IC-P-014 EFFECT OF HOMOCYSTEINE ON HIPPOCAMPAL ATROPHY INDEPENDENT OF CEREBRAL AMYLOID DEPOSITION AND VASCULAR BURDEN IN NORMAL AGING, MCI AND ALZHEIMER'S DISEASE

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Background: Although elevated levels of homocysteine have been associated with greater brain atrophy in elderly people, the pathogenetic linkage between the two is still unclear. This study aimed to clarify whether homocysteine has any independent effect, not medicated by cerebral beta amyloid protein (Aβ) deposition and vascular burden, on whole brain or hippocampal atrophy in elderly individuals with normal cognition, mild cognitive impairment (MCI) and AD. **Methods:** Fourteen cognitively normal, 19 MCI, and 24 AD individuals were included. All subjects received three-dimensional volumetric MRI, Pittsburgh Compound B - positron emission tomography and comprehensive clinical evaluation including vascular burden assessment for diabetes, hypertension, dyslipidemia, coronary artery disease, stroke and transient ischemic attack. Blood homocysteine, vitamin B 12, and folate levels were also measured. **Results:** Multiple linear regression analyses showed that plasma total homocysteine level was significantly associated with hippocampal atrophy even after controlling the degree of global cerebral Aβ deposition and vascular burden as well as other potential confounders including age, gender, education and apolipoprotein E ε4 genotype. In contrast, plasma total homocysteine level did not show any significant association with whole brain volume. **Conclusions:** Our finding of the independent negative association between plasma homocysteine and hippocampal volume suggests that homocysteine has a direct adverse effect, not mediated by cerebral Aβ deposition and vascular burden, on the hippocampus.

IC-P-015 EVALUATION OF THE PONS AS A REFERENCE REGION FOR AMYLOID PET IN ALZHEIMER'S DISEASE CLINICAL TRIALS

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Background: In observational Alzheimer's disease (AD) studies and clinical trials, amyloid PET data in cortical and subcortical regions of interest (ROIs) are typically quantified using a target-to-reference region (RR) approach which produces a standardized uptake value ratio (SUVr).This approach requires that the RR be reliably imaged, represent true background, i.e., not accumulate fibrillar amyloid, and, for clinical trials, not be affected by study medication. Cerebellar gray matter (cGM) is the most common RR, but it may not optimally satisfy these requirements, being vulnerable to confounding image acquisition factors and potential biological factors, i.e., amyloid accumulation and/or removal. Alternate RRs have been suggested, including the pons, subcortical white matter, and various combinations of regions. While the pons has attractive RR properties (e.g., well seen on PET, white-matter rich, amyloid-poor, with stable test-retest data), it has not previously been evaluated for clinical trial use, in which particular qualities may be especially important, eg, sensitivity to amyloid removal. **Methods:** We conducted a preplanned exploratory evaluation of the pons as RR in Pittsburgh Compound B (PiB) PET substudies of separate bapineuzumab Phase 3 studies enrolling apolipoprotein E4 non-carriers and carriers with mild-moderate AD. Subjects were scanned at baseline and after 45 and 71 weeks' treatment (bapineuzumab or placebo). Scans were originally analyzed using cGM as RR, producing SUVrs for anatomically defined ROIs and a global cortical average (GCA) composite ROI. Scans were reanalyzed substituting the pons as RR. Pons performance was evaluated by examining variability within and across subjects and on longitudinal changes, particularly within treatment arms. **Results:** Placebo-treated non-carriers' pons-based GCA SUVrs showed more longitudinal stability than their cGM-based SUVrs. Placebo-treated carriers showed more linear SUVr increase, compatible with findings in observational studies, eg, ADNI. Bapineuzumab-treated subjects showed either linear or more persistent GCA amyloid reduction using pons rather than cGM. Apparent reduced dataset variability merits further exploration. **Conclusions:** Using the pons as RR in an amyloid-removal trial produced intriguing results. Further investigation is warranted to understand the relative merits of various RRs, particularly concerning variability and longitudinal trends - both being critical for clinical trials.

IC-P-016 MR-LESS CORTICAL SURFACE-PROJECTION OF PET IMAGES FROM 11C- AND 18F-LABELED RADIOTRACERS

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Background: Clinical PET imaging in Alzheimer's disease relies in the visualisation of Aβ deposition and glucose metabolism in the cortical gray matter. Due to the limited structural information in PET images, automatic tissue-specific assessment is usually performed with the aid of MR images, which may not always be available. We evaluated a novel MR-less method to locally estimate and project the cortical tracer retention on a common surface template. **Methods:** Several subjects were scanned with different radiotracers: 18 F-Flutemetamol, 18 F-Florbetapir, 18 F-Florbetaben, 11 C-PIB, 18 F-NAV4694 and 18 F-FDG. First, each individual PET image was normalised in the MNI space and SUVR scaled with a common cortical cerebellum mask. Radiotracer retention was then estimated within several GM prior atlases. On scans acquired on a PET/CT scanner, CT was used to estimate the GM priors. Atlas selection and Bayesian fusion were then used for generating estimated surface values, reflecting the pattern of either high (Aβ ligands) or low (FDG) tracer retention. Surface projections and native transaxial, sagittal and coronal PET images were visually graded by clinicians blinded to clinical diagnosis. Images were read separately and graded as normal, possible AD or probable AD. For sensitivity and specificity calculations, "possible" and "probable AD" were combined. **Results:** In the visual readouts, surface projection images provided higher inter-rater reliability and much greater reader confidence than native PET images. Visual assessment of surface projections was both very sensitive and specific for AD and performed better than visual