RELATING FIBER CROSSING IN HARDI TO INTELLECTUAL FUNCTION

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Relating Fiber Crossing in HARDI to Intellectual Function

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Introduction: Localizing brain structures and pathways associated with intellectual performance and cognition may clarify the networks involved, their development, and their dysfunction in disease. Here we introduce a measure of fiber crossing computed from high angular resolution diffusion images (HARDI), with the goal of better characterizing complex white matter microstructure. We aimed to detect white matter features associated with intellectual performance, previously missed due to limitations of the single tensor diffusion model.

Methods: High magnetic field (4T) diffusion-weighted (94 gradients, 11 non-sensitized) MR images were acquired from 293 right-handed healthy young adult twins and their siblings (23.9 ± 1.9 years old; 112 monozygotic subjects, 153 dizygotic, and 28 siblings). Verbal, performance, and full-scale intelligence quotients were also measured (VIQ: 114.7 ± 15.2; PIQ: 114.2 ± 11.9; FIQ: 111.7 ± 10.4). Images were corrected for motion and eddy current distortions. Each subject's average b0 image was aligned to a common subject specific template using a nine-parameter affine transformation, and gradient directions were corrected accordingly. Orientation distribution functions (ODFs) in *constant solid angle* were computed as described in [1] from both the diffusion tensors [2] and q-balls [3]. We also created a mean map of the q-ball ODFs, averaged across all subjects. We computed the *geodesic distance* [4,5] between the two ODFs (from the fitted tensor and q-ball) at each voxel for each subject. Both the tensor and q-ball ODF models can correctly reconstruct isotropic and single-fiber geometries. However, only the q-ball ODF can correctly resolve fiber crossings, so the mentioned tensor–q-ball ODF distance (TQOd) is a reasonable measure of fiber crossing. Each individual's fractional anisotropy (FA) maps were elastically registered to a common FA template including only high FA regions, to improve white matter registration. Individual deformation fields were then applied to the TQOd to identically align each subject's FA and TQOd maps. Using a linear random effects regression analysis to account for familial relations in the twin samples, voxelwise FA and TQOd maps were each regressed against each intelligence score.

Results: Figures 1 and 2 show the mean q-ball ODF field overlaid on the mean FA and mean TQOd maps. The mean TQOd clearly identifies known crossings, e.g. where the corpus callosum, corona radiata and internal capsule all intersect. Known isotropic, single-fiber anisotropic, and fiber crossing regions were identifiable, respectively, as regions with low FA/low TQOd, high FA/low TQOd, and low FA/high TQOd. After correcting for multiple comparisons using the false discovery rate (FDR) method, performance IQ – which is thought to be related to neuronal processing speed – was associated with high anisotropy in several regions, as expected [6]. TQOd correlations with PIQ were also significant in regions of low FA located in the caudate head, where partial voluming occurs between the internal capsule and striatum. Here, fiber crossing and the presence of multiple tissue types per voxel prevent tensors from fitting correctly, but q-ball reconstruction is more accurate. **Figure 3** shows voxels that survived FDR correction, with uncorrected p-values of $p < 3.2 \times 10^{-5}$ for TQOd.

Conclusions: We introduced a new measure to identify white matter fiber crossings in HARDI; this measure was correlated with performance IQ in brain regions where correlation with FA was not detected. This highlights the importance of higher-order diffusion modeling to better localize fiber pathways relevant for cognition.

