(RAVLT and Trails B),hippocampal volume and cerebral glucose metabolism (CMRglu) with respect to APOE genotype (epsilon4+ or epsilon4-), age and AV-45 SUVR. The following path model was considered: APOE genotype and age as predictor variables; AV-45 SUVR as a mediator variable; and Trails B Score, RAVLT, hippocampal volume and mean FDG SUVR as outcomes. **Results:** Standardized regression weights for significant correlation are reported in Figure 1. In the path model, APOE genotype was strongly associated with amyloid SUVR, weakly associated with CMRglu and cognitive scores (and not at all to hippocampal volume). In contrast there was a stronger relationship between AV-45 SUVR, on the one hand, and CMRglu, hippocampal volume and cognitive function, on the other hand, independent of APOE genotype. Age was more strongly associated with hippocampal volume thanwith CMRglu and the cognitive measures. **Conclusions:** The effect of APOE genotype on cognition, hippocampal volume and CMRglu is mediated primarily by its effect on increasing amyloid deposition, with relatively little independent contribution by APOE genotype.

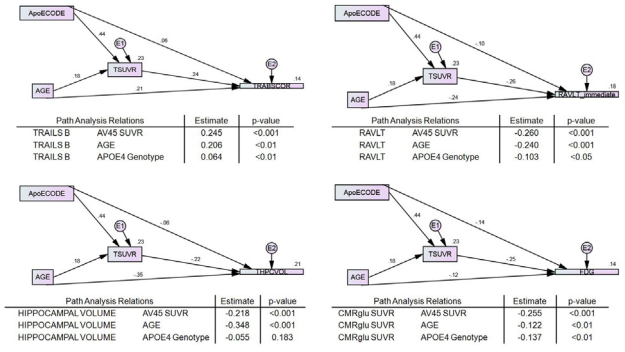

Figure 1. Path Analytic Models addressing dependencies of Cognitive Variables [Trails B (A) and RAVLT (B)], Volumetric variable [hippocampal volume] (C) and Metabolic variables [rCMRglu](D) to APOE e4 genotype, age and mean [18F]-florbetapir AV45 SUVRs, showing the Standardized Regression Weights for each correlation. The associations of Age (0.179, p<0.001) and APOE genotype (0.440 p<0.001) with AV-45 SUVR were found to be significant across all path models.

IC-P-004 THRESHOLDS FOR BRAIN AMYLOID CONCENTRATION IN RELATION TO DISEASE STAGE, COGNITION, BRAIN METABOLISM, BRAIN ATROPHY, AND APOE GENOTYPE IN THE ADNI COHORT

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Background: To determine vulnerability of cognitive, functional, cerebral metabolic rate of glucose (CMRglu) and brain volume variables to fibrillar amyloid burden, in relation to APOE genotype and disease stage in the ADNI Cohort. **Methods:** Data used in this study were obtained from the Alzheimer's Disease Neuroimaging Initiative (ADNI) database (adni.loni.usc.edu). Baseline demographic, clinical, neuropsychological, and volumetric MRI data for 385 subjects [55 diagnosed with mild Alzheimer's disease (AD), 91 with late MCI (LMCI), 114 early MCI (EMCI), and 125 cognitively normal (CN) cases] were explored in relation to APOE genotype (ApoE4+ (n=136) versus ApoE4- (n=211)). Piecewise Linear Models were used to assess the concurrent relationships between mean brain standardized uptake value ratios (SUVRs) of [18F]-florbetapir (AV45) uptake, auditory verbal learning test (AVLT), CDR sum of boxes (CDRsb) scores, regional CMRglu values and brain volumes on MRI, as a function of e4 status. Inflection points for SUVR scores in relationship to each of these regression curves were identified by computing points on the linear models at which the second derivative changes sign. **Results:** Overall, the association of SUVR scores was stronger for ApoE4+ than ApoE4- subjects (p<0.01). The coefficients of determination were: entorhinal cortex volume (R 2 for ApoE4+ = 18.14% and ApoE4- = 9.91%), mean CMRglu (R 2 for ApoE4+ = 13.89% and ApoE4- = 13.38%), RAVLT (R 2 for ApoE4+ = 9.36% and ApoE4- = 5.79%), and Hippocampal volume (R 2 for ApoE4+ = 16.71% and ApoE4- = 7.06%). Inflection points were identifiable for all the variables (Figure 1), and were at higher SUVR scores in ApoE4+ (μ =1.298, f = 0.13) than ApoE4- (μ =1.072, f = 0.08) subjects (p<0.001). The SUVR at the inflection points among cognitive (μ =1.270, f = 0.13), atrophy (μ =1.230, f = 0.16) and CMRglu (μ =1.201, f = 0.20) variables were different. **Conclusions:** For a given level of neurodegeneration (as reflected in cognitive scores, CMRglu values and regional brain atrophy in AD affected regions), the corresponding AV45 SUVRs and inflection points are strongly influenced by factors such as APOE genotype. These findings indicate the absence of a fixed threshold for "positive" or "negative" amyloid PET s cans.

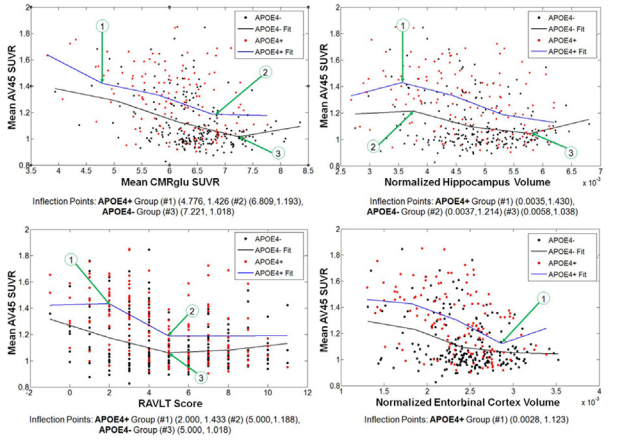

Figure 1. Fibrillar amyloid burden mean AV45 SUVR versus (A) Cerebral Metabolic Rate of glucose (CMRglu), (B) Rey Auditory Verbal Learning Test (RAVLT), (C) Normalized Hippocampus Volume and (D) Normalized Entorhinal Cortex Volume showing variations in mean AV45 SUVR for the inflection points of among cognitive, volumetric and functional measures. The inflection points are listed below each corresponding graph.

IC-P-005 DISCREPANCIES BETWEEN PIB AMYLOID IMAGING IN TYPICAL AND ATYPICAL CLINICAL DIAGNOSIS: PRACTICAL UTILITY IN A MEMORY CENTER

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Background: The 11C-PIB-PET is a tracer that specifically detects amyloid deposition in life. It has the advantage of being minimally invasive, but it is expensive and its use care in the clinical spectrum of degenerative diseases has not been stipulated. Our goal is to determine the utility of 11C-PIB-PET analyzing the presence of amyloid in patient groups high and low pretest probability. **Methods:** Observational cross-sectional study 144 patients underwent 11C-PIB-PET in our center. They were assigned into categories of high or low pretest probability according to clinical suspicion of AD pathology. The high probability group included: mild cognitive impairment (MCI), amnestic, amnestic and other domains MCI, Alzheimer disease (AD), posterior cortical atrophy (PCA), logopenic Primary Progressive Aphasia (PPA), amyloid angiopathy and mixed dementia. The low assumption group included: normal controls, non-amnestic MCI, non logopenic PPA and frontotemporal dementia (FTD). **Results:** 29.67% of patients with high pretest probability had 11C-PIB-PET negative, and 26.42% in