Background: Several studies highlighted the differential effect of normal and pathological aging on hippocampal subfield volumes, suggesting that these measurements may be more accurate than global hippocampal volumetry to detect early Alzheimer's disease (AD). For clinical application, validated automatic algorithms of hippocampal subfield segmentation are urgently needed. An increasing number of studies use the automatic segmentation algorithm implemented in FreeSurfer. However, this approach has not been validated so far on AD patients. This study aimed to compare the accuracy of T1-MRI-based FreeSurfer segmentation versus manual delineation on dedicated high-resolution scan in measuring hippocampal subfield volumes and the effects of age and AD on these volumes. **Methods:** Hippocampal subfields were segmented in 98 healthy individuals (aged 19 to 84), 17 MCI and 18 AD patients using both FreeSurfer (T1-MRI, resolution: 1*1*1mm) and manual delineation (proton density-MRI, resolution: 0.375*0.375*2mm). Intraclass correlation coefficients (ICC) and Bland-Altman plots were computed to assess the consistency between both methods, and the effects of age (regressions) and group (ANOVAs) were assessed for both Freesurfuer and manual measurements. **Results:** Moderate to high ICCs were found for the subiculum and other subfields as well as for the whole hippocampus, but the ICC was very low for CA1. Using manual delineation, age was found to have a linear effect on the subiculum and a nonlinear (later) effect on CA1 volumes. A graded effect of the pathology was found on CA1, subiculum and the other subfields volumes. FreeSurfer CA1 volumes were found to be lower than those obtained from manual segmentation. This bias was proportional to the volume of this structure so that no effect of age or AD could be detected on FreeSurfer CA1 volumes. **Conclusions:** This study highlights differences in the anatomic definition of the subfields, especially for CA1, between FreeSurfer and manual delineation based on histologic atlases. While FreeSurfer provides reasonable estimates of the subiculum and other subfields, it does not provide a reliable estimate of CA1 volume and fails in detecting normal aging and AD-related changes in this subfield. As earliest AD-related changes seem to occur in CA1, FreeSurfer needs to be improved especially for clinical application in early AD diagnosis.

IC-P-094 ALTERED FMRI ACTIVATION PATTERN DURING VISUAL SCENE ENCODING IN AFFECTED AND NON-AFFECTED CARRIERS OF PSEN1 AND APP MUTATIONS

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Background: Carriers of PSEN1 and APP mutations associated with familial autosomal dominant Alzheimer's disease (ADAD) have shown brain atrophy, amyloid deposition, and alterations in other biomarkers. However, the effect of these mutations on brain activation during memory processing has not been thoroughly explored. A visual scene encoding fMRI task was used to investigate activation changes in clinically affected and preclinical carriers of a PSEN 1 or APP mutation. **Methods:** 17 participants, including 5 clinically affected carriers of a PSEN1 or APP mutation (symptomatic mutation carrier (sMC); 4 PSEN1, 1 APP), 5 asymptomatic carriers (aMC; 4 PSEN1, 1 APP), and 7 healthy age-matched non-carriers (NC), were imaged using blood oxygen level dependent (BOLD) fMRI during a visual scene encoding task. After quality control, all fMRI scans were preprocessed using standard procedures in SPM8. Briefly, scans were spatially aligned, normalized to standard (MNI) space, resampled to 2mm isotropic voxels, and smoothed using a 6mm FWHM kernel. Contrast images were generated for each participant for the encoding > control conditions. These contrast images were then compared between groups using a one-way ANOVA in SPM8 and masked using a whole brain mask. Results were displayed at a significance threshold of $p<0.01$ (unc.) and a minimum cluster size of 25 voxels. **Results:** sMC showed significantly less activation than NC during visual scene encoding in the bilateral occipital, inferior temporal, and frontal lobes, as well as in the right medial temporal lobe (MTL; Figure 1A). sMC also showed significantly less activation than aMC in bilateral occipital, inferior temporal, frontal and MTL regions (Figure 1B). However, aMC showed greater activation than NC in the bilateral MTL (Figure 1C). Exclusion of the APP mutation carriers did not significantly alter the findings. **Conclusions:** Symptomatic carriers of a PSEN1 or APP mutation show reduced brain activation during visual encoding which suggests that the presence of clinical symptoms is associated with a decrease in brain activity during memory processing. Interestingly, asymptomatic carriers of these mutations showed increased activation in the bilateral MTL, which may represent a compensatory increase in activation in preclinical stage disease.

