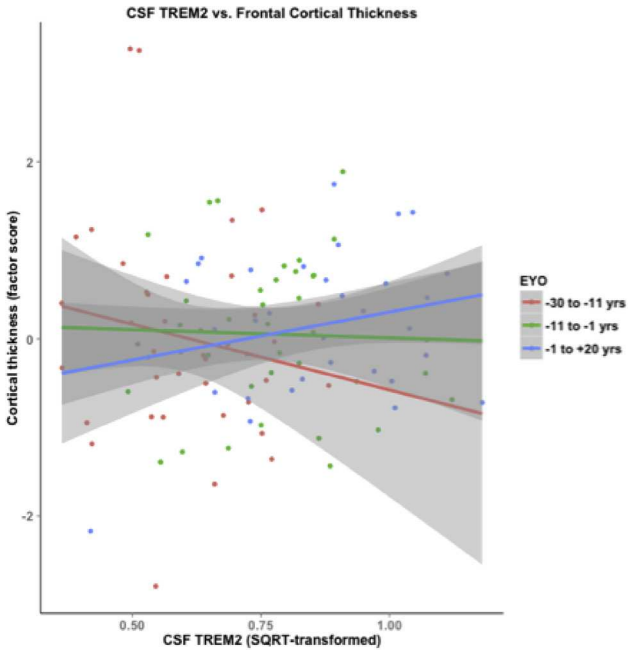

Figure. Regression plot showing interaction between CSF TREM2 and EYO onto factor scores of cortical thickness in predominantly frontal brain areas ($p = 0.03$) The shaded areas represent the 95% confidence interval of the regression lines.

genotype. **Results:** CSF sTREM2 levels were significantly higher in MC than in NC, and increased with more progressed EYO and higher dementia rating scale (CDR) scores in the MC subjects. For the factor analysis of cortical thickness, 3 factors explained 56% of the variance. Within the MC group, we observed a significant interaction between sTREM2 x EYO onto the factor scores of predominantly frontal cortical thickness (beta = 0.11, $p = 0.03$). Inspection of figure 1 shows that a positive association between higher sTREM2 and cortical thickness started to emerge after the estimated symptom onset. No associations were observed in NC. **Conclusions:** TREM2 increases during the course of AD. However, higher TREM2 is associated with greater frontal cortical thickness during more advanced stages, potentially due to compensatory processes in the frontal lobe or due to TREM2-mediated phagocytotic and non-inflammatory immune response to apoptotic processes.

IC-P-116 LATERAL ENTORHINAL CORTICAL THINNING PREDICTS COGNITIVE DECLINE IN THE ADNI SAMPLE

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Background: The entorhinal cortex is one of the earliest sites in the brain that is impacted by Alzheimer's disease pathology. In particular, aggregates of tau protein making up neurofibrillary tangles are prevalent in the transentorhinal region in the earliest stages of Alzheimer's disease. Recent data has also implicated the lateral entorhinal cortex as a potential ground zero for Alzheimer's disease and proposed the tau pathology may spread from the lateral entorhinal cortex to other neighboring sites in the medial temporal lobes as well as the neocortex. **Methods:** We used a novel structural cortical thickness pipeline to examine predictors of cognitive decline in the ADNI sample. We subdivided the entorhinal cortex into lateral (LEC) versus medial (MEC) portions and examined the degree to which neurodegeneration manifests in these two subregions and whether they differentially predict cognitive decline. **Results:** First, we analyzed baseline cortical thickness in the LEC and MEC by group status using an ANOVA. We found a significant interaction between region and group suggesting that there were greater differences between groups in the LEC than in the MEC. Next, we performed a regression analysis with separate models for LEC and MED both with MMSE as the predicted variable. In the MCI group, we found that greater EC baseline thickness was associated with higher MMSE scores and was also associated with greater preservation of MMSE scores over time. This association was greater for the LEC than for the MEC and persisted when confounding factors were accounted for. **Conclusions:** We suggest that lateral entorhinal cortical vulnerability maybe a site of early impairment in age-related cognitive decline that may serve as a viable biomarker and target for interventional trials in preclinical AD.

