Altered Fiber Radial Diffusivity in Schizophrenia Revealed by Diffusion MRI

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Introduction

Schizophrenia is a common mental disease affecting about 1% of the population. Various studies using Diffusion Tensor Imaging (DTI) have showed altered diffusion properties in the major fiber tracts connecting the frontal and temporal lobes including the cingulum bundles, arcuate fasciculi, and uncinate fasciculi (1-3). However, the underlying mechanism remains unclear since the tensor model is insufficient to distinguish the possible causes, such as a change in the fiber orientation coherence, a change in the intrinsic diffusivity of the fibers, or both. Fiber ORientation Estimated using Continuous Axially Symmetric Tensors (FORECAST) (4), a new approach to High Angular Resolution Diffusion (HARD) analysis, provides a reliable estimate of the fiber radial diffusivity and orientation distribution within each voxel. In this study, we performed a group comparison of the diffusivity properties estimated by the FORECAST analysis between schizophrenia patients and healthy controls, aiming to reveal white matter structural changes associated with schizophrenia.

Methods

HARD images of 20 schizophrenia patients (SZ, 10 with auditory hallucination, AH, 10 without, NAH) and 13 healthy controls (CO) were acquired on a 3T Philips scanner, using the following imaging parameters: b=1000s/mm^2, 92 diffusion-sensitizing directions, 2.5mm isotropic voxel size. For each subject, a number of voxels along bilateral cingulum bundles, uncinate fasciculi, and the left arcuate fasciculus were identified using a semi-automated fiber-based method (5) (data from 2 CO subjects and 1 NAH subject in the left arcuate, AL, were ignored due to failure in fiber tracking). A 6th order spherical harmonic FORECAST analysis was performed for each voxel to estimate the radial diffusivity, $\lambda_\perp$, FA (assuming axially symmetric diffusivity), and the fiber angular distribution (FAD). An intravoxel orientation coherence index (CI) was calculated based on the ratio of the amplitude of the FAD at the FWHM angle (for the noise-free FAD, about 17º) away from the principal orientation over the FAD maximum within each voxel (0 for isotropic diffusion, 1 for ideally coherent single fiber diffusion). FA, $\lambda_\perp$, and CI were averaged within each fiber tract, and a Student's t-test between the two groups was then performed to determine whether there is difference between the SZ group and the CO group.

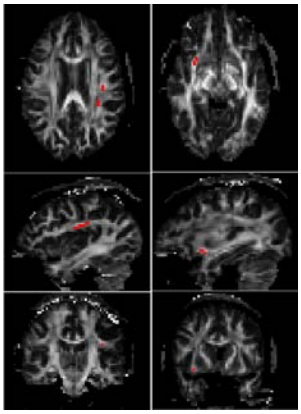

Figure 1. Locations of the chosen voxels in AL (left) and UR (right).

Results

As summarized in table 1, in AL, FA was significantly higher and $\lambda_\perp$ was significantly lower in SZ than in CO. In the right uncinate (UR), the SZ group showed significantly lower FA and higher $\lambda_\perp$ than CO group. No significant difference of CI was detected in either region between SZ and CO. Additionally, AH and NAH both had higher FA than CO in AL (not shown here).

Table 1. Comparison between SZ and CO (mean±std)

		SZ	CO	p value
AL	FA	0.56±0.07	0.53±0.06	**0.0003**
	$\lambda_\perp$ (1e-5cm^2/s)	0.45±0.06	0.47±0.05	**0.0018**
	CI	0.82±0.03	0.82±0.03	0.3535
UR	FA	0.54±0.11	0.57±0.11	**0.0321**
	$\lambda_\perp$ (1e-5cm^2/s)	0.50±0.10	0.47±0.10	**0.0256**
	CI	0.80±0.06	0.80±0.06	0.5185

Discussion and Conclusion

To the best of our knowledge, this is the first study that distinguishes between changes in intravoxel fiber coherence and intrinsic radial diffusivity in schizophrenia. The negative correlation between FA value and $\lambda_\perp$ confirms the hypothesis that in these SZ-affected tracts the change of diffusion anisotropy is predominantly due to a change of the fiber microstructure (change in the axon density or damage to myelin layers). In AL, the increase in FA for AH agrees with an earlier DTI study (1), though for NAH our study shows different results. The reduction of FA found in the UR is in accord with previous findings (2). The associated increase of $\lambda_\perp$ suggests damaged myelin layers in UR, which is consistent with a post mortem study showing lower expression of the oligodendrocyte-associated gene in the brain of schizophrenia (3). The lack of difference in CI between two groups suggests that the change of intravoxel orientation coherence may not be a major cause of the altered FA in either region.

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References: **1.** Hubl D et al. Archives of general psychiatry 2004;61(7):658-668. **2.** Nakamura M et al. Biological psychiatry 2005;58(6):468-478. **3.** Flynn SW et al. Molecular psychiatry 2003;8(9):811-820. **4.** Anderson AW et al. Magn Reson Med 2005;54(5):1194-1206. **5.** Arlinghaus L et al. Proc Intl Soc Mag Reson Med 2006;14:279.