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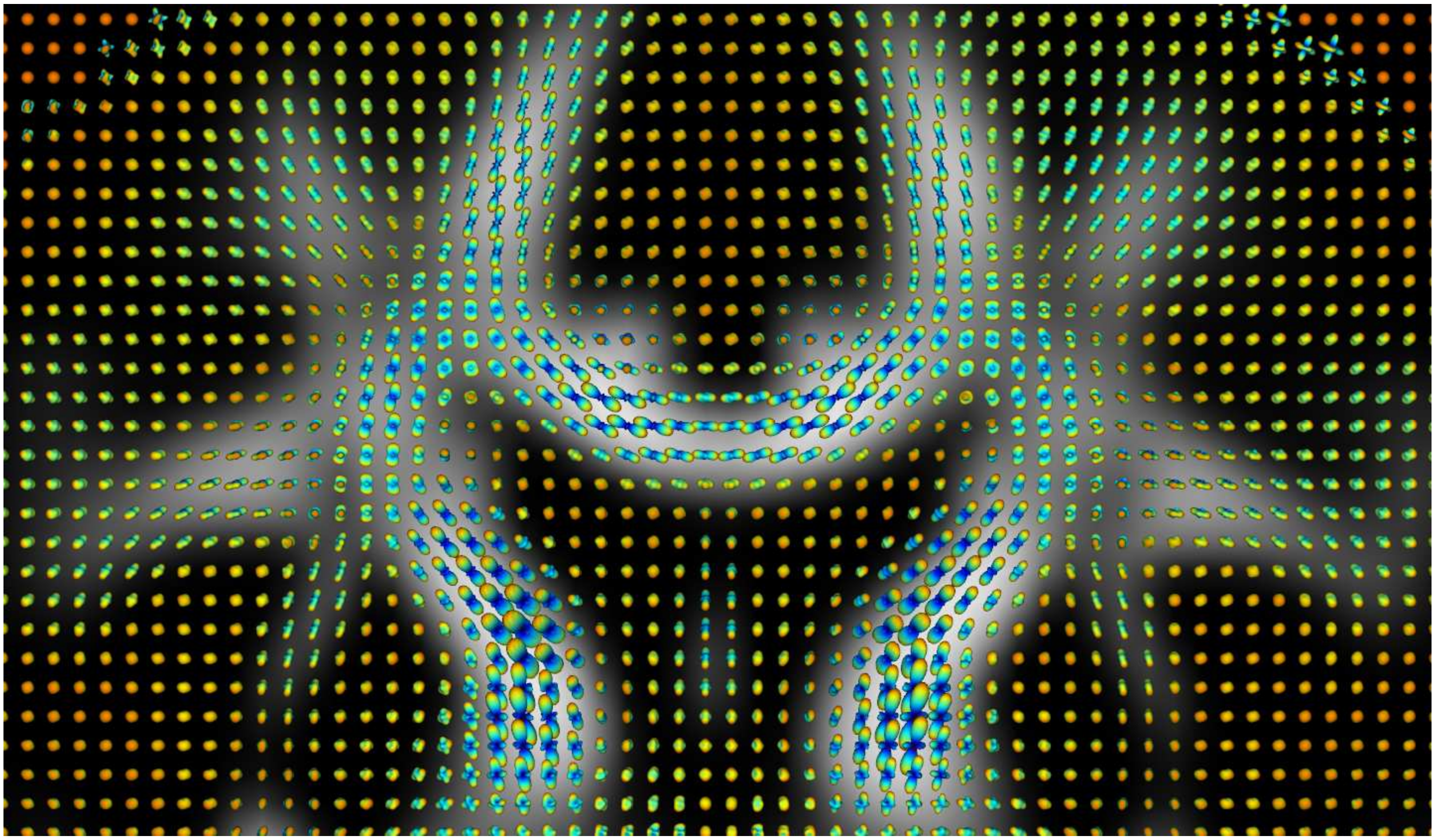

