Inter-Subject Correlations between DTI Indices and Tissue Fractions in Human Brain

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Introduction: Voxel-based analysis of diffusion tensor imaging (DTI) data has been widely used to access the alterations of white matter (WM) integrity at a group level [1]. However, the histological mechanism underlying the observed DTI index (FA/MD) changes is still poorly understood, posing a major difficulty in interpreting DTI findings [2]. For example, it remains unclear to what extent the inter-subject variations of FA measurements should be explained by the intra-voxel WM tissue fraction rather than the underlying WM integrity changes. A previous preliminary study has shown correlations of DTI indices with the tissue fractions estimated from a set of inversion-recovery (IR) procedures, although the results were limited to a 5-slice partial brain in a single subject [3]. Here we promote this investigation to a group-level whole-brain analysis by using a voxel-based DTI approach and a fast fractional signal mapping from inversion recovery (FRASIER) [4]. The major goals of this study are (I) to test whether significant correlations exist in WM between DTI and tissue fractions across the subjects, and (II) to identify the regions where the correlations between DTI and tissue fractions most likely occur. We expect the outcomes to provide useful information on whether and where we should take into account the effects of tissue fraction variations in a DTI group analysis.

Methods: Ten healthy volunteers (age=28±6 years, female/male= 7/3) participated in the MRI study under the guidance of local institutional review board (IRB). Each subject was scanned on a Siemens 3T Allegra system for the whole brain using a quadrature volume head coil. The DTI data were acquired using an EPI-based sequence (12 directions, b=1000 s/mm^2) at 35 axial slices of 128x128 matrix yielding a 1.72x1.72x4 mm resolution. A fast longitudinal relaxation (T1) measurement was obtained using inversion recovery Look-Locker segmented EPI between steady states (IR LL-EPI SS) [5] sequence (TR/TE= 400/13 ms, α= 16°, IT= 10 s, 5 lines per acquisition) with the same imaging prescription of the DTI acquisition. Structural images of the brain were also acquired with T1-MPRAGE at 1x1x1 mm resolution. Automatic segmentation for intra-voxel tissue fractions (f_{WM}, f_{GM}, and f_{CSF}) was performed for each subject as described in [4]. All DTI images were corrected for geometric distortion by PLACE [6] before fractional anisotropy (FA) and mean diffusivity (MD) indices were estimated using DTI tools in AFNI [7]. All FA (and then MD) maps were spatially normalized with an inter-subject nonlinear co-registration in FSL [8] and up-sampled to 1x1x1 mm resolution. The tissue fractions images (f_{WM} and f_{CSF}) were also wrapped into the normalized space by (1) applying an affine alignment between DTI and LL-EPI SS reference images within each subject, and (2) following the spatial transformation pipeline of the FA maps. Using the approaches similar to [9], we estimated FA vs. f_{WM} and MD vs. f_{CSF} correlations across the 10 subjects in the normalized space for each voxel within the WM mask defined as mean FA > 0.2.

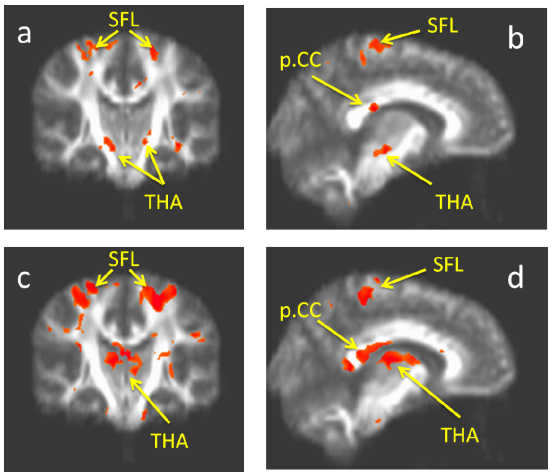

Fig.1: (a,b) FA vs. f_{WM}, (c,d) MD vs. f_{CSF} correlations.

Results: Overlaid on the mean FA map, red clusters in Fig.1 (a b) represent the significant correlations ($p<0.01$) between FA and f_{WM} variations across the subjects. Fig.1 (c d) show the correlations ($p<0.01$) between MD and f_{CSF} measurements at the same coronal and saggittal planes. It is shown that significant inter-subject correlations between DTI and tissue fractions do exist in WM, and that these correlations are not evenly distributed in WM but primarily focused on selective regions such as superior frontal lobes (SFL), posterior part of corpus callosum (p.CC), and thalamus (THA). Moreover, larger cluster sizes in (c d) indicate stronger effects of MD vs. f_{CSF} than FA vs. f_{WM} correlations. Results of region-of-interests (ROI) analysis also show the FA vs. f_{WM} correlations in manually-traced thalamus region (bilateral average), and the MD vs. f_{CSF} correlation in the whole brain WM mask, as plotted in Fig.2 (a) and (b), respectively.

Summary and Discussion: Both of our voxel- and ROI-based analysis indicate the existence of regional correlations between DTI and tissue fraction measurements across the subjects, and these correlations are primarily distributed in selective regions including superior frontal lobes, posterior CC, and thalamus. This result suggests the need to consider the effects of tissue fraction variations for a group DTI analysis in those correlation-sensitive regions. Further investigations are directed to obtain correlation maps for a larger group size, and to demonstrate improved statistical power of DTI group analysis when the measured tissue fractions are incorporated as a co-variance for correction.

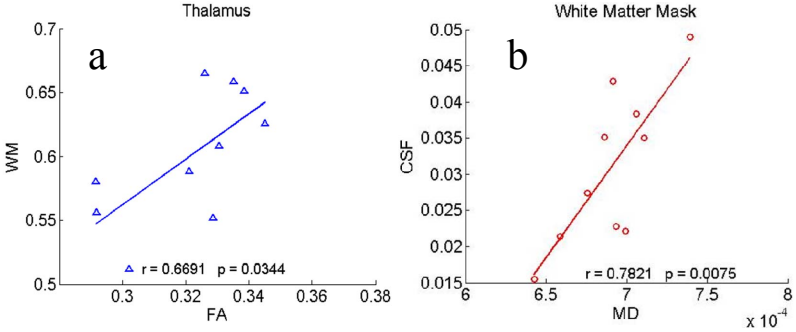

Fig.2: (a) FA vs. f_{WM} correlation in thalamus region for bilateral average, (b) MD vs. f_{CSF} correlation in the WM mask of whole brain.

References:

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