Effects of the 2-Repeat Allele of the DRD4 Gene on Neural Networks Associated With the Prefrontal Cortex in Children With ADHD


Abstract

Objective: Genetic variation, especially polymorphism of the dopamine D4 receptor gene (DRD4), has been linked to deficits in self-regulation and executive functions and to attention deficit hyperactivity disorder (ADHD), and is related to the structural and functional integrity of the default mode network (DMN), the executive control network (ECN) and the sensorimotor network (SMN). The aim of this study was to explore the effects of the 2-repeat allele of the DRD4 gene on brain network connectivity and behaviors in children with ADHD.

Methods: Using independent component analysis (ICA) and dimension analyses, we examined resting-state functional magnetic resonance imaging (fMRI) data obtained from 52 Asian medicine-naive children with ADHD (33 2-repeat absent and 19 2-repeat present).

Results: We found that individuals with 2-repeat absent demonstrated increased within-network connectivity in the right precuneus of the DMN, the right middle frontal gyrus (MFG) of the SMN compared with individuals with 2-repeat present. Within the ECN, 2-repeat absent showed decreased within-network connectivity in the left inferior frontal gyrus (IFG) and the left anterior cingulate cortex. A deeper study found that connectivity strength of the left IFG was directly proportional to the Stroop reaction time in 2-repeat absent group, and as well as the right MFG in 2-repeat present group.

Conclusion: Polymorphisms of the DRD4 gene, specifically 2-repeat allele, had effects on the ECN, the SMN and the DMN, especially in the prefrontal cortex (PFC) circles. ADHD children with DRD4 2-repeat allele have aberrant resting-state within-network connectivity patterns in the left IFG and the right MFG related to dysfunction in inattention symptom. This study provided novel insights into the neural mechanisms underlying the effects of DRD4 2-repeat allele on ADHD.