

Medical Center, Brooklyn, NY, USA. Contact e-mail: [megan.hogan@my.wheaton.edu](mailto:megan.hogan@my.wheaton.edu)

**Background:** Cross sectional analysis has shown an association between OSA severity and A $\beta$  burden using amyloid-PET, globally and regionally in the precuneus among MCI patients. However, whether OSA accelerates longitudinal increases in A $\beta$  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](http://adni.loni.usc.edu)). OSA was self-reported and participants were labeled either as OSA+, or OSA-. A $\beta$  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 A $\beta$  data at each time point by OSA status were determined. To test whether OSA is associated with the rate of change in A $\beta$  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 A $\beta$ -42 volumes (intercept) (mean SUVR; B = 0.0008, Z-value = 11.02,  $p < .0001$ ). A significant variation in the change (slope) in A $\beta$ -42 volumes over time was also seen (mean SUVR; B = 0.0084, Z-value = 11.63,  $p < .0001$ ). The covariance between the baseline A $\beta$ -42 level and A $\beta$ -42 volume change over time indicated that SDB subjects experienced a faster increase in brain A $\beta$ -42 volumes over time ( $p < .0001$ ). The rate of change in A $\beta$ -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 A $\beta$  burden is needed.

**IC-P-010 SLEEP DISORDERED BREATHING, APOE4 AND  $\beta$ -AMYLOID DEPOSITION IN COGNITIVELY NORMAL ELDERLY**



**Amanda Shim**<sup>1</sup>, Megan Hogan<sup>1</sup>, Kathryn Halldin<sup>1</sup>, Hannah Clark<sup>1</sup>, Beka Behrens<sup>1</sup>, Cassidy Griffith<sup>1</sup>, Ogie Queen Umasabor-Bubu<sup>2,3</sup>, Omonigho Michael Bubu<sup>1,2</sup>, <sup>1</sup>Wheaton College, Wheaton, IL, USA; <sup>2</sup>University of South Florida, Tampa, FL, USA; <sup>3</sup>Interfaith Medical Center, Brooklyn, NY, USA. Contact e-mail: [amanda.shim@my.wheaton.edu](mailto: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](http://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 A $\beta$ -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 A $\beta$ -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 A $\beta$ -42 volumes at baseline (intercept) (mean SUVR; B = 0.006,  $p > .0001$ ), as well as significant variation in the change in A $\beta$ -42 volumes over time (slope) (mean SUVR; B = 0.006,  $p > .0001$ ). The covariance between the baseline A $\beta$ -42 level and A $\beta$ -42 volume change over time indicated that SDB subjects experienced a faster increase in brain A $\beta$ -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  $\beta$ -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. Ikonovic**<sup>1</sup>, Eric E. Abrahamson<sup>1</sup>, Chris J. Buckley<sup>2</sup>, Chester Mathis<sup>1</sup>, Bill E. Klunk<sup>1,3</sup>, Gill Farrar<sup>2</sup>, <sup>1</sup>University of Pittsburgh, Pittsburgh, PA, USA; <sup>2</sup>GE Healthcare, Amersham, United Kingdom; <sup>3</sup>Alzheimer's Disease Research Center, Pittsburgh, PA, USA. Contact e-mail: [ikonovicmd@upmc.edu](mailto:ikonovicmd@upmc.edu)

**Background:** Specificity and sensitivity of Flutemetamol (Vizamyl<sup>TM</sup>) 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  $\pm$  0.64; FC = 5.81  $\pm$  1.18; t-test  $p = 0.15$ ), however, the integrated density in FC was greater than in the CD (CD = 5024  $\pm$  490.3; FC = 11742  $\pm$  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.