Diffusion Tensor Imaging (DTI) Reveals Evolving White Matter Abnormalities in Patients with Alzheimer's Disease

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Introductions: Alzheimer's disease (AD) is the most common cause of dementia in elderly people. White matter abnormalities, e.g. loss of myelinated axons in the deep and periventricular WM, have been demonstrated in AD patients. Although numerous studies report that diffusion tensor imaging (DTI) can detect changes in WM morphology or microstructures in AD patients [1,2], information on the spatial and temporal profiles of evolving WM abnormalities in AD patients, e.g., the location and rate of degeneration, has not yet been available. Such information is important for evaluation of disease progression and treatment efficacy. The aim of this study was to investigate evolving WM abnormalities in AD patients over a period of one year using DTI. The multi-scan DTI data were analyzed using voxel based analysis and advanced computational techniques to locate changes in WM morphology and diffusion properties over time.

Methods: AD patients (n=12) and healthy elderly volunteers (n=18) were scanned at least three times with approximately 4 months between scans. Data were acquired on a 3.0T MR system (Philips Medical Systems) using a single-shot, EPI sequence with SENSE (SENSE factor = 2.5). The imaging matrix was 96 x 96 with a field of view of 212 mm x 212 mm. A total of 60 2.2 mm thick transverse sections covered the brain without gaps. Diffusion weighting was encoded around 30 independent orientations with a b-value of 700 mm^2/s. Five additional images with minimal b-value of 33 mm^2/s were acquired. The total scanning time was about 18 minutes. The DTI data were processed using DTIStudio (H. Jiang and S. Mori, Johns Hopkins University, Kennedy Krieger Institute) [3] and normalized to the MNI coordinate system using rigid transformation. Nonlinear normalization of the group data to our single subject template was performed using large deformation diffeomorphic metric mapping (LDDMM) with T2-weighted and FA images as inputs. We calculated Jacobian maps for each subject and performed voxel based analysis on the normalized data. Two way ANOVA and cluster analysis were used to locate regions with significant ($p < 0.05$) difference in local tissue volume and FA between AD and healthy controls as well as regions with significant difference ($p<0.05$) in local tissue volume and FA over time in the AD patients.

Results: Group comparisons between AD patients and healthy volunteers (Fig. 1, top panel) revealed several brain regions in the AD patients with significantly ($p<0.001$) different FA from control subjects. For example, the fornix and part of the corpus callosum had reduced FA values. Our results also located several brain regions with significant ($p<0.001$) atrophy or hypertrophy (Fig. 2, bottom panel). For example, the lateral ventricles in AD patients were significantly enlarged. Further analysis of multiple scan data (two-way ANOVA) suggested that a region of the corpus callosum in AD patients, as indicated in Fig.2, had significant WM abnormalities evolving over the period of our study. For example, in one AD patients, the highlighted region of the corpus callosum in the FA images of the patient group had reduced thickness over time. In comparison, the same region in the FA image of a healthy volunteer maintained relatively consistent thickness over time.

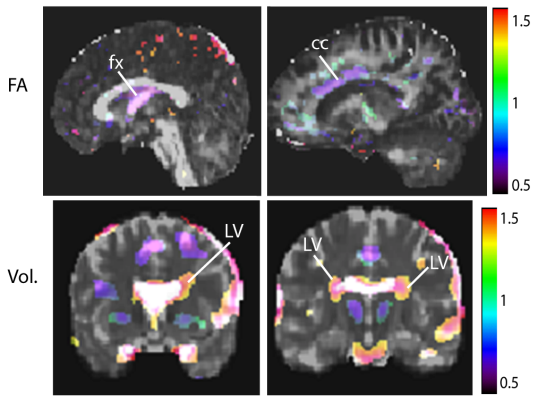

Fig. 1: Significant differences ($p<0.001$) in FA and local tissue volume (vol.) as measured by Jacobian maps between AD patients and healthy volunteers. Regions with significant changes are overlaid on sagittal FA images (top panel) and coronal B0 images (bottom panel). The color code represents the ratio of FA/tissue volume in AD patients to healthy volunteers. Blue or green indicates FA decrease/local atrophy while red or yellow indicates FA increase/local hypertrophy. fx = fornix. cc = corpus callosum; LV = lateral ventricle.

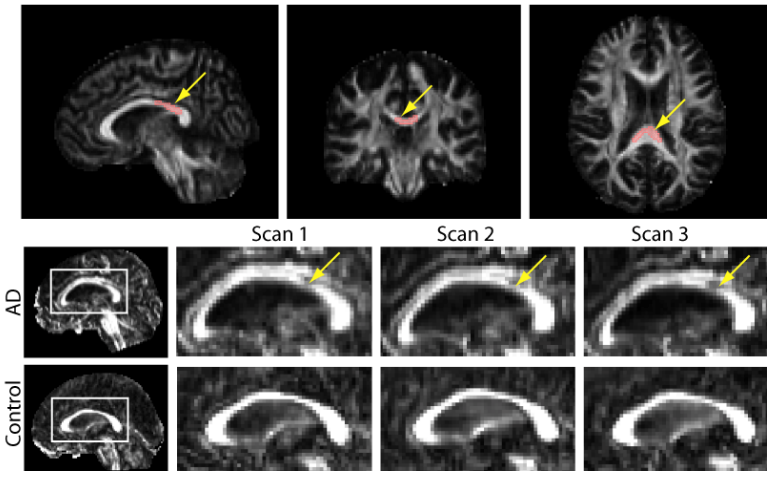

Fig. 2: Jacobian maps based on consecutive DTI scans of AD patients revealed significant ($p<0.05$) degeneration in the corpus callosum. Top panel: sagittal, coronal and transverse FA images of our single subject template. The region with significant changes in Jacobian maps over three scans is highlighted (red regions indicated by yellow arrows). Bottom panel: midsagittal FA images from three scans in a representative AD patient (AD) and a healthy volunteer (Control) showing an examples of degeneration in the corpus callosum (indicated by the yellow arrows) in the AD patient. The region indicated by the yellow arrows is the region highlighted in the top panel.

References: 1. Stahl, R. et. al. Radiology 243 (2) 483-92 (2007). **2.** Zhang, Y. et. al. Neurology 68 (1) 13-9 (2007) **3.** Jiang, H. et. al. Comput Methods Programs Biomed 81 106-116 (2006)

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