Effects of Interaction Between DRD4 Methylation and Prenatal Maternal Stress on Methylphenidate-Induced Changes in Continuous Performance Test Performance in Youth with Attention-Deficit/Hyperactivity Disorder

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Abstract

OBJECTIVES:
Environmental factors may interact with genetic factors via the epigenetic process, and this interaction can contribute to inter-individual variability in the treatment response. The purpose of this study was to investigate the interaction effects between dopamine receptor D4 (DRD4) methylation and prenatal maternal stress on the methylphenidate (MPH) response of youth with attention-deficit/hyperactivity disorder (ADHD).

METHODS:
This study was an 8-week open-label trial of MPH that included 74 ADHD youth. We investigated the associations between MPH treatment response, which was defined as a score ≤2 on the Clinical Global Impressions-Improvement (CGI-I) scale, and the methylation of 28 cytosine-guanine dinucleotide (CpG) sites of DRD4. Additionally, the interaction effects between DRD4 methylation and prenatal maternal stress on changes in Continuous Performance Test (CPT) scores after MPH treatment were investigated.

RESULTS:
Although there were no significant sites that showed significant association with treatment response, there was a significant interaction effect of the methylation of CpG7 and prenatal maternal stress on changes in omission errors of the CPT following treatment (p = 0.0001).

CONCLUSIONS:
The present findings indicate that the interaction between methylation of CpG7 of DRD4 and prenatal maternal stress may be predictive of the treatment response to MPH in youth with ADHD.