Voxelwise analysis of MR Diffusion Data from Recovering Alcoholics using Tract-Based Spatial Statistics

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Introduction: Neuropathological and neuroimaging studies in alcohol dependence demonstrate white matter (WM) volume loss [1], while DTI studies with region-of-interest (ROI) analyses indicated lower fractional anisotropy (FA) in regions of the corpus callosum and the centrum semiovale [2,3]. Current DTI data analysis methods, which include voxel-based morphometry (VBM), ROI, and tractography-based approaches, suffer from the low precision of cross-subject alignment, the residual misalignment due to group differences in gray and white matter partial volume and ventricular size, and the choice of correct smoothing extent. Tract-Based Spatial Statistics (TBSS) [4] is a newly developed technique that combines the strength of both VBM and tractography-based analyses. Here we demonstrate the application of TBSS to the investigation of the voxelwise difference of FA between recovering alcoholics and non/light-drinking controls using a 1.5 Tesla clinical scanner.

Materials and Methods: 1.5 Tesla DTI data from 5 male smoking alcoholics (sRA, sober for 7 ± 4 days, age 52.2 ± 5.6 years) and 5 male controls (41.3 ± 10.3 years) were used for this study. A single shot EPI DWI sequence (TR/TE/TI=5000/100/3000ms, 2.4x2.4x5mm^3) used a double refocusing SE acquisition, bipolar external diffusion gradients [5] with six encoding directions and five b-values (0, 160, 360, 640, and 1000 sec/mm^2). The diffusion-weighted images were preprocessed by aligning to the b=0 image using full affine transformation for the motion and eddy current correction. A simple least squares fit of the tensor model and diffusion tensor was calculated using four b values and tensor eigenvalues and FA were calculated. TBSS used four major analysis steps: 1) Nonlinear alignment: All 10 FA images were co-registered to each other and aligned into standard space using B-Spine free-form deformation. A single subject's FA image was targeted for all nonlinear registrations. 2) Creating the mean FA image and its skeleton: The perpendicular direction of the local surface tract was estimated and the highest FA along this direction was identified as the center of the tract (skeleton). 3) Projecting all individual FA values onto the mean FA skeleton (thresholded to FA=0.2): A "distance map" was created of voxelwise distances to the nearest skeleton point. The maximum FA value was searched and then assigned to the current skeleton voxel. 4) Voxelwise statistics on the skeletonized FA data: A permutation-based non-parametric approach [6] tested voxel t value and cluster size against the null distribution (generated via multiple random permutations) of maximum values of the test statistics. *p*-values were corrected for multiple comparisons using single threshold test of maximal statistics [6].

Results: Fig. 1a shows the overlay of the mean FA map on the FA mean skeleton image from 10 subjects. Fig. 1b displays the mean FA map after each subject has been nonlinearly aligned to the target subject in MNI 152.

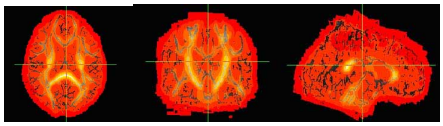

Fig. 1a

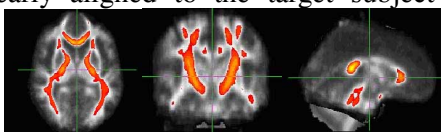

Fig. 1 b

Fig. 2 shows the mean FA skeleton overlaid with *t* values and aligned to the white matter tracts atlas using permutation-based inference on cluster size ($t > 1$, $p < 0.05$). Significantly lower FA (in blue) in sRA compared to controls is found in the left genu of the corpus callosum (Fig. 2a) and in thalamic fibers of the frontal and left parietal lobe (Fig. 2b).

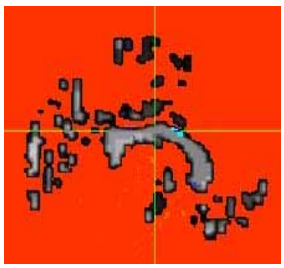

Fig.2a.

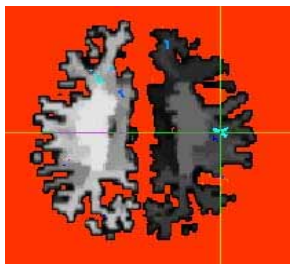

Fig.2b

Discussion: TBSS has been applied to 1.5 T DTI data in recovering alcoholics. The major regions of FA abnormalities coincide with compromised brain regions recently reported in deformation-based morphometric data from 1-week-abstinent alcoholics [7] and with FA abnormalities observed in previous DTI studies. The TBSS approach is believed to have distinct advantages over previous DTI data analyses methods and can be used for generating correlational maps.

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