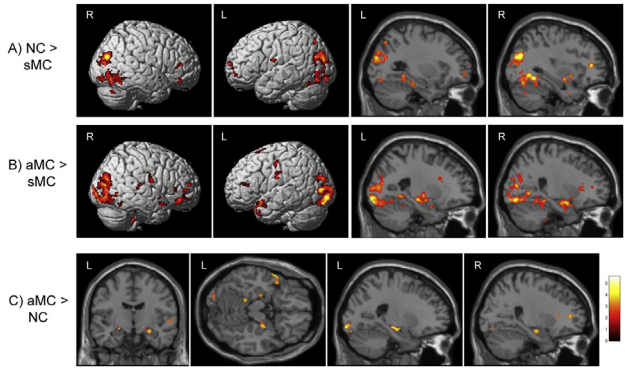

Figure 1. Altered brain activation during visual scene encoding in carriers of a *PSEN1* or *APP* mutation

IC-P-095 TWO-YEAR LONGITUDINAL CHANGE IN AMYLOID DEPOSITION, GLUCOSE METABOLISM, AND HIPPOCAMPAL ATROPHY IN ADNI-2 PARTICIPANTS: RELATION TO GENETIC RISK

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Background: Longitudinal change in amyloid deposition, glucose metabolism, and medial temporal lobe atrophy are important biomarkers for studies of Alzheimer's disease (AD). The goal of this study was a comparative assessment of two-year change in amyloid deposition, glucose metabolism, and hippocampal atrophy in

participants from the Alzheimer's Disease Neuroimaging Initiative (ADNI) with special emphasis on prodromal stages. **Methods:** 320 participants, including 106 healthy controls (HC), divided by genetic risk (family history of AD and/or APOE ε4 positive), 130 patients with early (EMCI) and 44 participants with late mild cognitive impairment (LMCI), and 29 patients with AD, were included in this analysis. Florbetapir PET scans and structural MRI scans were downloaded from the ADNI site for the baseline Florbetapir visit and the two-year follow-up visit and processed using previously described techniques [1]. FDG PET scans were also downloaded from these timepoints and processed using standard techniques. Average Florbetapir SUVR, FDG SUVR, and structural grey matter density (GMD) were extracted from target ROIs at both visits, including the global cortex for the PET and bilateral mean hippocampus for MRI. Annualized percent change (APC) was calculated from these regions and compared between groups. **Results:** No group differences were observed for change in amyloid deposition. However, glucose metabolism decline and hippocampal GMD atrophy rate showed significant group differences ($p<0.001$, Fig. 1A&B). AD showed faster glucose decline and hippocampal atrophy than all other groups except LMCI ($p<0.01$). LMCI had a greater hippocampal atrophy rate than HC without risk and EMCI ($p<0.05$). HC at genetic risk showed a non-significant trend toward greater decline in glucose metabolism and hippocampal GMD than HC without risk ($p=0.1$ for GMD). **Conclusions:** Mean amyloid deposition does not appear to significantly change over two years in any stage of cognitive impairment. However, declining glucose metabolism and hippocampal atrophy rates appear to accelerate in later disease stages (LMCI, AD). Cognitively normal older adults at risk for AD due to genetic background may show greater rates of hippocampal atrophy and glucose metabolic decline than those without genetic risk but larger samples and replication are needed to further investigate this issue.[1] Risacher et al. (2013) Front Aging Neurosci

