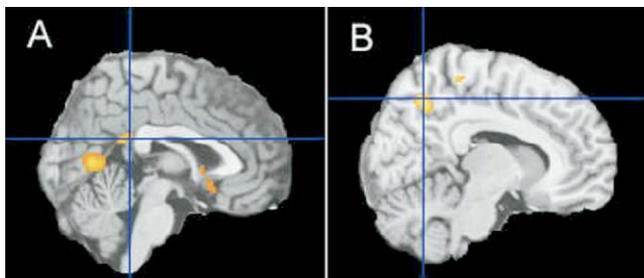


history of AD (mean age = 57.7 (1.8), mean education = 16.3 (2.1)) and six control participants with no parental history (mean age = 58.2 (3.1), mean education = 17.0 (3.0)). Participant groups were not significantly different with respect to age, education, or performance on visual and verbal memory tests. **Results:** Whole-brain random-effects analysis of the groups' statistical parametric maps revealed that controls showed greater medial parietal activation than the at-risk group during both episodic retrieval and self-appraisal. This is depicted in Figures A and B (crosshairs depict activation described here). During episodic retrieval, the at-risk group showed significantly less activation than control individuals in the retrosplenial aspect of the posterior cingulate cortex ($p = .01$; see Figure A). During self-appraisal, at risk individuals showed significantly less activation than controls in the precuneus ($p > .001$; see Figure B). **Conclusions:** The present study provides preliminary evidence for preclinical changes in medial parietal brain areas vulnerable to AD pathology. With continuing data collection, we will follow-up this work with an investigation of the influence of APO ϵ 4 and the interaction of family history and APO ϵ 4 on brain activity during both episodic retrieval and self-appraisal. Longitudinal follow-up of these participants will be needed to determine whether the findings we report are predictive of subsequent development of Mild Cognitive Impairment or AD.



P2-265 IMPROVED STATISTICAL POWER TO DETERMINE DISEASE MODIFYING EFFECTS USING A RANDOMIZED START MRI STUDY

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Background: Previous AD and MCI treatment trials have used a two-arm (treatment vs. placebo) approach. The between-subject variability of hippocampal volume change is usually large, requiring large sample sizes in two-arm treatment studies. One approach to reduce variability is to study subjects prior to and post-treatment, comparing hippocampal rates of change so that each subject serves as their own control. **Objective:** To compare the power of two types of treatment studies using hippocampal atrophy rates as measured with MRI. **Methods:** Subjects (15 male 10 female, mean age 75 years \pm 6) who met MCI criteria were scanned at 6-month intervals with T1-weighted volumetric MRI. Hippocampal volumes were measured, and data were used to simulate a 20% disease modifying effect with two types of treatment studies. The number of subjects required to detect a significant $p < 0.05$ effect with 90% power was calculated using a 2-tailed, unpaired t-test (2-arm study) and paired t-test (randomized start design). The 2-arm study simulates subjects scanned at the beginning and end of a 1-year study, powered with the annualized rate of change. The randomized start design has subjects scanned at 0, 6 and 12-months, with treatment at 6-months, powered using the 6-month rate of change data for the first 6-months, and a 20% slowing of the rate of change for each subject for the 2nd 6-months. **Results:** The 6-month rate of change for this group was $4.23\% \pm 5.72\%$ and the annualized rate of change was $7.42\%/year \pm 9.68\%/year$. The sample size required to detect a 20% slowing on the rate of atrophy using the traditional 2-arm treatment/placebo design is 736 subjects. In contrast, to detect the same rate of change in the randomized start design, a sample size of 19 is required. **Conclusions:** It should be emphasized that this simulation assumes that all

subjects respond equally to treatment. Nevertheless, this shows that a randomized start treatment trial potentially has higher statistical power to detect a disease modifying treatment effect than conventional 2-arm designs. Additional data is being collected and analyzed, and additional simulations are underway, to demonstrate the potential use of this approach.

P2-266 GREATER CEREBRAL ATROPHY PREDICTS MORE RAPID COGNITIVE DECLINE IN ALZHEIMER'S DISEASE

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Background: Cerebral atrophy is a feature of the neurodegeneration in AD and although nonspecific, is related to severity of disease. It is not established whether atrophy has prognostic significance with regard to course of AD. **Objective(s):** Determine whether visual quantitative methods of cerebral atrophy primarily assessing ventricular enlargement might relate to rapidity of cognitive decline in AD. **Methods:** We used extensive clinical data from a longitudinal, three-site study of patients with mild AD who were revisited with neuropsychological testing including modified Mini-Mental State (mMMS; scale 0-57) every 6 months, with average followup period of about 3 years. Entry criteria excluded patients with cortical infarcts or lacunes > 1 cm. Images from MRI studies performed close to baseline were available for 81 patients. These were 52% female, with mean age 73.4 ± 8.1 yr, education 13.9 ± 3.6 yr, and initial mMMS 40.0 ± 6.8 , 53% with an apoE ϵ 4 allele, 10% with diabetes, 16% with hyperlipidemia, 13% with coronary artery disease, and 34% with hypertension. Axial images with T1-weighted sequence acquired at 5 mm slice thickness were used in most cases, but when not available, FLAIR or T2-weighted images were used. Images were rated, blind to clinical data, for atrophy involving ventricular volume, using two measures: the bicaudate ratio and the biatrial ratio, measured in most cases at two levels which were then averaged. **Results:** Bicaudate and biatrial ratios (mean \pm SD, range) were 0.160 ± 0.038 (0.07-0.26) and 0.242 ± 0.056 (0.10-0.37). Average decline in mMMS was 3.46 points/year. Using GEE analysis, we found a significant relationship between bicaudate ($p < 0.001$) and biatrial ($p = 0.007$) atrophy scores and the rate of cognitive decline. Decline in mMMS was 0.41 (bicaudate) and 0.19 (biatrial) points/percentage point of atrophy /year, or about 14% and 18% increased speeds of decline per percentage point of atrophy. These relationships remained significant, even with adjustments for baseline mMMS, age, sex, education, cardiovascular risk factors, and apoE4. **Conclusions:** Brain atrophy is associated with increased rapidity of cognitive decline in AD. This association does not appear to relate to disease severity at baseline, nor apoE, age, or cardiovascular risk factors. AD may progress at different rates in different individuals.

P2-267 REGIONAL CEREBRAL GLUCOSE METABOLISM (CMRGLC) AS MEASURED BY 18FDG-PET AND ABETA1-42 AND TAU LEVELS IN CSF OF ALZHEIMER PATIENTS WHO ARE CARRIERS OR NON-CARRIERS OF THE APOE ϵ 4 ALLELE GENOTYPE

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Background: Pathological changes in CSF markers as well as functional changes in brain function have been found in Alzheimer's Disease (AD)