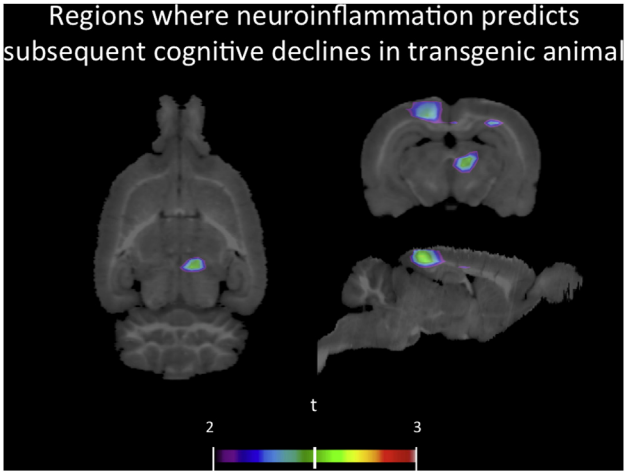
global cortical values, and t-statistical maps were generated to illustrate the regions of significance. **Results:** The association between baseline levels of cognition and inflammation was greater in the Tg than Wt rats in the right nucleus accumbens, whereas in the opposite was seen in the right inferior colliculus. The association between baseline levels of inflammation and change in cognition at follow-up, several regions including the left retrosplenial cortex, right hippocampus, and the right posterior commissure showed higher decrease in cognition of the Tg animals compared to the Wt (Figure 1). **Conclusions:** At baseline, there is no association between neuroinflammation and cognitive performance; however in more aged rats, baseline levels of PBR is able to predict cognitive decline. The results provide a framework that could potentially be applied in human studies focusing on the detrimental roles of neuroinflammation in AD.



IC-P-028 SLEEP QUALITY IN YOUNG AND MIDDLE AGE-PERIOD IS ASSOCIATED WITH CEREBRAL AMYLOID BURDEN IN COGNITIVELY NORMAL ELDERLY PEOPLE

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Background: Very little is known for the association between lifetime sleep experience and cerebral beta-amyloid protein (Aβ) deposition, which is the core pathological change related to Alzheimer's disease process. This study aimed to investigate the relationship of hours of sleep and sleep quality in young and middle age-period with cerebral Aβ burden in elderly individuals with normal cognition. **Methods:** One hundred and twenty-two cognitively normal old adults (age range: 60-87 years), who participated in the Korean Brain Aging Study for Early Diagnosis and Prediction of Alzheimer's Disease (KBASE), were included. All subjects underwent comprehensive clinical and neuropsychological assessment, ^{11}Clabelled Pittsburgh Compound B (PiB) positron emission tomography (PET). Through structured clinical interview for each participant, mean hours of sleep and sleep quality were assessed for the following age-periods: before 20 years, in their 20-30s, and 40-50s. Current sleep quality was also assessed by using the Pittsburgh Sleep Quality Index (PSQI). Global cerebral Aβ deposition was defined as mean cortical PiB retention of the cortical regions including the frontal, lateral temporal, lateral parietal and precuneus/posterior cingulate cortices. **Results:** The poorer sleep quality in all the three younger age-periods was associated with higher mean cortical PiB retention even after controlling for age, gender, apolipoprotein E e4 status, and Hamilton Depression Rating Scale score. In contrast, mean hours of sleep in any young or middle age-period or current sleep quality measured by the PSQI were not related to mean cortical PiB retention. **Conclusions:** These findings suggest that poorer sleep quality, but not hours of sleep, in young and middle age-period may contribute to increased cerebral amyloid burden in old age.

