Altered Fiber Radial Diffusivity in Schizophrenia Revealed by HARDI

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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 [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 Imaging (HARDI) analysis, provides a reliable estimate of the fiber radial diffusivity ($\lambda_\perp$) and fiber orientation distribution (FOD) within each voxel. A spatial normalization of the FOD function based on HARDI data was proposed recently [5], which makes it possible to compare the intra-voxel fiber distribution between subjects. In this study, we performed a group comparison of the diffusivity properties and intra-voxel fiber distribution between schizophrenia patients and healthy controls, aiming to reveal white matter structural changes associated with schizophrenia.

Methods

HARDI images of 33 schizophrenia patients (SZ) and 22 healthy controls (CO) were acquired on a 3T Philips scanner with b=1000s/mm^2, 92 diffusion-sensitizing directions, 2.5mm isotropic voxel size. Multi-step image registration was performed using linear [6] and nonlinear methods [7]. Datasets of 2 patients were excluded from further analysis due to poor registration and movement artifact. FODs were calculated in the common space using the FORECAST model through 6th order, with negative peak regularization [8], and transformed according to [5]. Voxel wise t-tests of group differences in fractional anisotropy (FA), $\lambda_\perp$, and fiber coherence index (κ) [9] were performed. In order to reduce false positive error, a threshold for cluster size of 6 voxels was applied. In clusters with significant FA difference between groups, a general linear model between these three measures was also applied.

Results

Significantly lower FA in SZ is found in the posterior part of the left superior longitudinal fasciculus (*slf*) and bilateral internal capsules (*ic*). In all three regions, the mean $\lambda_\perp$ of all voxels is significantly higher in SZ, though the group difference is not significant in all voxels. Similarly, the mean fiber coherence in each cluster is significantly lower in SZ, though the group difference does not reach the significant level in all voxels. Strong correlation between FA and $\lambda_\perp$ is found at both voxel and cluster levels in all three regions, even after controlling for fiber coherence variation.

Discussion

The negative correlation between FA value and $\lambda_\perp$ confirms the hypothesis that in these tracts the change of diffusion anisotropy between groups is predominantly due to the fiber microstructure (change in the axon density or myelin layers). This study will help advance our understanding of the structural alterations in schizophrenia, and the set of techniques will be helpful in other clinical studies of white matter.

Fig1. Scatter plots of FA vs. $\lambda_\perp$ (top) and FA vs. κ (bottom) in left *slf* (left), right *ic* (middle), and left *ic* (right). Points represent data from all voxels in the ROI for all subjects. The mean (mn) for each group is also shown. For each comparison, the p-value is shown for between-group differences in FA, radial diffusivity, and fiber coherence.

References

1. Hubl, D., et al., Arch Gen Psychiatry, 2004. 61(7): p. 658-68. 2. Nakamura, M., et al., Biol Psychiatry, 2005. 58(6): p. 468-78. 3. Flynn, S.W., et al., Mol Psychiatry, 2003. 8(9): p. 811-20. 4. Anderson, A.W., Magn Reson Med, 2005. 54(5): p. 1194-206. 5. Hong, X., et al., Magn Reson Med, 2009. 61(6): p. 1520-1527. 6. Li, R., in Electrical Engineering. 2001, Vanderbilt University: Nashville, TN, USA. 7. Rohde, G.K., et al., IEEE Trans Med Imaging, 2003. 22(11): p. 1470-9. 8. Tournier, J.D., et al., Proc Intl Soc Mag Reson Med, 2006. 14: p. 645. 9. Hong, X., et al., Proc I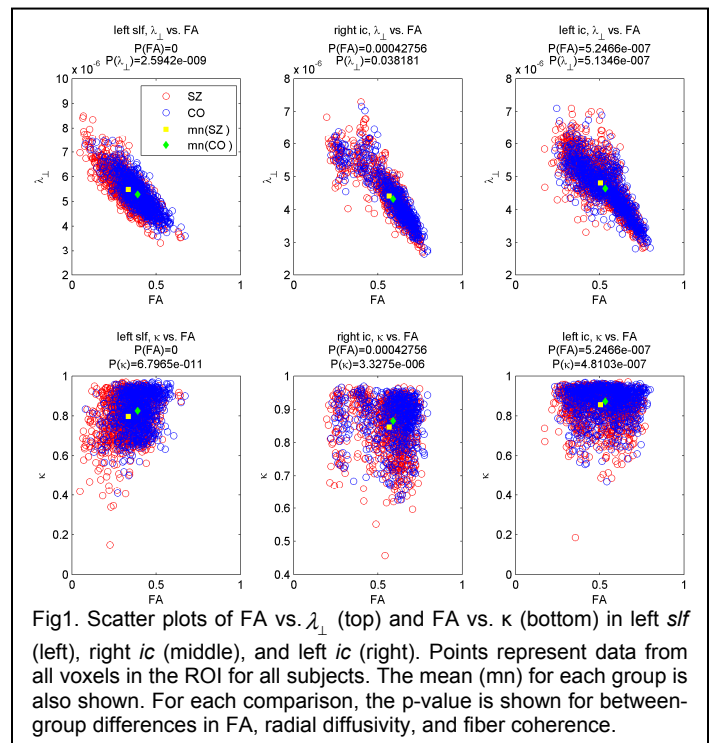ntl Soc Mag Reson Med, 2007. 15: p. 342.