contact e-mail: megan.hogan@my.wheaton.edu

Background: Cross sectional analysis has shown an association between OSA severity and Aβ burden using amyloid-PET, globally and regionally in the precuneus among MCI patients. However, whether OSA accelerates longitudinal increases in Aβ burden in MCI patients is presently unclear. **Methods:** Study participants included a total of 798 subjects with a diagnosis of MCI and were a subset of the ADNI cohort (adni.loni.usc.edu). OSA was self-reported and participants were labeled either as OSA+, or OSA−. Aβ burden was determined by florbetapir SUVRs calculated by averaging across the 4 cortical regions and dividing this cortical summary ROI by a composite reference region. Mean and variance of the Aβ data at each time point by OSA status were determined. To test whether OSA is associated with the rate of change in Aβ data longitudinally, SAS PROC MIXED was used to fit the model with randomly varying intercepts and slopes allowing dependence on OSA status. The final model was adjusted for sex, body mass index and CPAP use status since there was no difference between OSA groups for APOE e4 status, age and history of cardiovascular disease. **Results:** At baseline, there was significant variation between subjects in mean Aβ-42 volumes (intercept) (mean SUVR; B = 0.0008, Z-value =11.02, $p < .0001$). A significant variation in the change (slope) in Aβ-42 volumes over time was also seen (mean SUVR; B = 0.0084, Z-value =11.63, $p < .0001$). The covariance between the baseline Aβ-42 level and Aβ-42 volume change over time indicated that SDB subjects experienced a faster increase in brain Aβ-42 volumes over time ($p < .0001$). The rate of change in Aβ-42 deposition also varied significantly across OSA groups over the follow-up period. **Conclusions:** Obstructive Sleep Apnea possibly facilitates longitudinal increases in amyloid burden in elderly Mild Cognitive Impairment individuals. Further research examining mechanisms underlying effects of OSA on the longitudinal increases in Aβ burden is needed.

IC-P-010 SLEEP DISORDERED BREATHING, APOE4 AND β-AMYLOID DEPOSITION IN COGNITIVELY NORMAL ELDERLY

Amanda Shim[1], Megan Hogan[1], Kathryn Halldin[1], Hannah Clark[1], Beka Behrens[1], Cassidy Griffith[1], Ogie Queen Umasabor-Bubu[2,3], Omonigho Michael Bubu[1,2], *[1]Wheaton College, Wheaton, IL, USA; [2]University of South Florida, Tampa, FL, USA; [3]Interfaith Medical Center, Brooklyn, NY, USA. Contact e-mail: amanda.shim@my.wheaton.edu*

Background: Sleep Disordered Breathing (SDB) is commonly reported in the elderly, and recent studies in humans and animals describe associations between SDB and Alzheimer disease (AD). ApoE4 allele is considered the most important risk factor for sporadic AD. We examined whether SDB is associated with changes in amyloid burden in a sample of cognitively normal elderly. The interactive effect of SDB*APOE4 on amyloid burden was also examined. **Methods:** Data used were obtained from the ADNI database (adni.loni.usc.edu). Study participants included a total of 516 cognitively normal subjects and were a subset of the ADNI cohort. SDB was self-reported and participants were labeled SDB+, or SDB−. Brain Aβ-42 levels were determined at baseline and follow-up visits. Multi-level mixed effects linear regression models were used to examine the relationship between SDB and Aβ-42 volumes. First, we fit a linear regression model for each participant separately at each time point, and second, we regressed unknown time-specific regression coefficients against time. Our models were adjusted for sex, and body mass index. There was no difference between OSA groups for APOE e4 status, age and history of cardiovascular disease. The interactive effect of SDB*APOE4 on amyloid burden was also examined. **Results:** There was significant variation between subjects in mean Aβ-42 volumes at baseline (intercept) (mean SUVR; B = 0.006, $p > .0001$), as well as significant variation in the change in Aβ-42 volumes over time (slope) (mean SUVR; B = 0.006, $p > .0001$). The covariance between the baseline Aβ-42 level and Aβ-42 volume change over time indicated that SDB subjects experienced a faster increase in brain Aβ-42 volumes over time ($p > .0001$). The interactive effect of SDB*APOE4 on amyloid burden was not significant. **Conclusions:** Among community-dwelling cognitively normal older adults, SDB is associated with greater β-amyloid burden changes over time regardless of APOE4 status. This suggests that clinical interventions aimed at SDB, such as treatment with CPAP or dental appliances, implemented during the early phase in which tissue damage precedes clinical symptoms and neuronal dysfunction, may mitigate the progression of cognitive impairment.

