Multiple fiber diffusion anisotropy analysis in autistic children

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Introduction

Autism is a disorder of brain development characterized by impaired social interaction and communication, and restricted and repetitive behaviors. Increasing evidences from functional and structural neuroimaging studies show that an atypical developmental trajectory of white matter exists in patients with autism. Diffusion tensor imaging (DTI) is a biomedical imaging modality capable of revealing microstructural features of the brain or changes in white matter. In particular, fractional anisotropy (FA), a diffusion anisotropy index derived from DTI that is prevailingly in use, is highly sensitive to changes in nerve fibers. We herein present a novel diffusion anisotropy index for multiple fiber analysis that is based on a spherical harmonic function and that may effectively explain the morphological features that are responsible for changes in FA values. Our experiment using human MRI data showed that brain regions with low FA values may not necessarily indicate abnormal white matter, but could instead be linked to voxels containing fiber crossings or multiple fibers. Although FA is useful in many applications and appears to be a sensitive indicator for a broad spectrum of pathological conditions, FA may not be the best measure to characterize the full 3D shapes of a tensor. The mapping mechanism described here (R_4), which is based on a variation model may be an effective tool for studying diffusion anisotropy and providing a better explanation of the FA changes in the brains of autistic persons.

Materials and Methods

DT-MRI data from six autistic children and six matched healthy children were acquired using a 1.5-T GE MR scanner in Nanjing Brain Hospital, China. A single-shot, spin echo, echo planar sequence (SE-EPI) was used in DTI data acquisition, with diffusion gradients applied in 15 non-collinear directions and b-value at 1000s/mm^2. The subjects were imaged at thirty-nine axial slice locations, AC-PC aligned, with a thickness of 3mm and no gap, Other DWI parameters were: TE =104.4 ms; TR = 8000 ms; FOV = 24cm^2 and acquisition matrix = 128×128. The duration of the DTI scan was 4.4 minutes with 2 signal averages. The two groups of subjects were matched by age, gender, and IQ. The healthy volunteers had no history of psychiatric disease or neurological injury. Written consents were obtained and approved by the Southeast University's Institutional Review Board. Diffusion anisotropy was classified using a method based on apparent diffusion coefficient and spherical harmonic series. For non-Gaussian diffusion, SHS approximation (Eq. 1) of the ADC profiles estimated from HARDI data was used [1, 2] to characterize the diffusion anisotropy; and, the coefficients of SHS and the variance of ADC profiles from their mean were used to characterize diffusion anisotropy [3]. We have developed a novel measurement R_4 (Eq. 2) for studying diffusion anisotropy of tensor data in lieu of FA. The R_4 map is an indicator of diffusion anisotropy regarding crossing fibers or multiple fibers within a voxel, with higher intensity values corresponding to higher degrees of fiber crossing.

$$d(\mathbf{x},\theta,\phi) = \sum_{l=0}^{l_{\max}} \sum_{m=-l}^{l} A_{l,m}(\mathbf{x}) Y_{l,m}(\theta,\phi) \qquad (1)$$

$$R_4 =: \sum_{m=-4}^{m=4} |A_{4,m}| \Big/ \sum_{l=0,2,4} \sum_{m=-l}^{l} |A_{l,m}| \qquad (2)$$

where $Y_{l,m}(\theta,\phi)$ represents the spherical harmonics and $A_{l,m}(\mathbf{x})$ are coefficients.

Results and Discussion

Group differences in terms of FA and R4 were calculated and compared to characterize differences of anisotropy and fiber crossing across the autism and control groups (Fig.1). We found that in the region of corpus callosum and lateral ventricle (ROI1) and precentral gyrus (ROI2), the presence of multiple fibers within a voxel (producing an increase in the value of R_4) may reduce the value of FA (Fig. 2A/B). Therefore, the presence of multiple fibers within a voxel may be a reason for the change in diffusion anisotropy. Moreover, group differences in FA of white matter in the two ROIs (Fig. 2C) agreed with findings from previous autism studies [4]. FA is generally considered a marker of white matter integrity, although evidence for this claim is far from definitive [4]. Our findings suggest that regions in autistic brains that contain multi-fiber crossings have low FA values. Therefore, abnormal FA may not definitely indicate the white matter pathology per se, but may instead indicate different numbers of local crossing fibers.

References

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Acknowledgment

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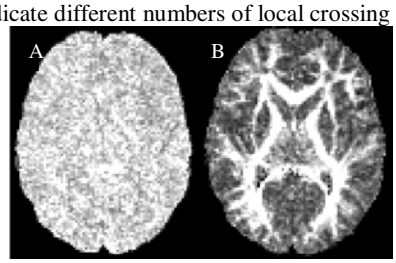
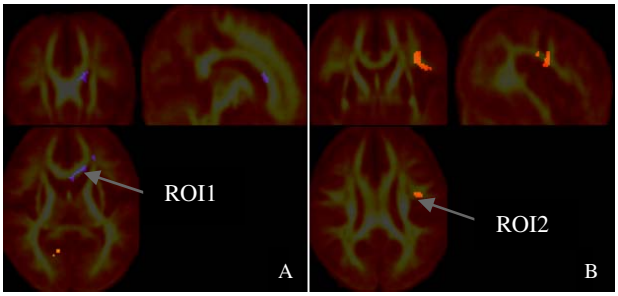
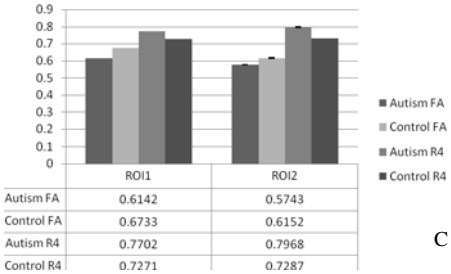


Figure 1 Results from one slice of the human MR datasets: A. map of multi-fiber classification of an axial slice (R_4 map); B. the corresponding FA map.





	ROI1	ROI2
Autism FA	0.6142	0.5743
Control FA	0.6733	0.6152
Autism R4	0.7702	0.7968
Control R4	0.7271	0.7287

C

Figure 2 A, B: Regions with significant changes of both FA and R_4, ($P < 0.01$); C: White matter change details in ROI1/2 between the autistic children and controls.