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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