IC-P-011 DETERMINATION OF NEURITIC VERSUS DIFFUSE PLAQUE CONTRIBUTION TO SIGNAL DERIVED FROM CN-FLUTEMETAMOL

Milos D. Ikonomovic[1], Eric E. Abrahamson[1], Chris J. Buckley[2], Chester Mathis[1], Bill E. Klunk[1,3], Gill Farrar[2], *[1]University of Pittsburgh, Pittsburgh, PA, USA; [2]GE Healthcare, Amersham, United Kingdom; [3]Alzheimer's Disease Research Center, Pittsburgh, PA, USA. Contact e-mail: ikonomovicmd@upmc.edu*

Background: Specificity and sensitivity of Flutemetamol (Vizamyl™) PET are high for detecting neuritic amyloid-beta plaques (NP). Several false-positive results from the Flutemetamol clinical-pathological study, as well as high retention of Flutemetamol in the striatum from AD cases, indicate that this radiotracer may also detect diffuse plaques (DP). The fluorescent derivative of Flutemetamol (CN-Flutemetamol) labels both plaque types in AD brain tissue sections, although NP show brighter fluorescence than DP. The current study explores quantitatively this relation in brain areas affected differentially by NP and DP. **Methods:** Tissue sections from the frontal cortex (FC, variable proportions of NP and DP) and caudate (CD, exclusively DP) from ten AD cases were processed using CN-Flutemetamol and analyzed for plaque load (% area occupied by plaques) and integrated density (a measure that integrates both size and fluorescence intensity of labeled plaques per defined field). A similar approach was used to assess total light output of individual NP and DP imaged using a DSU spinning disk confocal microscope. **Results:** All plaques in both regions were labeled with CN-Flutemetamol. CN-Flutemetamol positive total plaque load was similar in CD and FC (CD = 3.79 ± 0.64; FC = 5.81 ± 1.18; t-test p = 0.15), however, the integrated density in FC was greater than in the CD (CD=5024 ± 490.3; FC=11742 ± 568.2; t-test $p<0.0001$). Confocal analysis yielded similar results with total light output of NP greatly exceeding that of DP. **Conclusions:** For two regions with comparable plaque area coverage, but with different involvement of NP and DP, the region with a preponderance of NP yields greater overall CN-Flutemetamol fluorescence signal when area coverage and signal intensity are calculated as a single value (integrated density). These observations were confirmed by confocal image analysis of individual plaques, and they imply that in PET imaging studies, brain regions with high densities of NP exhibit greatest Flutemetamol retention.

However, DP can contribute to Flutemetamol PET signal in regions with very high DP area coverage. Thus, Flutemetamol PET may correlate better with NIA-AA 2012 AD neuropathology criteria that incorporate both CERAD (NP) and Thal phases (all types of Aβ plaques).

IC-P-012 ASSOCIATION OF RECENT MEMORY PERFORMANCE AND AMYLOID DEPOSITION IN AD CONTINUUM OF COGNITIVELY NORMAL ELDERLY SUBJECTS AND AMYLOID-POSITIVE MCI

Takashi Kato[1], Kaori Iwata[1,2], Go Kizawa[1], Izumi Kuratsubo[1], Naohiko Fukaya[1], Masahiko Bundo[1], Yutaka Arahata[1], Kengo Ito[1], Akinori Nakamura[1], MULNIAD, [1]*National Center for Geriatrics and Gerontology, Obu, Japan;* [2]*Micron, Tokyo, Japan. Contact e-mail: tkato@ncgg.go.jp*

