Estimation of the Angle Between Crossing Fibers as a Novel Structural Quantity

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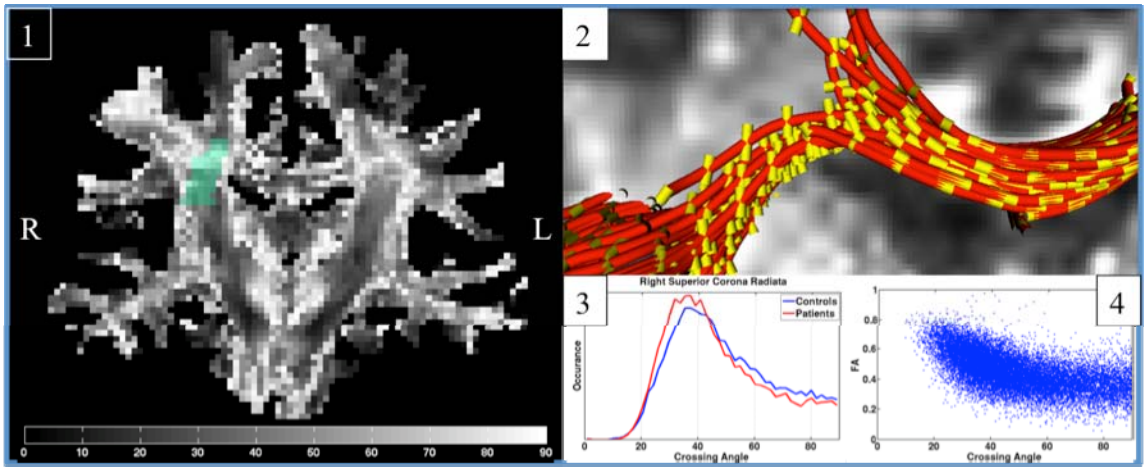
Introduction

In recent years a variety of high angular resolution diffusion imaging (HARDI) methods have been proposed to solve the "crossing fibers" problem, which occurs when two or more fibers pass within the same imaging voxel [1]. Usually the utilization of these methods is limited to improving tractography results. Interestingly, abnormal diffusion tensor imaging (DTI) indices in areas that are known to have crossing fibers are a common finding in a number of brain disorders. For example, an abnormality in the crossings of frontal connections is consistently reported in schizophrenia (SZ) [2]. Nevertheless, determining the underlying pathology in crossings is especially difficult, since the specificity of DTI parameters such as fractional anisotropy (FA) is dramatically decreased. Here, we propose the crossing-angle as a new contrast mechanism that describes a physical feature of fiber arrangement that has not been studied before. We introduce an algorithmic approach to extract crossing-angle maps from HARDI methods, and demonstrate the approach on a clinical dataset that compares first-episode SZ patients with matched healthy controls. We report a significant crossing-angle difference in the crossings of frontal connections between the two groups.

Algorithm and Methods

The crossing-angel map was constructed using the following algorithm: 1) Apply HARDI tractography to output a set of streamlines that describe either the entire white matter, or alternatively, a chosen set of fibers. Here we used whole brain Kalman filter based 2-tensor tractography [3], which is implemented as a Slicer3D module to acquire a whole brain set of streamlines. 2) Establish a voxel-wise heading direction for each fiber. Here the fiber direction was calculated in each voxel by principal orientation based 2-means clustering of all the estimated tensors (one per streamline). We then averaged each group to result with two estimated directions in each white matter voxel. 3) Calculate the angle between the fiber components; Due to the symmetry properties of the diffusion signal the angle is limited to the range of 0-90º. The algorithm was applied on a DTI dataset that included 18 patients diagnosed with a first episode of SZ, and 20 sex and age matched healthy controls (HC), acquired on a 3T GE Signa magnet using a double-refocused EPI-DTI that had 51 gradient directions with b=900 s/mm^2 and 8 additional b=0 images in 85 axial slices with (1.7mm)^3 isotropic voxels covering the entire brain. All diffusion images were corrected for motion and eddy currents artifacts (FSL) prior to applying tractography. We chose to compare the right superior Corona Radiata as defined in the ICBM DTI-81 atlas. The region of interest (ROI) was projected from the atlas space onto each individual subject space (FSL). We used t-test to group-compare the average value within the ROI across the two groups.



Results and Discussion

Figure 1 shows a crossing-angle map of a single healthy subject. Bright intensity - representing higher angle between fibers – is typically found at the boundaries between fibers, and in areas that are anatomically known to have crossing fibers. The ROI selected here (Fig. 1) is an example of an area in which part of the Corpus Callosum and the Cortico-spinal tracts are expected to cross. The crossing is demonstrated in Figure 2, where the two components obtained by the 2-tensor tractography are visualized (red and yellow) along the path of the Corpus Callosum. The average angle in the selected ROI of the SZ group was significantly lower than the average angle for the controls (p=0.0365), with 56º for the controls versus 53.6º for the HC. Figure 3 demonstrates that the distribution of crossing-angles over the HC group was different than the distribution over the SZ group. The HC group had more high-angular crossings, contrary to the SZ group that had more low-angular crossings. These findings suggest that the architecture of crossing fibers is different between the groups. In trauma cases such as injury or a tumor, the crossing-angle could change due to physical forces that the tissue endures. In SZ, however, physical trauma is less likely and the angular change could either be caused by developmental changes that caused abnormal alignment between the connected brain areas, or by local cytoskeletal alterations in the area of crossings. We predict that longitudinal comparison of the crossing-angle could further distinguish the pathology related to our findings. Figure 4 compares the crossing-angle with FA, where we found that the two measures were correlated for low crossing-angles (<45º), and that they were no longer correlated for higher crossing-angles. Low crossing-angles are predominantly found where a single fiber is expected, and it seems like the crossing-angle in that case provides a measure of dispersion, correlating with anisotropy [4]. The fact that the two measures do not correlate in higher crossing-angles suggests that FA is not sensitive to the angle between the fibers, thus this structural information is unique to the crossing-angle measure. The crossing-angle is therefore a promising new HARDI parameter to study the architecture of the brain.

References

[1]. Alexander D., *Ann N Y Acad Sci*, 1064:113-33 (2005). [2] Ellison-Wright I., and Bullmore E., *Schizophrenia Research*, 108:3-10 (2009). [3] Malcolm G. et al., *IEEE Trans Med Imaging*, 29:1664-1675 (2010). [4] Savadjiev P. et al., *Neuroimage*, 49:3175-86 (2010).