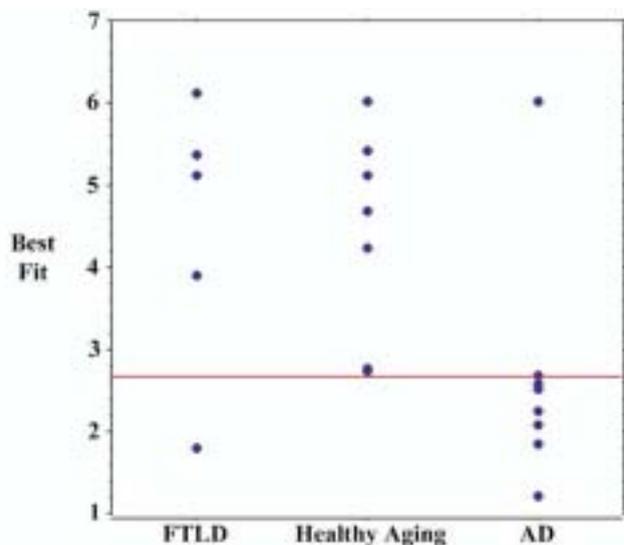


minute resting-state fMRI scans. AD and FTLN subjects were matched on age and mini-mental state examination scores. Healthy controls were slightly older than either the FTLN or AD patients. One AD subject could only complete a single 6-minute scan and one healthy control only had one usable scan. Preprocessing was done with SPM2. The smoothed, normalized images were subjected to independent component analysis. As in our previous study (Greicius et al., PNAS, 2004), an automated process was used to assign a goodness-of-fit score to each component reflecting how well the components matched a standard template of the default-mode network. The best-fit component was chosen as the default-mode component. Each subject's highest best-fit score (one from each of their two scans) was used as a dependent variable in an ANOVA and as a candidate biomarker. **Results:** The ANOVA showed a main effect of diagnosis and post-hoc tests showed that AD scores were significantly less than those of healthy controls and the FTLN group ($p < 0.05$). Scores did not differ significantly between the control and FTLN groups. Using a score of 2.7 as a cutoff, this method correctly classified 8/9 AD patients, 7/7 healthy controls, and 4/5 FTLN patients yielding a sensitivity of 89% in detecting AD and 100% specificity in distinguishing AD from healthy aging and 80% specificity in distinguishing AD from FTLN. **Conclusions:** These preliminary data suggest that resting-state fMRI merits wider-scale testing as a clinically useful biomarker of AD.



O1-04-08 DIFFERENT PATTERNS OF HYPOPERFUSION IN FRONTOTEMPORAL DEMENTIA AND ALZHEIMER'S DISEASE BY ARTERIAL SPIN LABELING MRI

Antao Du¹, Geon-Ho Jahng¹, Bruce Miller², Satoru Hayasaka¹, Howie Rosen², Joel H. Kramer², Michael W. Weiner¹, Norbert Schuff¹; ¹VA Medical Center, San Francisco, San Francisco, CA, USA; ²University of California, San Francisco, San Francisco, CA, USA

Background: A differential clinical diagnosis between Frontotemporal dementia (FTD) and Alzheimer's disease (AD) is sometimes difficult to make, especially at an early stage because of overlapping symptoms. Functional studies with PET and SPECT reported characteristic patterns of hypoperfusion in FTD and AD that might aid a differential diagnosis. However, PET and SPECT are not wide available and require injection of radioactive tracers. In contrast, arterial spin labeling MRI (ASL-MRI) provides an entirely non-invasive approach to measure cerebral perfusion. **Objective(s):** (1) To test if ASL-MRI detects different regional patterns of hypoperfusion between FTD and AD similar to results from PET and SPECT studies; (2) To determine the extent to which perfusion and gray matter (GM) loss classify FTD patients from cognitively normal (CN)

subjects and AD patients; (3) To explore the correlation between hypoperfusion and decline of cognitive functions. **Methods:** Twenty-one FTD patients (62 ± 7 yrs), 24 AD patients (64 ± 7 yrs), and 25 CN (62 ± 7 yrs) subjects were studied with ASL-MRI and volumetric T1-weighted structural MRI at 1.5 Tesla. Group effects on perfusion and the correlation between perfusion and cognitive function were tested voxel-wise using Statistical Parametric Mapping (SPM2). Group classification by perfusion and GM density was tested by a logistic regression. FTD patients showed hypoperfusion in bilaterally frontal lobe and anterior cingulate than CN subjects and in right frontal lobe than AD patients. On the other hand, AD patients had hypoperfusion in bilaterally parietal lobe and precuneus and left posterior cingulate than FTD patients. Overall classification reached 67% with perfusion and 60% with GM density between FTD and CN, and 78% with perfusion and 62% with GM density between FTD and AD. Furthermore, perfusion achieved a significantly better classification than GM density for separating FTD from CN and AD. In addition, hypoperfusion was positively correlated with cognitive decline, including language, spatial memory and executive function. **Conclusions:** ASL-MRI in combination with structural MRI may help a differential diagnosis between FTD and AD. Furthermore, ASL-MRI may be more sensitive than structural MRI in detecting FTD and AD pathology and thus, could be useful for staging early dementia and monitoring disease progression.

SUNDAY, JUNE 19, 2005
ORAL SESSION
O1-05
SCREENING I

O1-05-01 STATISTICAL ISSUES FOR DEVELOPING ALZHEIMER SCREENING TESTS

J. W. Ashford¹, Helena C. Kraemer²; ¹Stanford / VA Alzheimer Center, Palo Alto, CA, USA; ²Stanford University, Palo Alto, CA, USA

Background: What difference does it make that a test is to be used for screening, rather than for discrimination or definitive diagnosis? What difference does it make that a test is to be used in a general medical practice rather than in a specialty clinic? Such considerations must affect the statistical evaluation of tests, but are frequently ignored. **Objectives:** First, the continuum of pathology which is the target of the screen must be defined. This leads to selecting a "gold standard" for comparison, and its fallibility must also be considered. Other issues considered in the statistical evaluation of such screening tests are the prevalence in the population, the fixed cost of the test, the cost of false positives, the cost of false negatives, and the benefit of true positives. **Methods:** Item Response Theory and classification algorithms will be discussed. Optimally effective items for screening should be selective. Costs and benefits need to be analyzed with respect to the incidence of dementia for the age of the subject being tested. **Conclusions:** A screening test for Alzheimer's disease can be constructed and evaluated, but several issues must be addressed in the process. Further, iterative improvements of tests should be made.

O1-05-02 SCREENING FOR PRE-DEMENTIA ALZHEIMER'S DISEASE

Herman Buschke; Albert Einstein College of Medicine, New York, NY, USA

Background: If the criterion for memory impairment is low recall, memory impairment can only be detected when recall is low, and earlier memory impairment when memory is declining but is still in the normal range cannot be detected. Additional indicators of memory impairment are needed to detect early pre-dementia Alzheimer's disease when declining memory is still in the normal range and treatment may be more effective. **Objective(s):** Screen for pre-dementia AD when declining memory is still in the normal range. **Methods:** Controlled learning and cued recall of two coordinated lists was used to detect earlier memory impairment in a community-dwelling sample of