Fig. 1

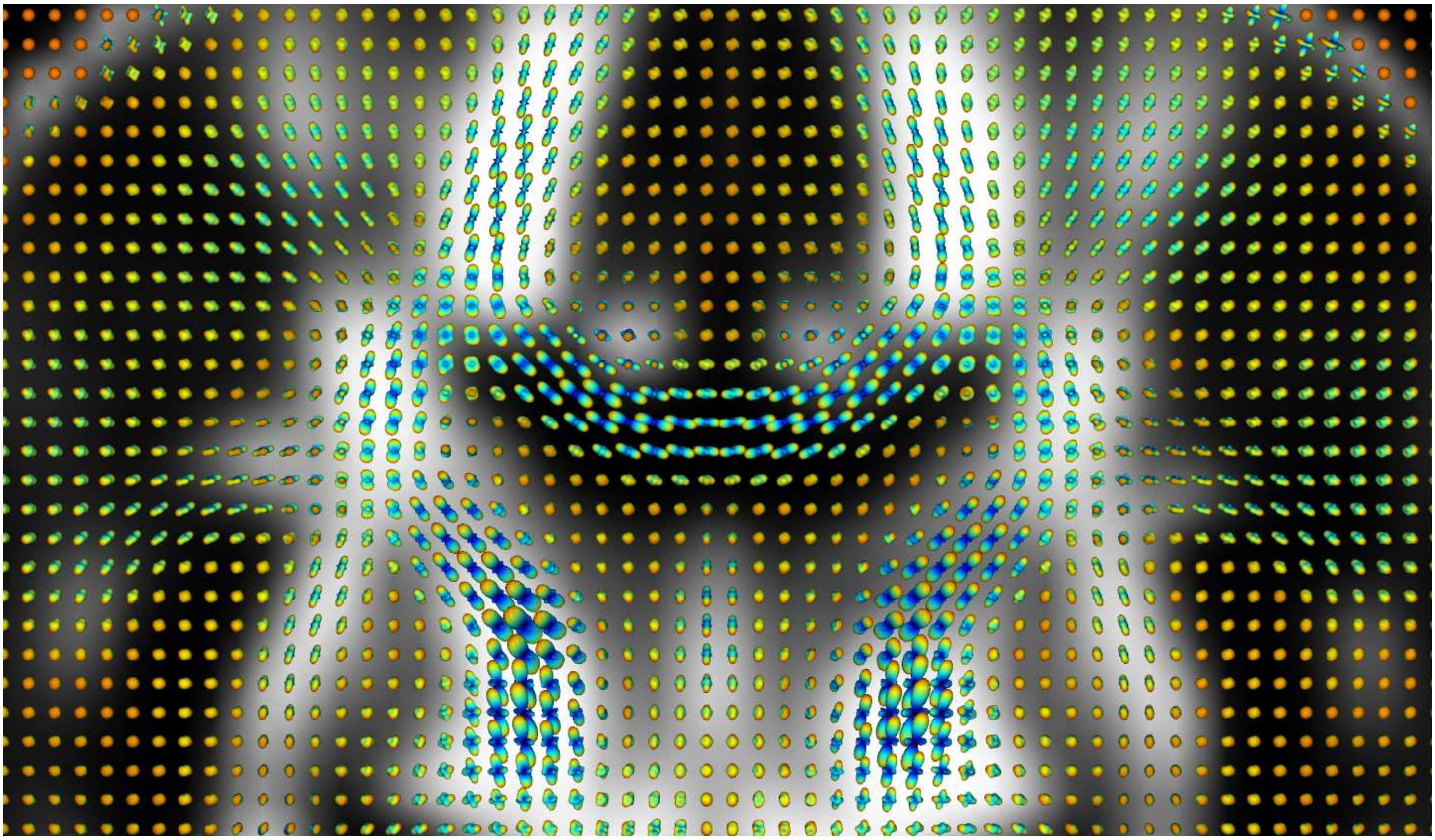

Fig. 2

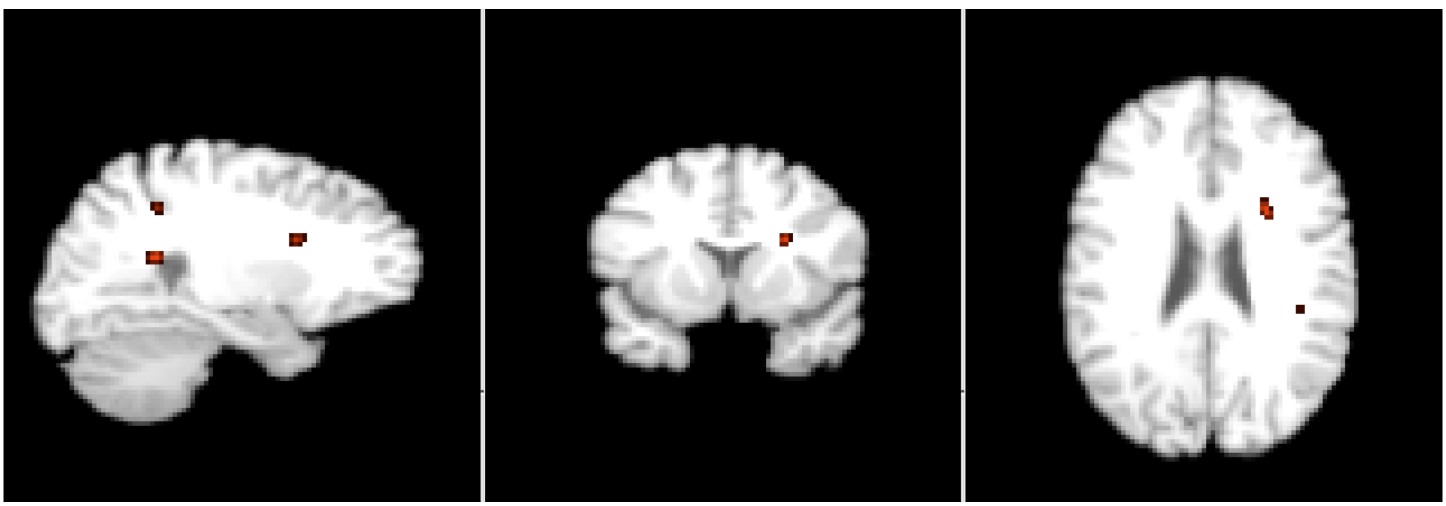

Fig. 3