Background: The purpose of this study was to investigate the decline of recent memory performance with amyloid PET and a surrogate maker of cognitive reserve in cognitively normal elderly people and amyloid positive patients with amnestic mild cognitive impairment (MCI). **Methods:** Subjects selected from in-house studies were 61 cognitively normal (CN) subjects (age: 69.8±5.7 (60-82) y.o., years of school education (YSE): 12.2±2.4 (9-18) years) and amyloid positive 17 patients with MCI (age: 74.6±6.1 (60-82) y.o.; YSE: 11.4±2.6 (8-16) years). They underwent a test of logical memory-II (LM-II) of Wechsler memory scale revised. Distribution volume ratio (DVR) image was calculated from dynamic PiB PET using simplified reference tissue mode 2. The DVR images spatially normalized using DARTEL method. Statistical analyses of the DVR images were performed with SPM8 for multiple regressions to assess the relationship with memory, age, and YSE. Correlation and regression analyses among regional DVR value, age, LM-II score and YSE were performed using SPSS. **Results:** Eleven out of 61 cases of CN were visually evaluated as amyloid-positive scan. LM-II score was 16.8 ± 6 (4-35) and 4.4±4.8 (0-15) in CN and MCI, respectively. A SPM analysis of the group of CN demonstrated that LM-II score was inversely associated with DVR values in the bilateral localized medial temporal cortices ($p<0.005$, ext>50). In CN a significant correlation was observed between LM-II and YSE ($r>0.5$, $p<0.001$). Multiple regression analyses with LM-II as a dependent variable represented that statistically significant terms were YSE ($p<0.001$) and an interaction term of YSE and regional DVR in the medial temporal lobe. In contrast, the combination group of CN and amyloid positive MCI showed an inverse association between DVR value and LM-II in wider areas such as anterior and posterior cingulate area, lateral temporal lobes, and basal forebrain in a SPM analysis ($p<0.005$, ext>50). **Conclusions:** The results suggest that, recent memory declines in association with amyloid deposition in the medial temporal lobe and cognitive reserve at cognitively normal stage, while recent memory performance goes down along with amyloid deposition spreading widely at the stage of cognitively normal to MCI in AD continuum.

IC-P-013 AMYLOID ACCUMULATION WITHIN THE NEGATIVE RANGE IS LINKED TO MEMORY DECLINE IN COGNITIVELY NORMAL OLDER INDIVIDUALS

Susan M. Landau[1], William J. Jagust[1,2], [1]*University of California Berkeley, Berkeley, CA, USA;* [2]*Lawrence Berkeley National Laboratory, Berkeley, CA, USA. Contact e-mail: slandau@berkeley.edu*

Background: The earliest phase of amyloid accumulation, before deposition is widespread throughout cortex, is of great interest for understanding the etiology of Alzheimer's disease and for developing amyloid-modifying treatments. A critical question that has emerged is whether amyloid accumulation can be detected prior to amyloid positivity, and whether this accumulation is accompanied by any subtle changes in cognition. **Methods:** We identified 160 normal older individuals from the Alzheimer's Disease Neuroimaging Initiative who were negative on 18F-florbetapir PET based on global uptake in cortical summary regions. We contrasted the baseline florbetapir scans of subjects who subsequently increased or did not increase over 2 or 3 scans (2-4 years) of longitudinal florbetapir imaging in order to define a set of early accumulation regions at baseline. Then we determined whether amyloid accumulation within these early accumulation regions was related to concurrent memory change. **Results:** Early accumulation regions (regions elevated at baseline for subjects who subsequently increased) were located in bilateral precuneus, posterior cingulate, and superior parietal lobes. Within these regions, 103/160 (64%) of baseline-negative normals had positive florbetapir slopes. 17 subjects (4 APOE4+) converted to florbetapir positive status over 3.4+-1.0 yrs (3.1% per year). Negative normals who increased on florbetapir did not differ from nonincreasing subjects with respect to age, sex, education, ApoE4 status, baseline temporoparietal glucose metabolism, or hippocampal volume but they did have slightly higher baseline cortical florbetapir, indicating that accumulation was ongoing. Increasing florbetapir was associated with memory decline regardless of whether florbetapir change was assessed as a dichotomous ($p=0.007$) or continuous ($p=0.03$) variable. Finally, the effect was stronger for subjects with longer florbetapir followup (3 scans over 4.1+/-0.3yrs compared with 2 scans over 2.4+/-0.8yrs). **Conclusions:** Despite considerable variability in longitudinal amyloid and memory measurements in amyloid negative healthy older individuals, those with increasing