Frontal White Matter Microstructure Predicts Response Control in Children With ADHD

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Abstract

A core feature of Attention-Deficit/ Hyperactivity Disorder (ADHD) is impaired response control. Recent fMRI evidence has suggested that, in contrast to typically developing (TD) children, those with ADHD may rely on prefrontal, rather than premotor regions for motor response control[1].

In this study we used Diffusion Tensor Imaging (DTI) to assess the microstructural integrity of white matter regions related to response control. We found that white matter integrity associated with prefrontal regions is correlated with response control in children with ADHD, but not among TD children.

Background

ADHD

Impaired or altered frontal circuits are thought to play a key role in the pathophysiology of Attention-Deficit/Hyperactivity Disorder (ADHD), a core feature of which is impared reponse control. Studies examining the neurologic basis of response control have suggested that children with ADHD recruit frontal regions differently than controls during tests of motor/cognitive control. This suggests that there may be a "hard-wired," anatomical basis for anomalous, and perhaps compensatory pattern of neural activity. fMRI studies of response control[1] suggest that, in contrast to typically developing children, those with ADHD may rely more on prefrontal, rather than premotor regions during motor response control.

Reaction Time Variability

In studies of motor and cognitive control, the trial-to-trial Intra-Subject Varability (ISV) in Reaction Time (RT) has been shown to be a sensitive measure of response control. Subjects with poor executive control show a wide variation in RT over a testing session, indicating difficulty in maintaining vigilance and sustained attention[2].

Diffusion Tensor Imaging (DTI)

DTI is an imaging methodology that is sensitive to the sub-voxel micostructure of white matter. Underdeveloped or dysmyelinated white matter commonly results in lower Fraction Anisotropy (FA) and higher Radial Diffusivity (RD)

We hypothesize that greater white matter integrity related to prefrontal regions will be associated with lower ISV among children with ADHD, but not among TD children.

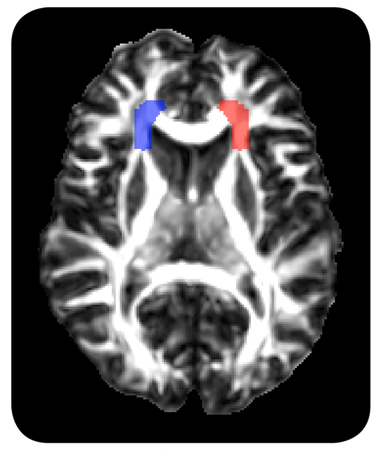
Methods

Participants

Data was collected on 24 children with ADHD (11 female, 13 male) and 35 typically-developing controls (17 female, 18 male) between the ages of 8 and 13 y/o (average 10.4). The two groups were matched on age, sex, IQ and handedness.

Imaging

DTI was collected using a standard imaging protocol[3]. A semi-automated atlas-based procedure[4] was used to parcellate DTI images into relevant regions of interest. Based on our a priori hypothesis, diffusion indices in the Anterior Corona Radiata (ACR) region from the JHU-ICBM atlas[3] were examined. The ACR region includes interhermispheric white matter connections, and connections between the prefrontal cortex and striatum.



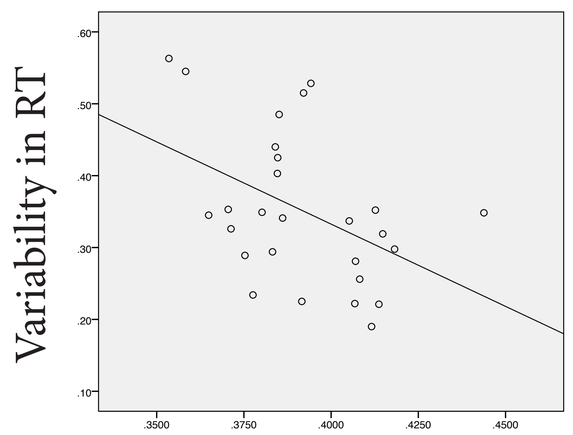
ACR atlas regions

Behavioral Measures

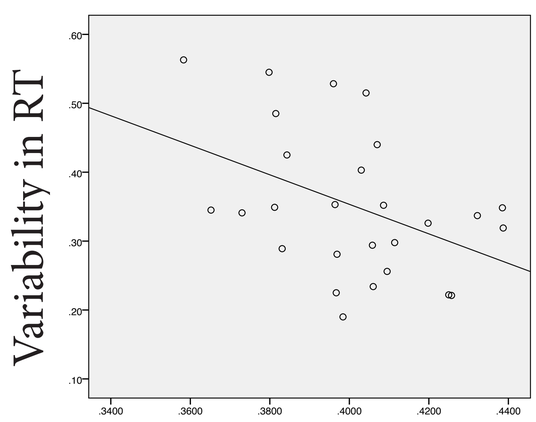
ISV in RT was assessed using a simple Go-No go task with a stimulus duration of 300ms and an inter-stimulus interval of 2s, with 4:1 ratio of "Go" to "No-go" trials. Total duration was 8min. ISV was calculated as the coefficent of variation (the mean divided by the standard deviation) of the RT within subjects.

Results

Among subjects with ADHD, Fractional Anisotropy (FA) in both the left and right Anterior Corona Radiata (ACR) inversely correlated with ISV (r=-0.451, p=0.018 for the left ACR; r=-0.426, p=0.027 for the right ACR).



FA in the left ACR



FA in the right ACR

Radial Diffusivity (RD) was positively correlated with ISV in the left (r=0.415, p=0.031) and right (r=0.522, p=0.005) ACR. ISV was not significantly correlated with any of the diffusion indices in the left nor the right ACR among the typically developing control participants.

Discussion

Consistent with our hypothesis, we found that response control was correlated with the integrity of prefrontal white matter connections in children with ADHD, but not among TD children. FA is negatively correlated with ISV in the ACR – so that higher FA (reflecting greater white matter integrity) is associated with lower ISV, indicating more effective, consistent response control. Additionally, greater ISV is correlated with greater RD, potentially indicating a lesser degree of myelination and/or more permeable axonal membranes in ADHD subjects with poor response control. These findings support previous studies suggesting greater prefrontal involvement in motor response control in ADHD.

References

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