



Title: Biomarkers for monitoring the progression of Alzheimer's disease in clinical trials: the Alzheimer's Disease Neuroimaging Initiative

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ADNI is a \$67 million observational longitudinal clinical trial with the overall goal of determining the value of MRI and PET imaging together with blood and CSF biomarkers for disease modifying Alzheimer's treatment trials. Specific aims are to: improve methods for clinical trials; determine the optimum methods for acquiring and processing images and biomarkers; "Validate" imaging and biomarker data by correlating with neuropsych and behavioral data. We have longitudinally studied: MCI (n= 400); AD (n= 200); Controls (n= 220). Clinical visits include neuropsychological assessments, MMSE, CDR, ADAS-cog, MRI (1.5 T), FDG PET blood and urine and CSF.

The rate of hippocampus atrophy appears to have the high statistical power for measuring change over time, and further that changes in this same region predict conversion from MCI to AD. FDG PET measures also have high predictive value of MCI conversion to AD and cognitive decline, and some FDG PET measures have high power as outcomes. Furthermore, analysis of data from the normal controls suggests that normal healthy elders with APOE4 and/or low CSF abeta amyloid have worse memory scores and higher rates of hippocampal atrophy than the non carrier controls or subjects with high CSF abeta; this is consistent with the hypothesis that some controls have preclinical AD pathology. Similar ADNI-like projects, with similar methods, are underway in Japan, Australia, and Europe. We recently received a \$24 million grant to enroll 200 early MCI, and to perform F18 amyloid imaging on all ADNI and GO subjects using AVIDs AV-45 ligand. World-wide standards and a world-wide network have been created for clinical trials. Updated analysis of ADNI data, including fully 2 yr followup data, will be presented.