IC-P-051 AMYLOID LOAD INCREASE AND CEREBRAL MICROBLEED PREVALENCE DIFFER AS A FUNCTION OF THE POSITION OF THE MUTATION WITHIN THE PSEN1 CODING SEQUENCE

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Background: Autosomal dominant Alzheimer's disease (ADAD) is a rare familial form of AD caused by mutations that alter metabolism of the β-amyloid protein. Most ADAD mutations concern the *PSEN1* gene with more than 185 mutations currently reported. Mann and colleagues have reported histological differences in terms of amyloidosis and angiopathy when *PSEN1*mutations are located before or after the codon 200 (Mann et al., 2001). The Dominantly Inherited Alzheimer Network (DIAN) aims to understand the changes occurring in the ADAD population. Here, we investigated amyloid PiB-PET retention and prevalence of microbleeds as imaging biomarkers, taking into account the mutation position relative to the codon 200. **Methods:** Carriers of a mutation on the *PSEN1*gene (n=119), before (n=34) or after (n=85) codon 200, underwent PiB-PET scan to quantify amyloid brain deposition, susceptibility-weighted imaging MR scan to detect microbleeds, and volumetric MRI. The volumetric MRI was used to register the PET images and calculate standardized uptake values ratio (SUVR) from segmented regions. Cross-sectional analyses with linear models were performed to evaluate the amyloid retention in function of estimated year of onset (EYO) of the symptoms. Prevalence of microbleeds in the participants and per group of mutation position was also analyzed. **Results:** Cross-sectionally estimated slopes of amyloid accumulation differed as a function of the mutation position. The group with mutations before codon 200 showed greater slope of amyloid accumulation at the mean cortical and caudate levels (p-value$<$0.005 and p-value$<$0.0005, respectively). Concerning microbleed evaluation, 12% of our cohort displayed one or more microbleeds. The percentage of carriers with microbleeds was up to 75% in the group carrying a mutation located after codon 200 compare to 25% in the group carrying a mutation located before codon 200. **Conclusions:** Our imaging findings are concordant with the previous histological description of particular phenotypes due to the position of the *PSEN1* mutation. They give new insights into the ADAD population who often display high subcortical, basal ganglia amyloidosis. These outcomes can be taken into account to address specific treatment trial designs, including screening participants likely to develop microbleeds during clinical trials.

IC-P-052 COMPARISON OF CEREBRAL GLUCOSE METABOLISM ^{18}F-FDG, EARLY FRAMES OF ^{11}C-PIB, AND CEREBRAL BLOOD FLOW ^{15}O-H_2O IN AUTOSOMAL DOMINANT ALZHEIMER'S DISEASE

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Background: Biomarkers characterizing Alzheimer's disease (AD) can estimate brain amyloid, tau accumulation, cerebral glucose metabolism decrease, and atrophy. In autosomal dominant AD similar biomarker changes have been observed (Bateman et al, 2012). Cerebral blood flow (CBF) may also change with the disease severity (Alsop et al, 2010). Cerebral glucose metabolism measured by ^{18}F-fluorodeoxyglucose (FDG)-PET is linked to CBF. Many studies have recently used early frames of ^{11}C-Pittsburgh Compound B (PiB)-PET (ePiB) as a proxy of CBF and have investigated associations with FDG (Rostomian et al, 2011). We evaluated in an autosomal dominant AD cohort the perfusion components of ePiB and FDG in comparison to a gold standard estimate of CBF, ^{15}O-H_2O. **Methods:** Thirty participants, including 11 mutation carriers (MC), underwent FDG, full dynamic PiB, ^{15}O-H2O PET and structural MRI scans. The PET images of each participant were registered with their structural MRI. The ePiB images were created using 1 to 9 min time frames, as best correlation with FDG. For each participant, voxel-wise spatial correlations were performed between FDG and ^{15}O-H2O, and between ePiB and ^{15}O-H2O images. The Pearson's correlation coefficient was used to assess the association between the different modalities for the whole brain and gray matter cortex, in PiB-positive and negative MC and non-carriers. PiB-positivity was defined with a threshold of $>$0.18 in mean cortical binding potential. **Results:** The FDG and ePiB images were visually similar and they displayed similar correlations for the whole brain and the cortex (0.8$\pm$0.01 and 0.7$\pm$0.01, respectively). Both FDG and ePiB had similar correlations with the ^{15}O-H2O, reaching an average of 0.6$\pm$0.01 and 0.4$\pm$0.01 for the whole brain and cortex, respectively. The same associations were observed in MC and non-carriers, and in the PiB-positive and PiB-negative participants from the MC group. **Conclusions:** Our results show that cerebral metabolism and early PiB perfusion frames are correlated to CBF irrespective of the level of AD pathology or mutation status. Evaluation of how these related phenomena evolve with the disease may give insight into the sequence of AD neuropathology. More studies are needed to determine whether these associations are maintained through the course of the disease.

IC-P-053 COMMON MEDIAL TEMPORAL LOBE ATROPHY ASSOCIATED WITH DISTINCT STRUCTURAL CONNECTIVITY INJURIES IN SEMANTIC DEMENTIA AND ALZHEIMER DISEASE

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Background: Semantic dementia (SD) and Alzheimer disease (AD) are both associated with medial temporal lobe (MTL) atrophy. However, while patients with AD present with anterograde