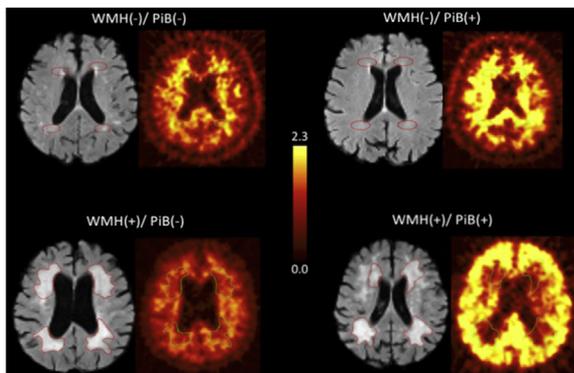


### IC-P-018 BINDING OF PITTSBURGH COMPOUND B TO BOTH NORMAL AND ABNORMAL WHITE MATTER IN ELDERLY COGNITIVELY NORMAL CONTROL

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**Background:** The amyloid imaging agent, Pittsburgh Compound B (PiB), binds with high affinity to  $\beta$ -amyloid (A $\beta$ ) in the brain and it is well established that PiB also shows non-specific retention in white matter (WM). However, little is known about retention of PiB in areas of white matter hyperintensities (WMH), abnormalities commonly seen in older adults. Further, WMH are hypothesized to be related to both cognitive dysfunction and A $\beta$  deposition. The goal of the present study was to explore PiB retention in both normal-appearing WM (NAWM) and WMH in a group of elderly, cognitively normal individuals. **Methods:** Cognitively normal elderly (n=64; 86.5 $\pm$ 2.6 years) who had a FLAIR-MRI, PiB-PET(SUVr 50-70, cerebellum reference) and visual WMH score were included in this analysis. Two ROI analyses were applied: (1) ROIs of standardized dimensions were placed over "typical" areas of periventricular WMH caps on all subjects, regardless of WMH burden or size. (2) Subject-specific maps of NAWM and WMH were created using C++ and ITK, these maps were then co-registered with the PiB-PET and mean SUVr values were calculated in these NAWM and WMH ROI. **Results:** PiB retention was significantly reduced in the "typical-WMH" ROIs of subjects with high WMH compared to subjects with low WMH (see figure below). Additionally, in subjects with high WMH, there was significantly lower PiB retention in subject-specific ROIs of WMH compared to NAWM, this was not observed in subjects with low WMH, likely because of the absence of WMH in this group. **Conclusions:** These data suggest that white matter in areas of WMH may have different binding characteristics to PiB than does normal WM. Further exploration of this phenomenon may lead to insights about the molecular basis of this non-specific interaction.



### IC-P-019 HIGH PUTAMEN 11C-PIB RETENTION IN MCI IS ASSOCIATED WITH AN INCREASED RISK OF CONVERSION TO AD

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**Background:** Alzheimer's disease (AD) pathology has most likely been ongoing in brain years before onset of cognitive symptoms. The challenge

is to detect the disease in its early stages and to be able to predict among patients who have the disease who will develop mild cognitive impairment (MCI) and convert to AD. High fibrillar A $\beta$  deposition in the cerebral cortex has been well established by 11 C-PiB-PET in MCI and AD patients. Furthermore, a high 11 C-PiB-PET retention was demonstrated in the striatum of PSN1 mutations carriers but is less studied in sporadic AD/MCI. The aim was to study the predictive value of high 11 C-PiB-PET retention in the striatum of MCI patients. **Methods:** We compared the caudate, putamen and neocortical 11 C-PiB-PET retention in 97 AD, 72 MCI patients, (mean age=68 ys). This population of patients was recently reported in a European multicenter imaging study (Nordberg et al. 2013). **Results:** In the evaluations we focused on the putamen as we found that the putamen 11 C-PiB retention exceeded the caudate 11 C-PiB retention in all subjects (p<0.001). No significant differences were found in the putamen 11 C-PiB retention between AD and MCI 11 C-PiB-positive patients. MCI patients, who converted to AD within 2 years, showed significantly higher 11 C-PiB retention in the putamen in comparison with the neocortex (p =0.006) while the MCI non-converting patients showed no significant differences between the two regions (p =0.15). These regional differences became somewhat less marked when compared MCI PiB-positive MCI converters (p =0.006) compared to MCI PiB-positive non-converters to AD (p =0.046). **Conclusions:** High putamen 11 C-PiB retention in MCI patients is associated with an increased risk of conversion to AD.

