Impact of a Common Genetic Variation Associated With Putamen Volume on Neural Mechanisms of Attention-Deficit/Hyperactivity Disorder

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Abstract

Objective
In a recent genome-wide association study of subcortical brain volumes, we identified common genetic variation at rs945270 as having the strongest effect on putamen volume, a brain measure linked to familial risk for attention-deficit/hyperactivity disorder (ADHD). To determine whether rs945270 is a genetic determinant of ADHD, we now explore its impacts on ADHD-related symptoms and neural mechanisms of ADHD, such as response inhibition and reward sensitivity.

Method
We used a large population sample of 1,834 14-year-old adolescents to test the effects of rs945270 on (i) ADHD symptoms accessed through the Strengths and Difficulties Questionnaire (SDQ) and (ii) region-of-interest (ROI) analyses of putamen activation by functional magnetic resonance imaging (fMRI) using the stop signal (SST) and monetary incentive delay (MID) tasks, assessing response inhibition and reward sensitivity, respectively.

Results
We found a significant link between rs945270 and ADHD symptom scores, with the C-allele associated with lower symptom scores, most notably hyperactivity. We also observed sex-specific effects of this variant on the brain. In boys, the C-allele was associated with lower putamen activity during successful response inhibition, a brain response that was not associated with ADHD symptoms. In girls, putamen activation during reward anticipation increased with the number of C-alleles, most significantly in the right putamen. Remarkably, right putamen activation during reward anticipation tended to negatively correlate with ADHD symptoms.

Conclusion
Our results indicate that rs945270 may contribute to the genetic risk of ADHD partly through its effects on hyperactivity and reward processing in girls.