P3-097 CHARACTERISTICS AND OUTCOME OF SUBJECTIVE AND MILD COGNITIVE IMPAIRMENT IN A U.K. MEMORY CLINIC POPULATION

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Background: As Alzheimer's disease (AD) research focuses increasingly on prevention and early treatment, interest in the identification of at-risk individuals is intensifying. The concept of mild cognitive impairment (MCI) as a risk state for AD has been established for several years. There is now growing interest in the possibility of an even earlier prodromal group where subjective memory impairment exists in the absence of any objective cognitive deficits; an increasingly accepted term for this is *Subjective Cognitive Impairment* (SCI). Evidence supports the existence of a clinically "silent" phase of AD where pathological, metabolic and functional changes are present in the brains of asymptomatic individuals. SCI may represent the earliest point on the continuum of clinical AD symptomatology; a better understanding of this group may enhance our knowledge of the underlying disease processes and also facilitate early diagnosis and the direction of future disease-modifying treatments. **Methods:** We completed a retrospective study of baseline characteristics and outcomes in patients presenting to our memory clinic between 2000 and 2010 who received an initial diagnosis of SCI or MCI. At each assessment point, all patients underwent a standard assessment, including a medical and psychiatric history and examination and cognitive testing. Inclusion criteria for SCI were: 1) cognitive complaint from patient, 2) performance on cognitive testing within normal limits for age and educational level, 3) intact activities of daily living, 4) absence of MCI or dementia. Criteria for MCI were: 1) cognitive complaint from patient or informant, 2) performance below expected for age and education, 3) preserved general cognitive function, 4) intact activities of daily living, 5) absence of dementia. **Results:** Demographic, clinical and cognitive data from baseline and follow-up assessments were collated and analysed. Descriptive data regarding characteristics and cognitive change over time for MCI and SCI groups will be presented in addition to comparisons between diagnostic groups and progressing and non-progressing groups. **Conclusions:** MCI and SCI most likely represent two distinctive early phases of the continuum of AD. We will discuss how each of these two groups fits into the concept of pre-clinical and prodromal AD and their utility in terms of future research and clinical practice.

P3-098 PREDICTING COGNITIVE DECLINE IN MCI SUBJECTS USING THE FUSION ICA TOOLBOX TO COMBINE MULTIMODALITY NEUROIMAGING DATA

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Background: The aim of this study was to combine structural MRI and FDG-PET in MCI subjects using a novel multimodality fusion tool to extract linked information useful in predicting cognitive decline. **Methods:** Alzheimer's Disease Neuroimaging Initiative (ADNI) baseline MRI and FDG-PET scans for 97 subjects with mild cognitive impairment (MCI) (mean/sd age 75 years/7.1, 54% ApoE4+) were used. As of 10/19/2010, 43 MCI subjects converted to AD and 54 did not. Converters did not differ from non converters in mean age, gender ratio, or education, but had lower baseline delayed recall memory scores ($p<0.05$) and higher ADAS-Cog ($p<0.05$). Whole brain gray matter probabilities were extracted from the MRIs using FSL-VBM. FDG-PET images were registered to the corresponding MRI and standard MNI space using FSL tools FLIRT and FNIRT. These biomarkers were combined with the Fusion ICA Toolbox (FIT Version 2.0b, 2009), which uses parallel ICA to isolate unique features from each biomarker. 16 components were extracted, 10 MRI and 6 PET, and the loading parameters for each component were analyzed, looking for linked components as well as individual components that predict conversion to AD. **Results:** Four sets of linked components were discovered: the MRI anterior per ventricular white matter/cerebellum correlated with PET thalamus/lentiform nucleus hypometabolism ($R=0.638$, $p<0.0001$), the MRI medial temporal lobe correlated with the PET posterior default network ($R=0.569$, $p<0.0001$), the MRI posterior frontal lobe component inversely correlated with the PET posterior default network ($R=-0.38$, $p=0.0001$), and the MRI basal ganglia/cerebellum component negatively correlated with PET parietal-occipital lobe hypometabolism ($R=-0.313$, $p=0.002$). The first 3 of these 4 sets showed significance in predicting cognitive decline, in that both the MRI and PET component in each set individually predicted conversion to AD. **Conclusions:** In conclusion, using a data driven method to extract independent sources of information from whole brain gray matter probability maps and FDG-PET, we have identified 3 sets of linked components which predict subsequent conversion from MCI to Alzheimer's disease. Such data driven methods may be useful in understanding the pathophysiology of early AD and aid in the development of diagnostic tools that combine imaging modalities to extract unique sources of clinically useful information.

P3-099 EVALUATION OF THE PLASMA PROTEOMICS DATA FROM THE ADNI DATABASE FOR ALZHEIMER'S DISEASE-STATE CLASSIFICATION AND PREDICTION OF 12-MONTH PROGRESSION FROM MCI TO AD

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Background: Blood-based biomarkers of Alzheimer disease (AD) are a more convenient and practical alternative to Imaging and Cerebral Spinal Fluid (CSF) biomarkers; both for drug development and as diagnostic aids for physicians. We report initial findings from our statistical evaluation of blood-based proteomic markers from AD, Mild Cognitive Impairment (MCI) and Normal (NL) subjects from the Alzheimer's disease NeuroImaging (ADNI) database. **Methods:** 1063 plasma samples from AD, MCI, and Normal subjects were sent to Rules Based Medicine (RBM) for measuring 190 analytes. Data were downloaded from the ADNI database. 146 analytes passed the ADNI quality-control criteria. Our analysis was geared towards identification of individual markers that significantly differentiate the disease states, and combinations of markers that are predictive of disease state. In addition, the ability of these markers to predict 12-month progression from MCI to AD was evaluated. Significance of individual markers was reported in terms of the False Discovery Rate (q-value). Predictive performance of multivariate signatures was estimated using rigorous internal cross-validation and pseudo-external validation. **Results:** For disease state differentiation, 41 markers were significant at $q < 0.05$ between AD and NL, out of which 23 were significant between MCI and NL, and 5 of which were significant between AD and MCI. These five markers are Alpha-1 Microglobulin (A1Micro), Heparin-binding EGF-like Growth Factor (HBELGF), Immunoglobulin-M (IgM), Macrophage Inflammatory Protein-1 Alpha (MIP-1a), and Pregnancy Associated Plasma Protein A (PAPPA). However, none of these individual markers showed impressive diagnostic accuracy to separate AD and NL. Multivariate methods revealed signature panels of 10-20 markers with over 80% predictive classification accuracy between AD and NL. For the prediction of 12-month progression from MCI to AD, PAPPA was statistically significant, however none of the individual or multivariate signatures showed over 60% sensitivity and specificity. **Conclusions:** Proteomic fingerprinting of plasma using the RBM panel has revealed some interesting findings, but none seem to stand alone as a predictive diagnostic marker. Multivariate methods provided fairly predictive signatures that require confirmation and further evaluations in independent cohorts. Nonetheless, blood-based markers in the ADNI cohort provide promising diagnostic potential, and we look forward to further scientific inquiry.