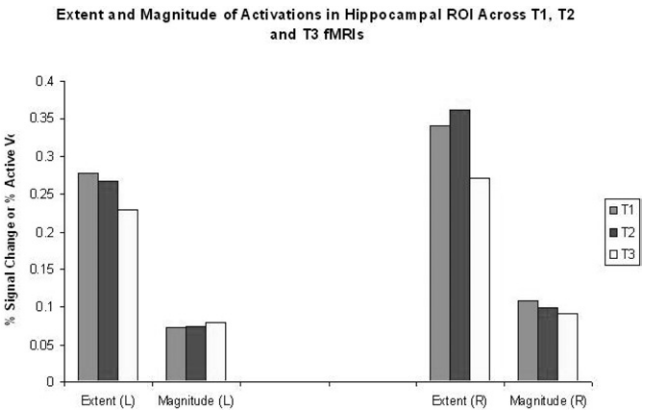

Atri et al. Feasibility and Test-retest Reliability of fMRI in an Alzheimer's Disease Clinical Trial

IC-P2-074 DIFFERENTIATING AMNESTIC MCI CONVERTING TO PROBABLE AD FROM STABLE AMNESTIC MCI USING FDG-PET AND AN AD-RELATED HYPOMETABOLISM OVERLAP INDEX

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Background: Alzheimer's disease (AD) is characterized by a characteristic pattern of reductions in the cerebral metabolic rate for glucose (CMRgl). We recently introduced use of an AD-Related Hypometabolism Overlap Index to determine the percentage of previously characterized AD-related hypometabolic brain voxels that are hypometabolic in an individual subject's fluorodeoxyglucose positron emission tomography (FDG-PET) image and help distinguish between probable AD patients, amnestic mild cognitive impairment (MCI) patients and normal controls (NC). The objective of this study is to evaluate the ability of our proposed Overlap Index to distinguish between probable AD patients, MCI patients who convert to probable AD within the next 18 months (MCIc), MCI patients who have so far remained stable (MCIs) and NC from the AD Neuroimaging Initiative (ADNI). **Methods:** The Overlap Index was computed in 74 AD patients, 14 MCIc, 124 MCIs patients, and 82 NC as follows: First, statistical parametric mapping (SPM5) was used to generate individual cerebral hypometabolism z-score maps, comparing each person to a database of 82 NC. Next, the individual hypometabolism map was superimposed on an AD-related hypometabolic map generated from a previous study (Alexander et al, 2002). Finally, the Overlap Index was computed as $V_{ADI}/V_{AD} \times 100\%$, such that V_{ADI} is the hypometabolic volume in both previous AD-NC group comparison and the subsequent individual-NC comparison, and V_{AD} is the hypometabolic volume in only the previous AD-NC group comparison. **Results:** The Overlap Index significantly distinguished the four subject groups (ANOVA P=8.8e-15). As predicted, the overlap index had the following rank order: AD>MCIc>MCIs>NC (ANOVA with linear trend P=3.9e-16). Moreover, the Overlap Index significantly distinguished between the MCIc group and the MCIs group (t-test P=0.013). **Conclusions:** Our preliminary findings suggest that the AD Overlap Index can help identify hypometabolic patterns consistent with AD and help differentiate MCI patients converting to AD from stable MCI patients without the need to correct for multiple comparisons.

IC-P2-075 USE OF REGIONAL THICKNESS MEASURES TO PREDICT DECLINE IN QUESTIONABLE AD DEMENTIA: COMPARISON TO STANDARD VOLUMETRIC MEASURES

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Background: We previously used exploratory analyses to determine that clinically mild Alzheimer's disease (AD) is reliably associated with a "cortical signature" of thinning in a specific set of regions in medial (MTL), inferior (ITG), and polar temporal (TP), inferior, superior (SPL), and medial parietal, and inferior and superior frontal cortices. We sought to determine whether the pattern of AD-related thinning is present in individuals with questionable dementia of the Alzheimer type (QAD) prior to mild AD and whether a greater degree of regional thinning predicts mild AD dementia. **Methods:** Participants included 49 older adults with QAD (Clinical Dementia Rating (CDR)=0.5) at the time of structural MRI scanning. Nine regions of interest (ROIs) identified from an exploratory analysis comparing a separate sample of Older Controls to mild AD (CDR=1) patients were used to measure AD signature cortical thickness in these participants. We also measured "mean AD signature" thickness across all 9 regions. In addition, mean thickness across the entire cortex, and whole brain, hippocampal and entorhinal volumes were calculated. Longitudinal clinical follow-up after scanning was used to classify participants as progressors to CDR=1 or non-progressors. **Results:** Longitudinal follow-up revealed that 20 participants converted to mild AD dementia after approximately 2.5 years. At baseline, these QADs showed milder thinning in the cortical ROIs as well as milder hippocampal and entorhinal atrophy than is typically seen in mild AD. Compared to the non-progressors, the progressors showed thinning in MTL, ITG, TP and SPL. Effect sizes for group differences were higher for many regional thickness as compared to volume measures. Using receiver operating characteristic curves, mean AD signature cortical thickness was the best at predicting progression to mild AD with 83% sensitivity and 65% specificity as compared to entorhinal volume, which achieved 72% sensitivity and 65% specificity. **Conclusions:** Thinning in specific cortical areas known to be affected by AD is detectable in individuals with QAD and predicts conversion to mild AD dementia. This method could be useful for identifying individuals at relatively high risk for progression from QAD to mild AD dementia within a few years, which may be of use in clinical trials.

IC-P2-076 WHITE MATTER VOLUME IN INDIVIDUALS AT INCREASED RISK FOR ALZHEIMER'S DISEASE

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Background: While much of structural imaging has focused on gray matter, the quantification of white matter integrity is of interest not only because of the noted white matter pathology seen in Alzheimer's disease (AD), but also because of the apparent breakdown of myelin in AD. To date there has been no longitudinal study of white matter integrity within asymptomatic samples at elevated risk for late-onset AD, the purpose of this study. **Methods:** Cognitively normal participants age 50 years and above were chosen from an ongoing longitudinal study, comparing those with increased genetic risk for AD to matched controls. 95 of the high-risk and 91 of the controls had structural scans at baseline (Time 1) and 87 high-risk and 74 controls at three-year follow-up (Time 2). Participants were imaged at each time point on the same 1.5 Tesla Philips Intera-NT system equipped with Galaxy gradients (66mT/m at 110 mT/m/s). High resolution anatomical images of the brain for structural measurements were acquired using a T_1-weighted, 3D MP-RAGE (Magnetization Prepared Rapid Acquisition Gradient Echo) sequence with the following parameters: TR=8.6 ms, TE=3.9 ms, FOV=240 mm, $\theta=8^o$, matrix size =256x256, slice thickness=1.5 mm, 124 slices). Pre-processing was performed using a semi-automated method, followed by the manual removal