DLGAP1 and NMDA receptor-associated postsynaptic density protein genes influence executive function in attention deficit hyperactivity disorder.

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Abstract

OBJECTIVE:
To explore the association of DLGAP1 gene with executive function (EF) in attention deficit hyperactivity disorder (ADHD) children.

METHOD:
A total of 763 ADHD children and 140 healthy controls were enrolled. The difference of EF between ADHD and controls was analyzed using the analysis of covariance (ANCOVA), with IQ, sex, and age as covariates. Both the associations of SNPs with EF and three symptom traits of ADHD were conducted using an additive linear regression model by PLINK with the same covariates as ANCOVA.

RESULTS:
Compared with controls, children with ADHD showed poorer cognitive flexibility and inhibition. Two SNPs (rs2049161, p-value = 5.08e-7, adjusted p-value = 1.63e-4, rs16946051, p-value = 5.18e-7, adjusted p-value = 1.66e-4) survived multiple tests in Trail Making Test. Both SNPs also showed association with TOH (rs2049161, p = 6.82e-4, rs16946051, p = 7.91e-4). Set-based analysis for gene DLGAP1 and its functional pathway DLGAP1-DLG4-NMDA showed they were associated with cognitive flexibility at both gene (p = .0057) and pathway level (p = .0321). Furthermore, the gene and pathway also showed association with ADHD symptom score. The associated SNPs and their LD proxies were related to the expression of DLGAPI in medulla and frontal cortex.

CONCLUSION:
Children with ADHD showed deficit in EF, especially, cognitive flexibility and inhibition. DLGAP1 was associated with cognitive flexibility and plan, and the role of DLGAP1 might be implemented through the complex of DLGAPI-DLG4-NMDA.