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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 ± 2.4 years at vascular risk assessment and 68.8 ± 2.3y 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 ± 4.6 words vs 12.2 ± 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 (frontotemporal 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±7.6 and MMSE was 21.3±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 reads 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.

IC-P-024 BIN1 AND CR1 VARIANTS AFFECT COGNITIVE PERFORMANCE, NEURODEGENERATION, AND BRAIN AMYLOIDOSIS IN ADNI SUBJECTS

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Background: Genome-wide association studies (GWAS) have identified many risk genes for Alzheimer's disease (AD). The precise mechanism through which many of these genes exert their effect on AD remains unknown. **Methods:** We downloaded the top 10 AD gene single nucleotide polymorphism, baseline clinical and MR volumetric data (hippocampal, ventricular, fusiform and entorhinal volumes) of 33 ADNI-2/GO cognitively normal and 126 mild cognitive impairment subjects. The corresponding AV45 images were downloaded and processed with the FDA-approved AmyQ software. For each individual AmyQ derived the mean SUVR in 46 ROIs across the brain with whole cerebellum as a reference. We employed ANOVA with Bonferroni correction for multiple comparisons to investigate the effect of minor allele dosage on cognitive and functional performance, neurodegeneration and brain amyloidosis. **Results:** CR1 rs6691117 and BIN1 rs749008 had significant effects on multiple measures. The minor allele of CR1 rs6691117 showed significant association with functional decline at 6, 12 and 24 months as measured with the Functional Activity Questionnaire (FAQ). The minor allele of CR1 rs6691117 also associated with lower entorhinal and fusiform volumes as well as with greater brain amyloidosis in the lateral temporal, parietal and occipital association cortices at baseline. The minor allele of BIN1 showed a negative association with ventricular size and amyloid load in the frontal association, sensorimotor, posterior cingulate, medial temporal cortices, the pons, the midbrain and the lentiform nuclei. **Conclusions:** Both CR1 rs6691117 and BIN1 rs749008 demonstrate significant associations with brain amyloidosis and neurodegeneration providing further support for the relevance of these two genes to AD pathophysiology. The minor allele of CR1 rs6691117 appears to have a disease-promoting effect while the minor allele of BIN1 rs749008 seems to convey a disease-protective effect. The associations differed significantly in terms of localization in the brain.

IC-P-025 AGE IS A SIGNIFICANT FACTOR IN DETERMINING PATHOLOGICAL POSITIVITY MEASURED WITH [18F]FLORBETAPIR PET

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Background: The effect of age on amyloid burden in Alzheimer's Disease patients and in the discriminative power of amyloid imaging needs to be determined. **Methods:** 246 Healthy Control (HC), 342 Mild Cognitive Impairment (MCI) and 138 AD with raw [18F]Florbetapir- and [18F] FDG-PET data were downloaded from the Alzheimer's Disease Neuroimaging Initiative (ADNI) database. Florbetapir data were analysed using a Florbetapir-PET population template and atlas. Two age groups were created; mean = 70.9 ± 3.5 (young) and 80.9 ± 3.9 (old) years, matched for gender and disease severity (MMSE). A Receiver Operating Characteristic Analysis derived a composite neocortex ratio (cctxr) cut-off of 1.34. The AD patients with Amyloid negative scans had their Florbetapir and FDG scan read visually. **Results:** The Florbetapir cut-off displayed lower sensitivity and specificity in the old ADNI group in comparison to the young one (87/87 vs 73/74). The young HC displayed significant lower amyloid in the Posterior Cingulate (1.16 vs 1.24) and the Putamen (1.18 vs 1.25) in comparison to the older HC. The cctxr values of the old AD patients (oAD) were bimodal in mixture model analysis whereas the values of the younger AD (yAD) patients followed a normal distribution. The yAD patients, whether analysed dichotomously or continuously, displayed significantly higher values in all ROI examined in comparison to the oAD, except in Putamen and Occipital lobe. The neocortical FDG pattern of amyloid negative AD patients (n=27; 10 yAD vs 17 oAD) were all consistent with AD; whereas 10 of the same individuals had negative Florbetapir scans when read visually. In agreement with the PET template analysis the amyloid negative oAD had a greater number of Florbetapir scans read as negative (n=8) in comparison to the yAD (n=2). **Conclusions:** The Florbetapir cut-off, as well as the visual read of the Florbetapir scans, displayed a diminished discriminative ability in the old ADNI group in comparison to the younger patients. The oAD patients showed less prominent amyloid burden and different distribution of their values in comparison to the yAD group. This might have important implications for the clinical diagnostic use of Florbetapir imaging in the oldest patients.

IC-P-026 HIGH BLOOD PRESSURE, BUT NOT CEREBRAL AMYLOIDOSIS, IS ASSOCIATED WITH LATE-LIFE ONSET DEPRESSION IN NON-DEMENTED ELDERLY

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Background: Previous researches on the late-life onset depression (LLOD) have revealed its association with vascular risk factors, which supported vascular depression hypothesis. However, several recent studies raised the possibility of the role of cerebral amyloidosis in LLOD. We aimed to investigate the independent association of vascular risk factors and cerebral amyloidosis with the experience of LLOD. **Methods:** Twenty eight non-demented subjects who first experienced major depressive episode after age of 60 years were recruited as LLOD patients. Twenty seven non-demented elderly individuals who had no experience of major depressive episode were also included as normal control (NC) subjects. All participants received comprehensive clinical assessment including vascular risk evaluation, 11 C labeled Pittsburgh Compound B (PiB) positron emission tomography (PET), and magnetic resonance imaging (MRI). **Results:** There were no group differences in age, education level but the frequency of female participants was significantly higher in LLOD patients compared to NC subjects. Univariate group comparison demonstrated that LLOD subjects had significantly higher systolic blood pressure than NC. In contrast, no significant between-group differences were found in regard of mean cortical PiB retention, and the frequency of PiB-positive and ApoE e4 carriers. Multiple logistic regression analysis including diagnostic group (LLOD vs. NC) as a dependent variable showed that systolic blood pressure was significantly associated with LLOD diagnostic state after controlling age, education, gender, and mean cortical PiB retention as covariates. Mean cortical PiB retention did not show any significant association with LLOD state in the same regression model. **Conclusions:** The results suggest that while vascular risk, hypertension in particular, is closely related to LLOD as indicated by vascular depression hypothesis, cerebral amyloidosis per se is probably not a major contributor to LLOD.

IC-P-027 VALUE OF AMYLOID IMAGING FOR PREDICTING CONVERSION TO DEMENTIA IN MCI SUBJECTS WITH INITIALLY INDETERMINATE FDG-PET SCANS

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