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ALZHEIMER'S IMAGING CONSORTIUM
POSTER PRESENTATIONS
IC-P

IC-P-001 THE INCREMENTAL DIAGNOSTIC VALUE OF 18F-FLORBETAPIR IMAGING IN NATURALISTIC PATIENTS WITH COGNITIVE IMPAIRMENT: THE INDIA-FBP STUDY

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Background: Amyloid PET imaging enables the in vivo estimation of brain β-amyloid neuritic plaque density and can be used to support an Alzheimer's Disease (AD) diagnosis in research settings (Albert et al., 2011). The added value of amyloid PET imaging in clinical settings is less known. Data are starting to emerge but still limited (Vandenberghe et al., 2013; Grundman et al., 2012). We report preliminary findings about the incremental diagnostic value of 18F-Florbetapir amyloid PET on top of routine assessment in an Italian naturalistic setting. **Methods:** The study started in Sept 2013 and plans to enroll 250 patients coming to observation of 21 Alzheimer's Evaluation Unit in Eastern Lombardy, Italy, until Dec-2014. 30 healthy elderly controls (HC) will also be enrolled. Patients will undergo a diagnostic work-up according to usual local practice. Physicians will formulate a clinical diagnosis and rate their diagnostic confidence (range between 15% and 85%). Patients will undergo 18F-Florbetapir PET. Diagnosis, diagnostic confidence and treatment plan will be revised based on 18F-Florbetapir scan results. **Results:** During the first 5 months, 73 patients and 9 HC were enrolled. Of these, 57 patients completed their diagnostic work-up. Clinical diagnosis were as follows n=15 MCI due to AD; n= 23 AD; n=3 FTD; n=7 MCI not due to AD; n=9 had other dementias (PDD, DBL, CBS). 56 patients and 8 HC underwent 18F-Florbetapir PET. Negative scans occurred in 18% of AD, 33% of MCI due to AD, 29% of MCI not due to AD, 33% of FTD, 33% of patients with other dementias. Two HC had a positive amyloid-PET scan. To date, the diagnosis was re-evaluated post-amyloid imaging in 40 patients, and 18F-florbetapir results led to a change in diagnosis in 42% of these patients. The diagnostic confidence increased significantly after amyloid imaging for both confirmed and changed clinical diagnoses (15% and 17% increase in confidence respectively, $p<0.0005$). Amyloid PET positivity had a significant impact on the therapeutic plans of patients with an initial diagnosis of AD, MCI due to AD or DLB, with an increase of 29% in the prescription of AChE ($p=0.01$). **Conclusions:** 18F-Florbetapir PET has a significant impact on diagnosis, diagnostic confidence and treatment plan of dementia experts.

IC-P-002 DEMENTIA EXPERTS' PERCEIVED DIAGNOSTIC VALUE OF PET AMYLOID IMAGING

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Background: Amyloid PET imaging is a biomarker of amyloid pathology and can assist in the differential diagnosis of Alzheimer's Disease (AD) from other non-AD dementias. Evidence that amyloid PET has an impact on the diagnostic thinking of dementia experts is starting to emerge but is still limited (Vandenberghe et al., 2013; Grudman et al., 2012). This study was aimed at assessing whether amyloid positivity/negativity has an impact on the diagnostic thinking of dementia experts (DEs) as assessed through an ad-hoc questionnaire. **Methods:** This study was carried out in the context of a larger one on the diagnostic valueof amyloid PET imaging in Eastern Lombardy, Italy. Twenty-two DEs of second level referral centres participated to the study. Six clinical case-vignettes representative of patients with diagnostic uncertainty were developed and submitted to the DEs. Each case-vignette included the following information: patient's age, sex, cognitive/behavioural symptoms, FDG-PET and MRI results, and initial diagnosis before amyloid-PET scan. DEs were then asked to rate the probability (from 0 to 100) of a change in diagnosis after knowledge of amyloid-PET results (positive Aβ+/negative Aβ-). **Results:** When assessing the 6 case-vignettes, the highest probability of a change in diagnosis was for cases with an initial diagnosis of (i) AD with atypical profile (logopenic variant) and Aβ- (66% probability), and of (ii) subcortical ischemic vascular dementia and Aβ+ (62%). There was no significant difference between the two case-vignettes ($p>0.05$ on post-hoc ANOVA). The lowest probability was in the cases with an initial diagnosis of (iii) LBD and Aβ- (14%), and of (iv) AD and Aβ- (33%). These case-vignettes were significantly different from case-vignettes (i) and (ii) ($p<0.01$). For cases with an initial diagnosis of bvFTD and CBD and Aβ+ the probability of a change in diagnosis was intermediate (43 and 44%). These values were significantly higher compared with those of case-vignette (iii) ($p<0.01$). **Conclusions:** Amyloid biomarkers proved to be most informative to rule out an AD etiology in cases with atypical AD, and to support an AD etiology in cases with a non-AD dementia. A change in the diagnosis was less frequent in cases of suspected non-amyloid pathology.

