A Diffusion Tensor Imaging Study of Adolescents with Disruptive Behavior Disorder

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Introduction: The objective of the present study was to use diffusion tensor imaging (DTI) to find possible white matter micro-structural abnormalities associated with disruptive behavior disorder (DBD) in adolescents. DBD is among the most common psychiatric disorders and is associated with substantial short-term and long-term risks. Despite improvement in psychotherapeutic and evaluation techniques, a substantial number of adolescents fail to respond to treatment, posing threats to the community and to the adolescents themselves. One factor hindering the treatment of adolescents with DBD is the lack of neurobiological knowledge. A neurobiological investigation is important for improving the understanding of the neurological underpinnings to the aggressiveness of this patient group and may suggest directions for medical treatment of adolescents at risk for dangerous behavior.

Methods: 76 adolescents with an average age of 14±1 years old were studied. 36 subjects (male/female=25/11) were diagnosed as DBD patients and 40 were normal controls (male/female=21/19) with no psychiatric disorder. All subjects were screened with the DSM-IV criteria for Conduct Disorder and Oppositional-Defiant Disorder, using the K-SADS diagnostic interview[1]. DBD subjects were also required to have aggression symptoms to people or animals within the past 6 months. The control subjects underwent the same battery of tests and were required to have no psychiatric diagnosis in the past. The MR measurements were conducted on a 1.5T GE MRI scanner. All subjects underwent an MRI exam using a protocol included a high-resolution T_1-weighted 3D whole brain scan and DTI measurements using a custom-made pulse sequence based on single-shot echo-planar imaging acquisition[2]. The main DTI data acquisition parameters were: TR=6s, spatial resolution=1.9×1.9×5 mm^3, matrix size=128×128, 22 contiguous slices parallel to AC-PC line. The distribution of the diffusion-weighting gradients was optimized[2] by minimizing the error propagation from the diffusion-weighted images to the final DTI parameters. The design of DTI schemes consisted of 20 distributed diffusion-weighting gradient with b=1000 s/mm^2 and 3 samplings at b=0. Each DTI scan lasted 138 sec. At least double measurements were performed in each subject. Each subject used an individually fitted bite-bar during the entire MRI scans to reduce motion artifacts. The DTI data were analyzed using an optimization algorithm that takes into consideration the three models simultaneously: 1) eddy current artifacts correction by estimating the whole brain based shearing, scaling, and translation effects; 2) motion correction based on 3D rigid-body motions; 3) second order self-diffusion tensor model. The optimization was performed globally in a least square sense for all the voxels inside the brain simultaneously instead of voxel-by-voxel. After calculating the fractional anisotropy (FA) index, spatial normalization of the FA parameter maps into the Talairch template was performed using SPM2 with the help of the high resolution 3D anatomical scan. For group comparison, the student t-test statistics was applied to the normalized FA image data. The statistical significance was assessed by using a pixel-wise t-score threshold of 3.2 ($p<0.001$) and a minimum in-plane cluster size of 3 inter-connected voxels. For each brain region with significant FA deficit, the average region of interest (ROI) FA value for each subject was also determined.

Results: Fig. 1a shows three cross sections of the normalized average FA data for the normal controls with overlaid t-score results illustrating the brain regions where DBD patients have significantly lowered FA. The displayed cross sections were chosen to reveal the largest ROI where DBD patients have significantly FA reduction in comparison to the normal adolescents. The ROI center is located at (-40, -20, 26) on the Talairch coordinate and was identified as the arcuate fasciculus. The ROI average FA values from individual subjects are shown in fig. 1b. The average FA in the arcuate fasciculus for the DBD group is 0.39 ±0.02, which is about 13% lower than that for the normal group (0.45 ±0.02). In addition, the DBD patients have also less extensive but significant FA deficits in the prefrontal regions.

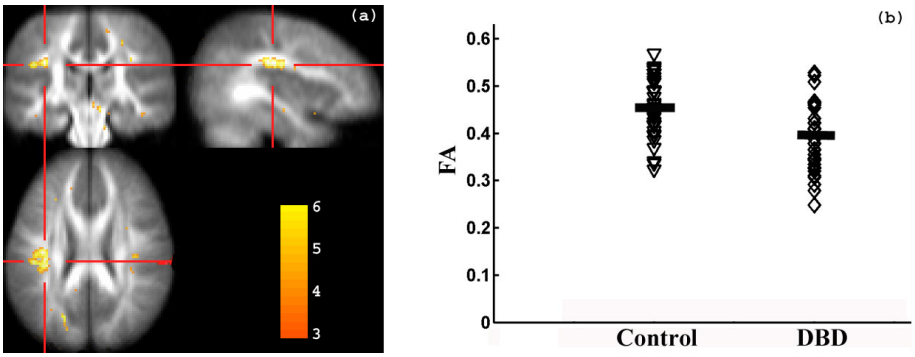

Fig. 1: The student t-test results overlaid on to the spatially normalized average FA data. The cross sections were chosen along the crossing red lines, which locate the largest ROI with significant FA deficit in the DBD patient group (a). The average FA values from individual subjects as evaluated from the ROI at the arcuate fasciculus (b). The lines indicate the group averages for the normal controls and DBD patients.

Discussion: It has been previously shown that DTI is a promising tool to study white matter abnormalities in children with various brain disorders. The more intriguing findings are the relationships between FA deficiencies in specific brain regions and cognitive performances. For example, it was reported [3] that reading disability and FA in the temporo-pariental region is closely correlated. The results from the current study on DBD population indicate significantly reduced FA in the arcuate fasciculus, which is comprised of white matter fibers extending from the temporal lobe to the frontal lobe. The involved pathways play also very important role in normal language capability. Analysis of the neuropsychological results showed that DBD patients perform poorer than the age-matched control on reading and vocabulary capability. This is apparently in line with the findings from Klingberg's study[3]. If vigorous correlations between FA in a specific brain area and cognitive deficits associated with a specific neuropsychiatric disorder can be established, this would provide a neurological basis for diagnosis and treatment. Similar lines of support evidence for this notion can also be found in anatomical MRI and DTI studies of normal subjects at different ages. Both the myelination time course in normal children and demyelination in the elderly were found to be related to the changes in cognitive functions.

References: 1. Li, TQ et al. *Ann NY Scie Acad* 2004, **in press**; 2. Li TQ et al. *Dev Sci*, 2002, **5**:293; 3. Klinberg et al. *Neuron* 2000, **25**:493.