Table
Correlation between sleep variables and Pittsburgh Compound B (PiB) retention

	Unadjusted		Mutivariable Adjusted*	
	Correlation Coefficient	P Value	Partial Correlation Coefficient	P Value
<20y sleep quality	0.246	0.006	0.224	0.015
<20y sleep duration	-0.050	0.582	-0.030	0.748
20-39y sleep quality	0.175	0.055	0.174	0.060
20-39y sleep duration	-0.002	0.984	-0.013	0.889
40-59y sleep quality	0.203	0.025	0.198	0.032
40-59y sleep duration	-0.058	0.526	-0.085	0.360
Total PSQI	0.010	0.912	0.044	0.637

*Adjusted for age, gender, apolipoprotein E e4 status, and Hamilton Depression Rating Scale score

IC-P-029 POLYMORPHISM IN CYTOCHROME P450 GENE IS ASSOCIATED WITH ALZHEIMER'S PATHOLOGY

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Background: The cytochromes P450 (CYP) are known for their role in metabolizing several endogenous and exogenous substrates. In

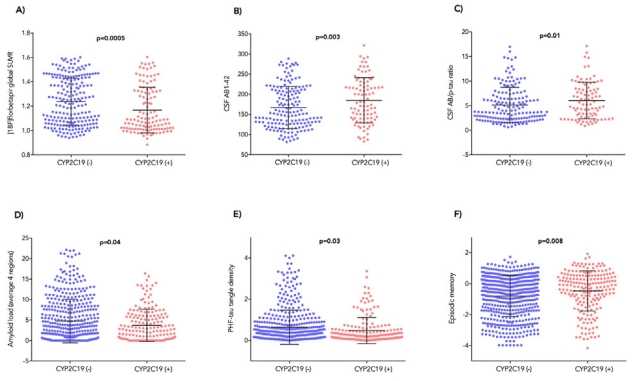

Figure 1. Comparison between non-carriers(-) and carriers(+) of the minor allele of rs4388808 (CYP2C19). A significant difference was observed in brain amyloid load (A), CSF Aβ levels (B) and CSF Aβ/p-tau ratio (C) using ADNI cohort. Results were generalized using post-mortem data from Rush ROS and MAP cohorts, where a concordant pattern was observed in amyloid load (D), PHF-tau tangle density (E) and episodic memory scores (F). The linear models were adjusted for age, gender and ApoE-e4 carriage status.

the brain, they modulate blood-flow regulation, metabolize cholesterol, and participate in neuroinflammatory processes. CYP activity is also implicated in Alzheimer's disease (AD), particularly in amyloid-β (Aβ) accumulation in CSF. We examined whether genetic polymorphisms of CYP are associated with AD pathology. **Methods:** [18F]florbetapir-PET imaging was employed to assess brain Aβ levels in 256 subjects from a discovery cohort (ADNI: 186CN, 105 lMCI, 47AD). Linear regression models examined the association of 30 SNPs from four genes of CYP (CYP3A4, CYP2C9, CYP2C19 and CYP1A1) with global [18F]florbetapir-SUVR, adjusting for age, sex, and ApoE-e4carriage status. Significant signals were interrogated at the voxel level using RMINC-tool, and, separately, tested for associations with CSF Aβ and Aβ/p-tau ratio. Neuropathologic data from the Rush ROS and MAP cohorts were used to generalize the findings to Aβ load and PHFtau tangle density by immunocytochemistry in post-mortem brains (302 CN, 180 aMCI, 259 AD). **Results:** The analysis of [18F]florbetapir identified an intronic variant in the CYP2C19 gene (rs4388808; P=0.0005), in which carriers of the minor-allele (G) had lower global SUVR (Figure 1). The voxel-wise analysis showed a significant effect of the SNP in the frontal and posterior cingulate cortices, as well as in the inferior parietal cortex (Figure 2). Carriers of the minor-allele were also associated with higher CSF Aβ (P=0.003) and higher Aβ/p-tau ratio (P=0.01). In post-mortem brains, minor-allele carriers had a lower Aβ load (P=0.04), lower PHFtau tangle density (P=0.03) as well as better episodic memory (P=0.008). **Conclusions:** The rs4388808, an intronic variant of the CYP2C19 gene is implicated in Aβ load, tau pathology and episodic memory, where the minor-allele protects against AD pathology.