### IC-P-020 EVIDENCE OF AMYLOID ON FLORBETABEN-PET IS ASSOCIATED WITH REDUCED EPISODIC MEMORY 10 YEARS PRIOR: RESULTS FROM THE WOMEN'S HEALTHY AGEING PROJECT

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**Background:** Positron emission tomography (PET) has shown that accumulation of brain amyloid begins 20-30 years prior to AD dementia. It is less clear when decline in cognitive function begins. We sought to identify whether reduced episodic memory (EM) was present a decade earlier in participants of the Women's Healthy Ageing Project (WHAP) who showed evidence of amyloid accumulation on a recent amyloid PET scan. **Methods:** 92 participants with cognitive measures at 1999, 2002, 2004 and 2012-13 and 18F-Florbetaben PET (FBB-PET) imaging in 2012-13 were studied. All participants had normal range cognition at the 1999-2004 time points. FBB Standardised Uptake Value Ratio (SUVr) was calculated for the neocortical regions normalized to cerebellar cortex. Cognitive assessment included the CERAD word list recall (1999, 2002 and 2004) and CVLT-delay (2002, 2004 and 2012-13). EM scores were compared between tertile of FBB SUVr using ANOVA, and linear regression to adjust for age, education and E4 status. **Results:** No results submitted. **Conclusions:** Individuals with higher amounts of AD-pathology in later life demonstrate subtle decrements in episodic memory function up to ten years earlier.

### IC-P-021 MIDLIFE VASCULAR RISK, APOLIPOPROTEIN E4, AND AMYLOID STATUS 20 YEARS LATER: RESULTS FROM THE WOMEN'S HEALTHY AGEING PROJECT

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**Background:** There are conflicting reports linking vascular risk factors and Alzheimer's disease biomarkers and histopathology. Timing of exposure to risk factors may be critical in mediating their association. However there is little literature to date examining mid-life risk measurements with later-life disease-specific biomarkers such as amyloid PET imaging. **Methods:** 125 participants from the Women's Healthy Ageing Project, a longitudinal study of Australian women, with vascular risk measurements in 1992 and cognitive assessment and 18F-Florbetaben (FBB) PET imaging in 2012. FBB PET Standardized Uptake Value Ratio (normalized to the cerebellar cortex [SUVR]), and episodic memory measured by CVLT-long delay score, were compared by tertile of midlife PROCAM and Framingham Coronary Risk Scores. Groups were compared using ANOVA and linear regression models were performed including Risk Score tertile, age, education, apolipoprotein E- e 4 status, and e 4 x Risk Tertile. **Results:** Mean age was  $49.9 \pm 2.4$  years at vascular risk assessment and  $68.8 \pm 2.3$ y at time of PET scan/CVLT. Participants in the highest PROCAM tertile had significantly higher late-life mean FBB SUVR than those in intermediate ( $p < 0.04$ ) or low tertiles ( $p < 0.03$ ), and poorer mean CVLT performance ( $10.5 \pm 4.6$  words vs  $12.2 \pm 3.0$  words,  $p < 0.02$ ). Similar, though non-significant trends were also seen with midlife FCRP and late-life SUVR and CVLT. Midlife PROCAM tertile, e 4 status and e 4 x PROCAM were each significantly associated with late-life FBB burden, correcting for age and education. Age, years of education, and PROCAM tertile were independently associated with later-life CVLT-LD performance. In addition, the interaction between E4 status and PROCAM was significantly associated with CVLT-LD score, such that e 4+ with high PROCAM risk score performed much worse than e 4 non-carriers or low-risk PROCAM tertiles. Of component parts of the PROCAM, only LDL-cholesterol was associated with late-life SUVR in univariate analyses. This was largely attenuated when e 4 status was added to the model. **Conclusions:** Mid-life vascular risk factors are associated with both amyloid burden, assessed by Florbetaben PET, and poorer episodic memory function 20 years later. The presence of e 4 interacted to increase this association.

