Human Brain Mapping 2008

Print

3D Mapping of Brain Atrophy in Alzheimer's Disease and Mild Cognitive Impairment with Tensor-Based Morphometry

Xue Hua[1], Alex Leow[1], Suh Lee[1], Neelroop Parikshak[1], Andrea Klunder[1], Arthur Toga[1], Natasha Lepore[1], Yi-Yu Chou[1], Caroline Brun[1], Ming-Chang Chiang[1], Marina Barysheva[1], Clifford Jack Jr[2], Michael Weiner[3], Paul Thompson[1]

[1]*Laboratory of Neuro Imaging, Dept. of Neurology, UCLA School of Medicine, Los Angeles, CA, United States/[2]Mayo Clinic College of Medicine, Rochester, MN, United States/[3]Dept. Radiology, Medicine and Psychiatry, UC San Francisco, San Francisco, CA, United States*

Introduction: We used tensor-based morphometry (TBM) to create 3D maps of disease-related structural atrophy in Alzheimer's disease (AD) and mild cognitive impairment (MCI), relative to healthy elderly control subjects. Correlations between atrophic changes and clinical measures were investigated.

Methods: We compared the anatomical distribution of brain atrophy in 40 AD patients (age: 76.0 ± 8.5 years), 40 individuals with amnestic MCI (age: 75.9 ± 8.3 years), and 40 controls (age: 76.2 ± 6.9 years). Each group included 21 males and 19 females. Using a non-linear inverse-consistent elastic intensity-based registration algorithm [1], we warped each individual brain image ($N = 120$) to the control group average template to create Jacobian maps, which show the local expansion or compression factor at each point in the image, reflecting individual volumetric differences. We created statistical maps of group differences, whose overall significance was assessed with permutation tests, to correct for multiple comparisons. Using the general linear model, voxel-level correlations were assessed, between the Jacobian value and several clinical measures, including Mini-Mental State Examination (MMSE) scores and the Clinical Dementia Rating (CDR). To discover which methodological choices best sensitize TBM for detecting atrophy, using cumulative p-value plots, we compared the detection power of different study designs with various sample sizes, search regions (whole brain, temporal lobe, hippocampus), and initial global registration methods (9- versus 12-parameter).

Results: Figure 1 show the average 3D maps of brain atrophy in AD and MCI as a percentage reduction in volume relative to controls (the top rows of a,b). The bottom rows show the significance of these reductions, revealing highly significant atrophy in AD but a more anatomically restricted atrophic pattern in MCI. Permutation tests confirmed that atrophic was significant overall in MCI (two tailed: $P = 0.04$; negative one tail: $P = 0.02$, ROI: left temporal lobe) and AD (two tailed: $P = 0.002$, ROI: whole brain), when compared to controls, corrected for multiple comparisons. Jacobian values were strongly correlated with the clinical measures (MMSE and CDR summary and sum-of-boxes scores; Table 1).

Cumulative distribution function (CDF) curves (Figure 2), illustrate the power to detect significant brain atrophy in MCI and AD, with various sample sizes ($N = 10, 20, 30,$ or 40 per group) and different linear registration schemes (9P vs. 12P).

Conclusions: The cumulative p-value plots obtained with 9P linear registration (solid lines in Figure 2) generally outperform those from 12P linear registration (dotted lines),

suggesting that the 9P registration scheme may have superior power for detecting atrophy in MCI and AD and differentiating these groups from normal subjects. Sample size greatly influences the power to detect brain atrophy in MCI and AD; effect sizes increase monotonically with sample size.

References: [1]. Leow AD et al., Longitudinal Stability of MRI for Mapping Brain Change using Tensor-Based Morphometry, NeuroImage, Feb. 2006.
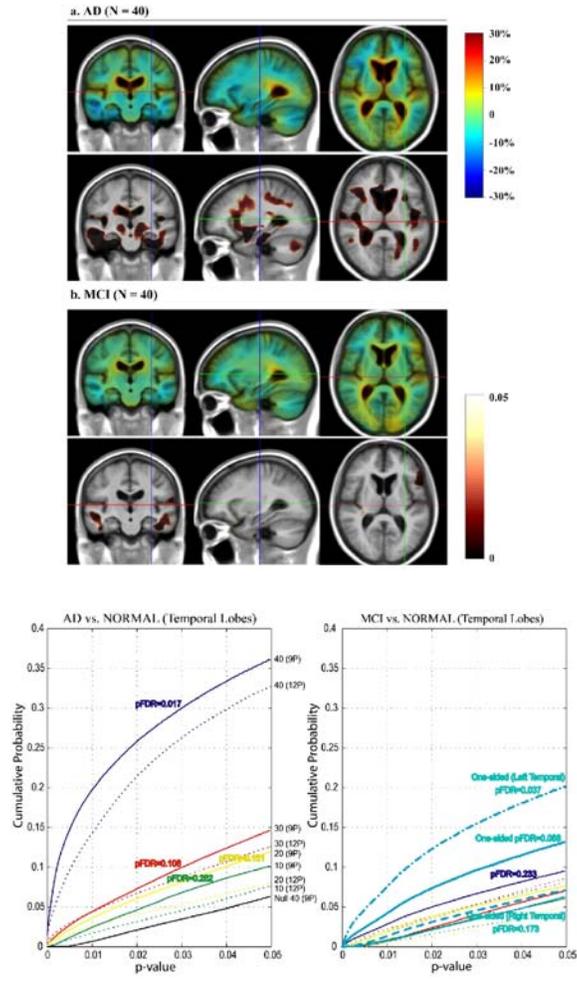

Table 1: Correlations with Clinical Measures of Dementia Severity.

	MMSE Score	Global CDR	Sum-of-Boxes CDR
Negative correlations (-1)	0.079	0.006	0.002
Two-tailed correlations (0)	0.001	0.007	0.001
Positive correlations (+1)	0.001	0.048	0.011