

Genetic variant for behavioral regulation factor of executive function and its possible brain mechanism in attention deficit hyperactivity disorder

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Abstract

As a childhood-onset psychiatric disorder, attention deficit hyperactivity disorder (ADHD) is complicated by phenotypic and genetic heterogeneity. Lifelong executive function deficits in ADHD are described in many literatures and have been proposed as endophenotypes of ADHD. However, its genetic basis is still elusive. In this study, we performed a genome-wide association study of executive function, rated with Behavioral Rating Inventory of Executive Function (BRIEF), in ADHD children. We identified one significant variant (rs852004, $P = 2.51e-08$) for the overall score of BRIEF. The association analyses for each component of executive function found this locus was more associated with inhibit and monitor components. Further principle component analysis and confirmatory factor analysis provided an ADHD-specific executive function pattern including inhibit and monitor factors. SNP rs852004 was mainly associated with the Behavioral Regulation factor. Meanwhile, we found the significant locus was associated with ADHD symptom. The Behavioral Regulation factor mediated its effect on ADHD symptom. Functional magnetic resonance imaging (fMRI) analyses further showed evidence that this variant affected the activity of inhibition control related brain regions. It provided new insights for the genetic basis of executive function in ADHD.