Alteration of White Matter Tract Integrity in Adults with ADHD as Compared to Healthy Adults: A Diffusion Spectrum Imaging Study Using Whole Brain Tract-Based Automatic Analysis

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Purpose:

Attention deficit/hyperactivity disorder (ADHD) lasts to adulthood with recent evidence of widespread brain abnormalities. Diffusion tensor imaging (DTI) studies have revealed disturbed white matter microstructure integrity in several brain regions in ADHD, such as the frontostriatal circuit, cingulum, superior longitudinal fasciculus, inferior longitudinal fasciculus, corona radiata, corticospinal tracts, etc [1, 2]. As the first study to examine the microstructure integrity using diffusion spectrum imaging (DSI) in adults with ADHD, this study aimed to identify the fiber tracts which can distinguish adults with ADHD and healthy adults.

Methods:

Forty-seven adults with ADHD and forty-eight healthy adults received psychiatric and DSI assessments. After acquisition of the DSI, whole brain tractography was reconstructed by tract-based automatic analysis (TBAA). The procedure of TBAA method was briefly described as follows. 1) Study subjects were coregistered to create a study specific template (SST) using large deformation diffeomorphic metric mapping (LDDMM) [3]. 2) The SST was coregistered to the DSI template. 3) Sampling coordinates of 117 tracts were transformed from the DSI template to individual DSI datasets via the transformation matrix between DSI template and SST as well as the transformation between SST and individual DSI. 4) Generalized fractional anisotropy (GFA) values were sampled in the native DSI space using the transformed sampling coordinates and a 2D array of GFA profiles, named connectogram, was created for each subject. A threshold free cluster weighted (TFCW) method was used following Smith's approach [4] to estimate weighted scores ($S(\mathrm{p}) = \sum_{\mathrm{h=h_0}}^{\mathrm{h_5}} \mathrm{e_p}(\mathrm{h})$, where e_p is the cluster extent level which survives at the given threshold h at step p) of effect size of each step between two groups. A 99% cut-point of the histogram of TFCW scores was then estimated to determine the most different clusters between these two groups. The participants also reported on ADHD symptoms and received the Conner's continuous performance test (CCPT). We also conducted correlation and regression analyses to investigate the relationship between the tracts with significant differences and attention performance assessed by CCPT indexes.

Results:

According to the 2D array TFCW score map, the most significantly (>99% cut-point) different clusters between healthy adults and adults with ADHD were determined, mainly located in the fornix, corpus callosum, frontostriatal tracts, and thalamocortical tracts (Figure 1). Adults with ADHD performed worse in focus attention, sustained attention, cognitive inhibition, and vigilance as assessed by the CCPT. There were different patterns of correlations of the microstructural property of the fiber tracts with CCPT performance between adults with ADHD and healthy adults. None of the tracts were correlated with the CCPT indexes in adults with ADHD while some of these tracts were significantly correlated with CCPT indexes in healthy adults. Furthermore, the tracts could only predict the CCPT indexes in healthy adults rather than adults with ADHD.

Conclusions:

Using the proposed TBAA method to assess the white matter microstructure over the whole brain, this work demonstrated altered microstructural integrity in 13 tracts located in the fornix, corpus callosum, frontostriatal tracts, and thalamocortical tracts (Figure 2). These results implied the disturbance of the fronto-striato-thalamic circuit in adults with ADHD. Moreover, our findings also suggested markedly different neural correlates for attention performance, demonstrated by lack of correlations between fronto-striato-thalamic circuit integrity and CCPT indexes, in adults with ADHD from healthy adults.

References:

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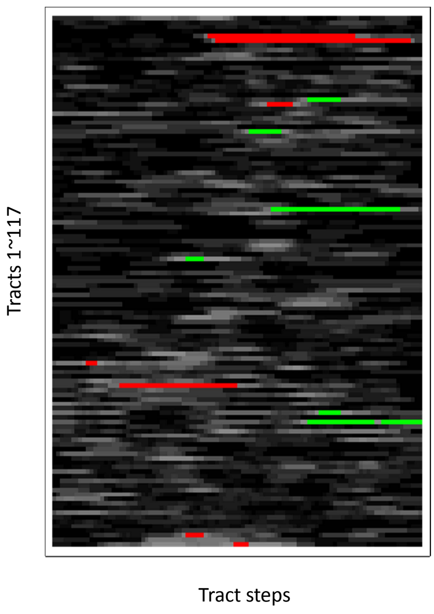

Figure 1. Comparison of GFA values, red means control group > ADHD group, and green means ADHD group > control group.

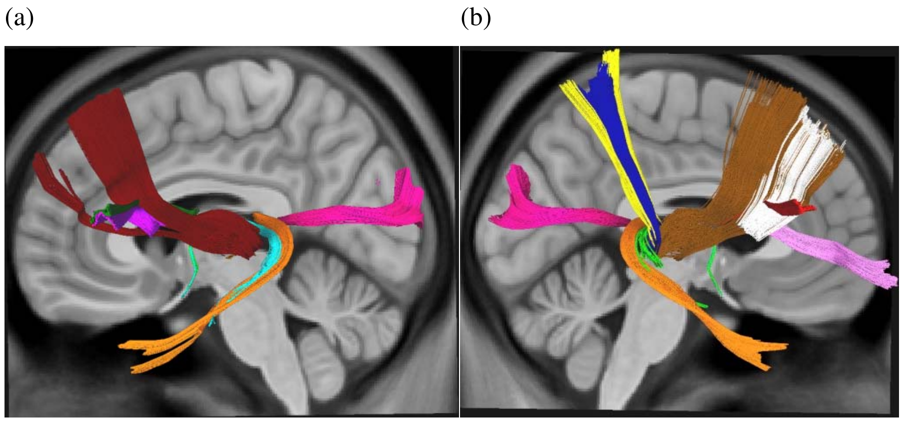

Figure 2. (a) Left side view of the tracts. (b) Right side view of the tracts. This figure illustrates the locations of the 13 tracts with significant differences between adults with ADHD from healthy ones. Left fornix (light blue), right fornix (light green), left caudate to inferior frontal gyrus-opercular part (dark green), right caudate to inferior frontal gyrus-opercular part (red), right caudate to middle frontal gyrus (light pink), left putamen to inferior frontal gyrus-opercular part (purple), right putamen to superior frontal gyrus (white), left thalamus to superior frontal gyrus (dark red), right thalamus to superior frontal gyrus-orbital part (brown),right thalamus to inferior parietal gyrus (dark blue), right thalamus to superior parietal gyrus (yellow), corpus callosum to bilateral cuneus (pink), and corpus callosum to bilateral temporal pole (orange).