A Preliminary Result of Principal Diffusion Direction Comparison in Attention-Deficit/Hyperactivity Disorder

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Introduction

Attention deficit/hyperactivity disorder (ADHD) was conceptualized to be relative to neurodevelopment in the origin [1]. Neuroimaging studies focusing on gray matter volume have interrogated the frontal-striatal circuitry associated with dopamine regulation was related to ADHD [2-4]. And several research results provide the evidence that suggest white matter abnormalities during development may be a factor [1].

Diffusion tensor imaging (DTI) is an MRI technique that could reveal white matter microstructure integrity and orientations. The structural integrity information could be reflected by fractional anisotropy (FA) which is one of the major indices in DTI. Despite the fact that discrepancies of FA in ADHD and normal subjects have been reported [1], it was once suggested that the fiber integrity may remain similar even if the white matter fiber orientation become altered [5]. Therefore, we hypothesized that microstructural orientation of certain circuit might be different between ADHD and normal subjects which may underscore the pathophysiology of ADHD. In this work, we performed statistical comparisons of the fiber orientations in pediatric patients with ADHD and age- and gender-matched control subjects [5], using the index principal direction derived from DTI.

Materials and Methods

A total of eighteen male pediatric subjects were included in this work (ranging from 8-15 years of age, all males), and every subject was psychologically examined. Nine were diagnosed as ADHD, whereas the other nine age-matched subjects were recruited as control. Patients with comorbid disorder were excluded.

MR imaging experiments were performed on a 1.5T system (GE Signa CVi, Milwaukee, WI). A 13-direction EPI DTI protocol was adopted for acquisition with b-value of 1000 s/mm^2. Slice thickness was 5 mm with in-plane resolution of 0.86x0.86 mm^2. 30 slices were obtained covering the whole brain. 3D T1-weighted images (124 slices) were also acquired with voxel size of 0.98x0.98x1.1 mm^3. For diffusion tensor reorientation during image deformation as needed in inter-subject averaging, we adopted the procedure proposed in Ref.[6]. Scalar image registration and normalization was performed using SPM99. The b = 0 EPI images in DTI were coregistered to T1 images to obtain an affine matrix from b0 to T1. Subsequently, this matrix was applied to the tensor components coregistration. The original T1 images were then normalized to a T1 template, from which the normalization parameters could be obtained to derive the transformation matrices using the deformation toolbox in SPM99. The two transformation matrices were applied into the tensor reorientation algorithm to normalize the DTI images [6].

For statistical analysis, the f score of the comparison of f-test was calculated using the method proposed by Schwartzman et al. as the following equation,

$$F = \frac{(N-2)\,(Ns - N_1 s_1 - N_2 s_2)}{(N_1 s_1 + N_2 s_2)}.$$

where N_1 and N_2 were number of subjects in each group and s_1 and s_2 were the corresponding dispersion indices; N was equal to N_1+N_2 and s denoted the total sampled dispersion [5].

The region of interest for the analysis of the principal direction was selected as voxels having FA values greater than 0.2 in the averaged FA map from all subjects, where the microstructure of fibers can be regarded as relatively well-oriented.

Results

The voxels showing statistically significant difference between ADHD and normal controls in principal direction were colorized on the T1 template in Fig.1 (neurological convention). Clusters with more than fifty contiguous voxels whose p-values were less than 0.001 were displayed. The white matter near the dorsal cingulated gyrus and the bilateral white matter within the striatal region were identified to exhibit significantly different principal directions.

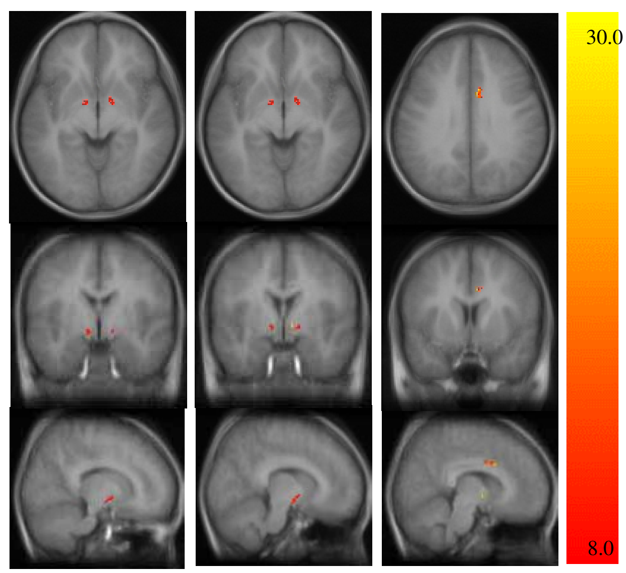

Fig 1. The Left column showed the region of significant differences in the left hemisphere. The middle and the right columns showed the regions in the right hemisphere. And the overlaid pseudo-colors denoted for the f-scores as the color bar indicated.

Discussion

The cingulate gyrus was known to be a region concerning the attention and many other cognitive activities in human behaviors. Therefore, our findings on the change of principal fiber direction in nearby white matter on ADHD may have important clinical significance. In addition, the difference in the bilateral striatum suggests that the frontostriatal circuitry may be associated with ADHD. Since these two areas played important roles in the transport of dopamine which was considered as a neurotransmitter responsible for regulation of some inhibitory tasks, our findings on white matter alterations of ADHD patients are in agreement with the literature reports[2-4].

We conclude that in addition to volumetric comparison and integrity indices in DTI such as FA and ADC, the principal direction analysis also provided valuable insights to the understanding of the relationship between white matter microstructure, orientation, and human cognition and behavior. The preliminary results suggested that principal direction analysis may shed light on unexplored neurobiological alteration in ADHD.

References

1. Ashtari, M., et al., Biol Psychiatry, 2005. **57**(5): p. 448-55.
2. Seidman, L.J., E.M. Valera, and N. Makris, Biol Psychiatry, 2005. **57**(11): p. 1263-72.
3. Durston, S., Ment Retard Dev Disabil Res Rev, 2003. **9**(3): p. 184-95.
4. Yang, P., et al., Psychiatry Clin Neurosci, 2004. **58**(6): p. 619-23.
5. Schwartzman, A., R.F. Dougherty, and J.E. Taylor, Magn Reson Med, 2005. **53**(6): p. 1423-31.
6. T-C. Chao, C.-W.K., H-W. Chung, M-T. Wu. in *ISMRM 13th SCIENTIFIC MEETING & EXHIBITION*. 2005. Miami Beach, Florida, USA.No. Abstract No.628.