IC-P-117 NEURONAL INJURY AND DEGENERATION EVALUATED WITH IMAGING AND CSF BIOMARKERS IN AUTOSOMAL DOMINANT AD: RESULTS FROM THE DIAN STUDY

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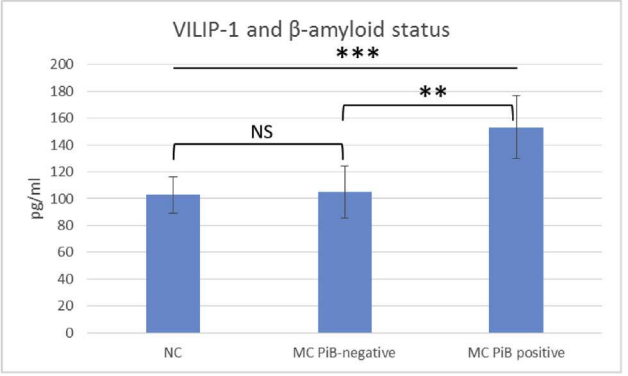
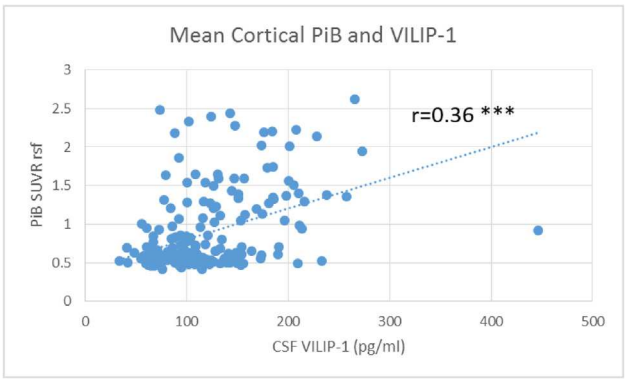
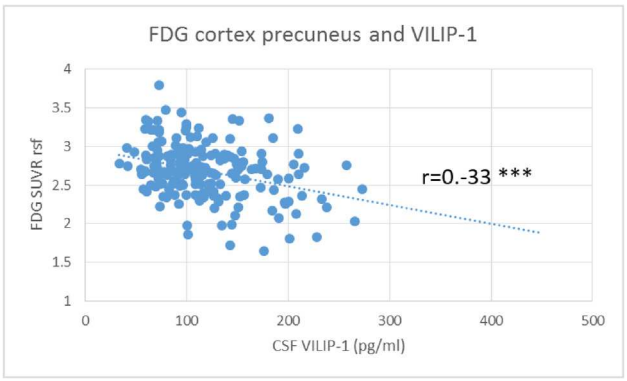
Background: Changes in Alzheimer's disease (AD) biomarkers can be detected before cognitive decline using neuroimaging and CSF measures. In autosomal dominant AD (ADAD), PET imaging biomarkers of amyloidosis and hypometabolism (measured with Pittsburgh compound B [PiB] and







