Structural abnormalities of adolescent males with attention-deficit/hyperactivity disorder: a DTI study

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Introduction

Attention-deficit/hyperactivity disorder (ADHD) has been evidenced as a developmental disorder [1]. Growing numbers of reports also suggest that abnormalities in white matter (WM) development might be an important factor to the pathophysiology of ADHD [2]. To gain a fully understand of brain structural development in ADHD, studies in WM abnormalities of different age levels are necessary. Recent advent diffusion tensor MRI (DTI) is unique for exploring the organization of WM tracts in vivo [3] and has great potential for the study of WM abnormalities in neuropsychiatric disorders [4, 5]. In this study, healthy males and ADHD patients aged between 12 to 17 years old were recruited for DTI analysis. Voxelwise analysis was applied on fractional anisotropy (FA) of DTI. The data showed the alternations in brain WM integrity in corticospinal tracts, cerebellum, parietal lobe, occipital lobe, and ventricle in adolescent. And the results are consistent with previous functional and volumetric studies. It also implicates the developmental manipulation when links this study with previous finding [2].

Methods

15 healthy males (mean age is 13.6±1.1 y/o, right handed) and 17 ADHD males (mean age is 13.5±0.5 y/o, right handed) who were diagnosed and confirmed by DSM-IV criteria were recruited. Exclusion criteria included the history of head injury, neurological symptoms, and any contraindications to MRI scanning, such as metal implants and claustrophobia. All MR scan was performed at 1.5T MR system (Excite II; GE Medical Systems, Milwaukee, Wis., USA) in TPE-VGH. Using single shot diffusion spin-echo EPI sequence with TR/TE = 17000/68.9 ms, voxel size = 2 x 2 x 2.2 mm3, b = 900 s/mm², 13 directions, and NEX = 6, whole brain anatomy was acquired. T1 structural images were also acquired with TR/TE= 8.54/1.84ms, voxel size=1*1*1.5 mm^3. All MR images were acquired within 40 minutes. DTI and FA analysis were programmed in-house. Subsequent voxelwise analysis including scalar image registration and normalization was performed by SPM2 (Wellcome Department of Cognitive Neurology, Institute of Neurology, London, UK). DTI null images of each participant was coregistered to T1 images for an affine matrix from b_0 to T1. The original T1 images were then normalized to a T1 template, which is available in SPM2. Deformation parameters from the coregistration and normalization procedure mentioned above were applied to FA volume of each participant of which was smoothed with an 10 x 10 x 10 mm^3 Gaussian kernel. Regional differences between patient-control groups were explored through two-tailed unpaired t-tests with a statistic threshold of $p < 0.01$ and 50 continuous voxels.

Results

As compared with healthy group, a significant FA decrease in ADHD was observed in four regions (Figure a-d): left internal capsule, middle cerebellar peduncle exiting pons into the cerebellum, right internal capsule, and right cerebellum. A significant FA increase was observed in other four regions (Figure e-h): left parietal lobe, ventricle, corpus callosum, and right parietal lobe. With a more flexible threshold ($p < 0.01$ and 40 continuous voxels), right occipital lobe was observed

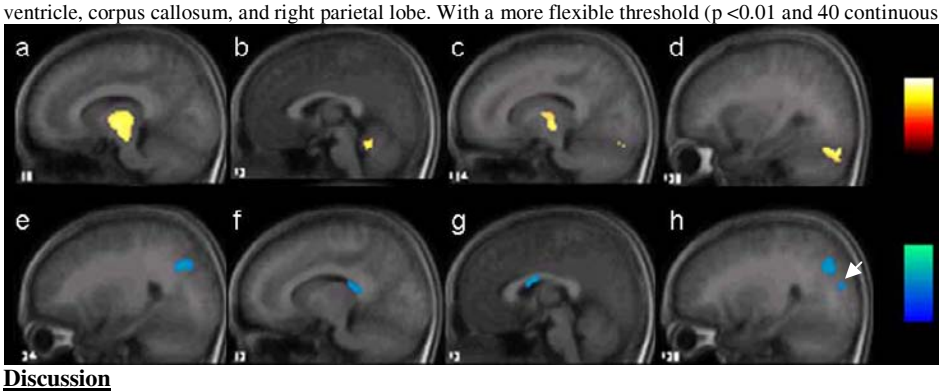

Figure 1, FA decrease in ADHD patients is shown in areas of left internal capsule (a), middle cerebellar peduncle exiting pons into the cerebellum (b), right internal capsule (c), and right cerebellum (d) as compared with age matched healthy group. FA increase in ADHD is shown in areas of left parietal lobe (e), ventricle (f), corpus callosum (g), and right parietal lobe (f). With a more flexible threshold, right occipital lobe was observed (arrow).

Discussion

FA decrease in the bilateral internal capsule, middle cerebellar peduncle, and right cerebellum in adolescent males with ADHD was found as compared with age matched healthy males. These areas are important to the supplementary motor area in planning and execution of motor acts and are consistent with previous studies on ADHD [2, 6]. However, in our study, voxel clusters in left internal capsule are statistically much more than those in right internal capsule. The result might be due to the brain maturation of the subjects when compared with previous study, where ADHD patients were within 7-11 age level. And our ADHD patients were constrained to be male and right handed group. In addition to FA decrease in some brain areas, our results also showed FA increase in several brain areas, left parietal lobe, ventricle, corpus callosum, right parietal lobe, and right occipital lobe. The precise etiology of these differences is unclear nevertheless the results are in good agreement with previous findings [7]. FA increase in ventricle and corpus callosum implicated their volume alternation which might induce severe error in voxelwise analysis in ventricle boundary after T1 template coregistration. Structure studies have also shown the reduced volume in parietal lobe, corpus callosum, ventricle, and occipital lobe [8]. Functional imaging studies via fMRI also found abnormal brain activation patterns during attention tasks and response inhibition in parietal lobe [9]. Linking this study with previous ADHD study [2], developmental manipulation in ADHD is better clarified.

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