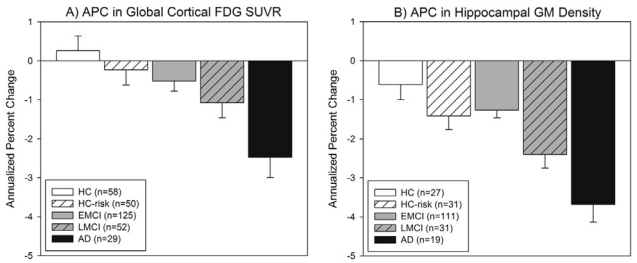

Figure 1. APC in Glucose Metabolism and Hippocampal GM Density

IC-P-096 INCREASED AMYLOID DEPOSITION IN OLDER ADULTS AT RISK FOR PROGRESSION TO ALZHEIMER'S DISEASE DUE TO GENETIC BACKGROUND AND/OR THE PRESENCE OF SIGNIFICANT MEMORY CONCERNS

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Background: Older adults with significant memory concerns (SMC) and/or genetic risk for AD are key groups of interest due to risk of progression. Our goal was to evaluate amyloid deposition, glucose metabolism, and medial temporal lobe (MTL) atrophy in SMC participants from ADNI. **Methods:** 569 participants were selected from the ADNI cohort, including 177 healthy controls (HC), 93 participants with SMC, and 299 patients with early mild cognitive impairment (EMCI). The HC participants were further divided into those with genetic risk (APOE ε4 positive and/or family history of AD (HC-risk)) and those without genetic risk (HC). The SMC participants were also further divided by the presence or absence of informant complaints about the participant's memory. SMC participants were considered to have self-only concerns (SMC) if the informant did not endorse >1.5 SD above the HC mean on the ECog Memory domain (~62% of items) and to have self-plus-informant concerns if the informant endorsed > 62% (SMC-plus). Florbetapir and structural MRI scans were downloaded from the ADNI site for the baseline visit and processed as previously described [1]. FDG PET scans were also downloaded from this timepoint and processed using standard techniques. Average Florbetapir SUVR, FDG SUVR, and structural grey matter density were extracted from the global cortex (PET) and bilateral hippocampus (MRI). Florbetapir PET scans were also compared between groups on a voxel-wise level in SPM8. **Results:** A significant difference in amyloid deposition was observed between groups on both voxel-wise and ROI analyses. HC-risk, SMC, and SMC-plus demonstrated more global and regional amyloid deposition than HC without risk, including in the global cortex ($p=0.004$) and precuneus ($p<0.001$). Differences in glucose metabolism and MTL atrophy were more variable with some regions showing a trend towards hypometabolism and MTL atrophy in HC-risk and SMC groups. **Conclusions:** Participants with SMC and HC participants at risk for progression to AD due to genetic background show increased amyloid deposition relative to HC without risk. This suggests that older adults with SMC, especially those with informant corroboration, are at increased risk for future cognitive decline and therefore may be a good target population for enrichment of clinical trials.[1] Risacher et al. (2013) Frontiers in Aging Neuroscience.

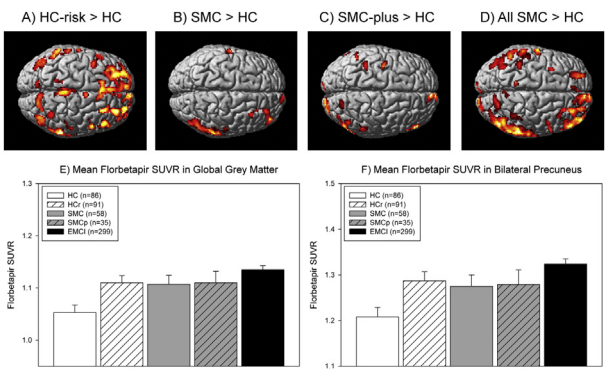

Figure 1. Increased Amyloid Deposition in Older Adults at Risk for AD

IC-P-097 VISUAL AND AUDITORY CHANGES ARE ASSOCIATED WITH NEUROIMAGING BIOMARKERS DURING PRODROMAL STAGES OF ALZHEIMER'S DISEASE

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