IC-P-003 RELATIONSHIP OF MEDIAL TEMPORAL VOLUME TO MEAN BRAIN AMYLOID CONCENTRATION, APOE GENOTYPE, AND DISEASE STAGE IN ADNI

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Background: The amyloid cascade hypothesis of Alzheimer's Disease was initially proposed over 20 years ago. Recent data from studies such as the Alzheimer's Disease Neuroimaging Initiative (ADNI) suggest that the relationship between brain amyloid burden, biomarkers of neurodegeneration, genetics, age and disease stage may be complex. **Methods:** Data used in this study, including brain measures, was downloaded from the ADNI public database. Subjects were 154 with late mild cognitive impairment (lMCI), 238 with early MCI (eMCI), and 183 who were cognitively normal (CN). Neuropsychological evaluations included tests of memory (Rey Auditory Verbal Learning Test) and executive function (Trails B score). Subjects also had an F-18 AV-45 amyloid PET scan, an FDG PET scan and a structural MRI scan. Imaging measures included hippocampal volume, the average normalized CMRglu of 6 AD-sensitive regions, and average SUVR for the amyloid scans of the following regions: anterior and posterior cingulate, prefrontal, lateral temporal and parietal (AV-45 SUVR). Path analysis was carried out to explore the dependencies of cognitive scores

(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.

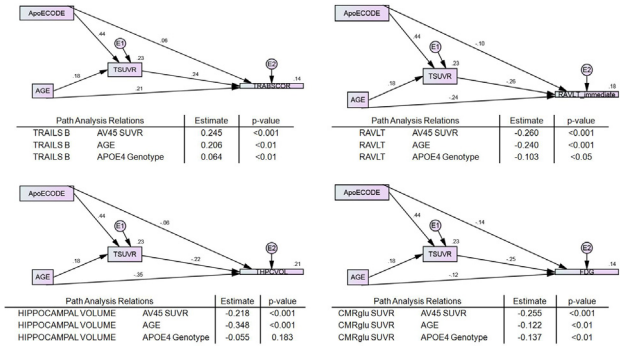

Figure 1. Path Analytic Models addressing dependencies of Cognitive Variables [Trails B (A) and RAVLT (B)], Volumetric variable [hippocampal volume] (C) and Metabolic variables [rCMRglu](D) to APOE e4 genotype, age and mean [18F]-florbetapir AV45 SUVRs, showing the Standardized Regression Weights for 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.

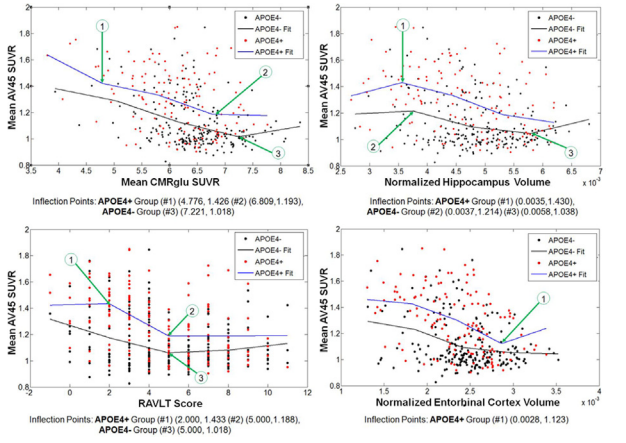

Figure 1. Fibrillar amyloid burden mean AV45 SUVR versus (A) Cerebral Metabolic Rate of glucose (CMRglu), (B) Rey Auditory Verbal Learning Test (RAVLT), (C) Normalized Hippocampus Volume and (D) Normalized Entorhinal Cortex Volume showing variations in mean AV45 SUVR for the inflection points of among 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