DAT1 methylation is associated with methylphenidate response on oppositional and hyperactive-impulsive symptoms in children and adolescents with ADHD.


Abstract

OBJECTIVES:
To examine the association of the DNA methylation of DAT1 and DRD4 gene with methylphenidate (MPH) response in attention deficit hyperactivity disorder (ADHD).

METHODS:
One hundred and eleven DSM-IV defined ADHD Chinese Han children were recruited. Inattention, hyperactivity-impulsivity and oppositional symptoms were evaluated by the Swanson, Nolan and Pelham-IV-parent rating scale (SNAP-IV-P) at baseline and 6 weeks after MPH treatment. DNA methylation of CpG sites in the promoter sequences of DAT1 and DRD4 was examined for association with treatment response.

RESULTS:
Greater improvement on the SNAP-IV-P total score and percentage change from baseline score were both significantly correlated with DAT1 methylation (rho = -0.222, P = .019 and rho = -0.203, P = .032, respectively). A secondary analysis demonstrated that the effect of DAT1 methylation on symptom response was primarily related to the percentage change in oppositional symptoms (rho = -0.242; P = .012), with a smaller significant effect on hyperactivity-impulsivity (rho = -0.192; P = .045). No significant correlation was found between the treatment effect on inattention and DAT1 methylation (rho = -0.101; P = .292). No significant correlation was observed between mean DRD4 methylation and measures of treatment outcome or baseline symptoms.

CONCLUSIONS:
Our findings provide initial evidence for the involvement of the epigenetic alterations of DAT1 in modulating the response to MPH treatment in ADHD, primarily on oppositional and hyperactive-impulsive symptoms.