Stimulant treatment history predicts frontal-striatal structural connectivity in adolescents with attention-deficit/hyperactivity disorder.

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Abstract

Diffusion tensor imaging (DTI) has revealed white matter abnormalities in individuals with attention-deficit/hyperactivity disorder (ADHD). Stimulant treatment may affect such abnormalities. The current study investigated associations between long-term stimulant treatment and white matter integrity within the frontal-striatal and mesolimbic pathways, in a large sample of children, adolescents and young adults with ADHD. Participants with ADHD (N=172; mean age 17, range 9-26) underwent diffusion-weighted MRI scanning, along with an age- and gendermatched group of 96 control participants. Five study-specific white matter tract masks (orbitofrontal-striatal, orbitofrontal-amygdalar, amygdalar-striatal, dorsolateral-prefrontal-striatal and medial-prefrontal-striatal) were created. First we analyzed case-control differences in fractional anisotropy (FA) and mean diffusivity (MD) within each tract. Second, FA and MD in each tract was predicted from cumulative stimulant intake within the ADHD group. After correction for multiple testing, participants with ADHD showed reduced FA in the orbitofrontal-striatal pathway (p=0.010, effect size=0.269). Within the ADHD group, higher cumulative stimulant intake was associated with lower MD in the same pathway (p=0.011, effect size=-0.164), but not with FA. The association between stimulant treatment and orbitofrontal-striatal MD was of modest effect size. It fell short of significance after adding ADHD severity or ADHD type to the model (p=0.036 and p=0.094, respectively), while the effect size changed little. Our findings are compatible with stimulant treatment enhancing orbitofrontal-striatal white matter connectivity, and emphasize the importance of the orbitofrontal cortex and its connections in ADHD. Longitudinal studies including a drug-naïve baseline assessment are needed to distinguish between-subject variability in ADHD severity from treatment effects.