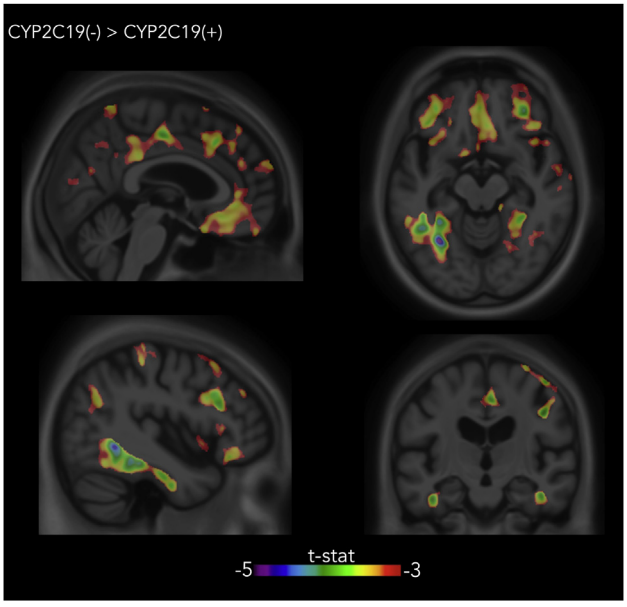

Figure 2. Voxel-wise comparison between minor allele non-carriers(-) and carriers(+) of the polymorphism rs4388808 of CYP2C19. A significant difference was observed in the frontal and posterior cingulate cortices, as well as in the inferior parietal cortex. The voxel-wise analysis was adjusted for age, gender and ApoE-e4 carriage status.

IC-P-030 *IN VIVO* NADH FLUORESCENCE IMAGING OF DOUBLE TRANSGENIC AD MICE REVEALS CHRONIC TISSUE HYPOXIA

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Background: Vascular and metabolic dysfunctions are well known features of Alzheimer's disease (AD) and they precede clinical dementia. Undoubtedly vascular changes are expected as amyloid accumulates in the arterial vessel walls in cerebral amyloid angiopathy (CAA), leading to the death of smooth muscle cells, cerebral hypoperfusion and inadequate oxygen supply. These vascular events could also contribute to metabolic alterations in glucose homeostasis. High resolution *in vivo* study of the dynamic vascular and metabolic events may reveal which tissue regions and cell populations are affected and cast light on the mechanisms that contribute to AD pathogenesis. **Methods:** We used fluorescence imaging of nicotinamide adenine dinucleotide (NADH) as an intrinsic marker for cellular metabolic states and tissue oxygen supply *in vivo*. We resolved the tissue boundaries of NADH fluorescence in the cortex of transgenic AD mice (B6C3.Tg(APPswe-PSEN1de9), n=4, 12-24 months old) and observed NADH pattern relative to vessels during hyperoxia and normoxia. We then used *in vivo* two-photon fluorescence microscopy together with cell-type specific labeling to determine the cellular origin of the intrinsic signal and the locality of CAA. **Results:** Reduction of oxygen supply from hyperoxia to normoxia produced no detectable changes in controls, however AD mice showed characteristic NADH pattern (Figure 1A), indicative of reduced oxygen gradient and rise in glycolysis in tissues further away from the arterial oxygen supply. Areas around capillary beds showed decreased NADH signal. Two-photon imaging under the same conditions revealed numerous cells with increased signal (Figure 1B) and only some of those cells stained positive for the astrocyte marker Sulforhodamine-101 (Figure 1C). All AD mice had CAA and tissue plaques seen with Methoxy-X04 staining (Figure 1D) and there appeared to be no association of the NADH signal with the plaques location. **Conclusions:** In agreement with previous findings, double transgenic AD mice display chronic tissue hypoxia. Our preliminary results also