fluorodeoxyglucose [FDG], respectively) are detectable 15 and 10 years before any symptoms develop. A new marker of neurodegeneration, increased CSF visinin-like protein 1 (VILIP-1), may predict cognitive decline and has been shown to be increased in carriers of an ADAD mutation. We wanted to further characterize in ADAD this new marker of neurodegeneration by evaluating its relationship with well-known AD biomarkers, in particular FDG hypometabolism, which is believed to reflect neuronal dysfunction and injury. **Methods:** Participants from the Dominantly Inherited Alzheimer Network (DIAN) study (n=202, including 124 mutation carriers [MC], 43 of whom were symptomatic) underwent MRI, PiB and FDG PET scans and CSF VILIP-1 measurement. Dementia severity was defined by the Clinical Dementia Rating (CDR). The cohort was divided by mutation status (non-carriers [NC] vs. MC) and β-amyloid status (PiB-negative vs. PiB-positive) for group comparisons. The standardized uptake value ratio (SUVR) of PiB and FDG, obtained from an MRI-based PET processing method, were corrected and normalized to the brainstem. Partial correlations between PET SUVR data and CSF-VILIP-1 levels controlling for age and family history were performed. **Results:** This study confirmed increased CSF VILIP-1 levels and decreased FDG SUVR values in MC compared to NC. Among carriers, PiB-positive participants had higher VILIP-1 levels compared to PiB-negative ($p<0.005$). VILIP-1 trended higher in PiB-positive asymptomatic participants compared to PiB-negative ($p=0.07$). A positive correlation between mean cortical PiB SUVR and VILIP-1 ($r=0.36$, $p<0.0001$) and a negative correlation between FDG PET in the precuneus and VILIP-1 in all participants ($r=-0.33$, $p<0.0001$) were observed. The negative correlation between CSF-VILIP-1 and FDG PET was driven by the PiB-positve MC participants. **Conclusions:** These preliminary results show that increased CSF VILIP-1, a marker of neuronal injury, is associated with both abnormal amyloid deposition and cerebral glucose hypometabolism in the DIAN population. Longitudinal investigation and evaluation of other AD features are still needed. Support: NIH/NIA U01AG032438.

IC-P-118 VALIDATED DEMENTIA RISK MEASURE IS ASSOCIATED WITH REGIONAL BRAIN VOLUMES: THE ANU ALZHEIMER'S DISEASE RISK INDEX (ANU-ADRI)

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Background: Effective dementia prevention requires the identification of modifiable risk factors, reliable estimation of their combined risk and identification of individuals at risk. The ANU Alzheimer Risk Index (ANU-ADRI) was developed to assess a person's future risk of developing Alzheimer disease given their current exposure to known risk factors. It is based on current evidence on AD modifiable risk factors and reliable effect sizes from meta-analyses. The ANU-ADRI methodology is published and has been validated on three large international studies. The aim of this study was to further demonstrate the validity of this instrument by investigating associations between risk scores and brain structure. **Methods:** Cognitively healthy individuals (n=358, 46.1% female, 63.1 years, MMSE: 27-30) living in the community and participating in the neuroimaging sub-study of the PATH Through Life project were included in this investigation. Cortical volumes were measured with the Freesurfer 5.3 package. Dementia risk was assessed with the ANU-ADRI which produces a composite measure based on robust effect size from systematic reviews and meta-analyses of demonstrated risk factors. The cross-sectional relationship between ANU-ADRI scores (lower=less risk) and orbito-frontal, medial temporal and posterior cingulate cortex volumes were investigated with multiple regression analyses while controlling for age, sex and intra-cranial volume. **Results:** The ANU-ADRI ranged from -17 to +10 (mean -8.50, SD=5.34). Higher ANU-ADRI scores (greater risk) were associated with lower left (Beta: -25.52mm3; SE 11.36; p=0.025) and right (Beta: -29.36mm3; SE 10.67; p=0.006) fusiform volumes, left (Trend, Beta: -5.24mm3; SE 2.94; p=0.075) para-hippocampal volume, and right (Beta: -12.57mm3; SE 6.00; p=0.037) orbito-frontal volumes. No significant association was detected for the right para-hipocampal, posterior cingulate, and left orbito-frontal cortex although these regions were also mostly negatively associated with the ANU-ADRI. **Conclusions:** These results indicate that increased dementia risk exposure is associated with lower regional volumes in regions theoretically relevant to AD pathology. They provide further validation that the ANU-ADRI is a useful and biologically relevant measure of Alzheimer risk factors exposure.