#### IC-P-022 BRAIN BETA-AMYLOID, VASCULAR FACTORS, AND COGNITION: 54-MONTH FOLLOWUP RESULTS FROM THE AIBL STUDY

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**Background:** There is great interest in interplay between cerebrovascular disease (CVD) and amyloid in mediating cognitive decline. Vascular disease risk factors increase risk for dementia, however whether this is synergistic or additive to concurrent AD-pathology is unclear. **Methods:** 287 participants from the Australian Imaging, Biomarkers and Lifestyle Study of Ageing, ranging from normal cognition through MCI to AD dementia, assessed four times over 54 months with 11C-PiB PET, 3T-MRI and neuropsychology assessment. 174 also had SWI MRI for microbleeds and 80 had carotid intima-media thickness (CIMT) measurement. Linear mixed models regression was used to compare outcome (cognitive score, PET SUVR, atrophy) between groups with and without significant PiB and CVD burden over time. Subanalyses also tested whether greater carotid intima-media thickness (CIMT) or lobar microbleeds (LMB) influenced change in PiB. **Results:** 21/151 NC and 24/32 MCI had declined (e.g. NC-MCI, MCI-AD) by 54 months. A similar proportion of PiB+CVD+ and PiB+CVD-

NC declined at 54 months (25.0% vs 26.7%) compared with PiB-CVD+ (14.3%) and PiB-CVD- (9.1%) ( $X^2 = 6.3$ ,  $p = 0.01$ ). For MCI, 100% (4/4) of PiB+CVD+ MCI vs 69.2% of PiB+CVD- declined, 2/2 PiB-CVD+ and 1/10 PiB-CD- ( $X^2 = 15.3$ ,  $p = 0.002$ ). Both PiB+ and CVD+ were associated with cognitive decline in univariate models, however after correcting for age, E4, gender and education, PiB+ remained significant, whereas CVD+ was not. In mixed models analyses adjusted for age, education and E4 status, PiB and CVD were additive, but not interactive, in influencing longitudinal change in episodic memory (CVLT-long delay) and global cognitive function (CDR-SOB). There was no significant difference seen in the accumulation of PiB over time between CVD+/-, nor in subanalyses by CIMT or lobar microbleeds. **Conclusions:** In this sample, PiB and CVD were additive but not interactive processes in mediating cognitive decline, and no association was seen between markers of vascular pathology and longitudinal PiB accumulation.

#### IC-P-023 AMYLOID PET HAS GREATER CLINICAL IMPACT THAN FDG PET IN THE DIFFERENTIAL DIAGNOSIS OF AD AND FTD

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**Background:** Differentiating AD (Alzheimer's disease) and FTD (fronto-temporal dementia) is a promising application of amyloid imaging. We prospectively assessed the clinical impact of florbetapir PET in this scenario, and compared to FDG PET, the current standard. **Methods:** Patients with suspected AD (N=24) or FTD (N=13) were assessed by behavioral neurology fellows and attending physicians at an academic dementia center (10 by fellows, 2 by attendings, 25 by both). Mean age was  $63.6 \pm 7.6$  and MMSE was  $21.3 \pm 6.6$ . All patients underwent florbetapir PET and 35/37 underwent FDG PET. Scans were visually interpreted blinded to clinical information. Written reports of scan results were released to clinicians sequentially using a balanced design (50% florbetapir results disclosed first, balanced between fellows and attendings). Clinicians independently rated their top clinical diagnosis, diagnostic confidence and management plan prior to PET and following disclosure of each scan result. **Results:** Florbetapir PET was positive in 63% of patients with suspected AD and negative in 85% of FTD patients. FDG visual reads agreed with the clinical diagnosis in 73% of AD and 69% of FTD patients. Florbetapir and FDG PET agreed in 86% of patients ( $\kappa = 0.72$ ). There was no relationship between the order in which scans were disclosed and concordance with pre-PET diagnosis ( $p > 0.54$ ). Fellows changed their primary clinical diagnosis in 15% of cases after florbetapir results were disclosed and 0% after FDG results disclosure ( $p < 0.001$ ). Attending physician diagnoses changed in 11% of patients following florbetapir results and 4% after FDG results ( $p = 0.08$ ). Clinicians reported high diagnostic confidence in 37% of patients pre-PET, 45% post-FDG PET and 71% post-florbetapir PET ( $p = 0.004$  vs. FDG). Changes in management were more frequent after florbetapir (32%) than FDG results disclosure (12%), but this was not significant ( $p = 0.67$ ). Changes in management included starting or stopping AD medications, referring patients to clinical trials or further clinical work-up. Clinicians reported that amyloid results were more helpful than FDG results in guiding clinical management in 76% of cases. **Conclusions:** Amyloid PET had greater clinical impact than FDG PET and should be considered the PET scan of choice for the discrimination of AD and FTD.