Multiple epigenetic factors predict the Attention Deficit/Hyperactivity Disorder among the Chinese Han children

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Abstract
Attention deficit/hyperactivity disorder (ADHD) is one of the most common psychiatric disorders of childhood. Despite its prevalence, the critical factors involved in its development remain to be identified. It was recently suggested that epigenetic mechanisms probably contribute to the etiology of ADHD. The present study was designed to examine the associations of epigenetic markers with ADHD among Chinese Han children, aiming to establish the prediction model for this syndrome from the epigenetic perspective. We conducted a pair-matching case–control study, and the ADHD children were systematically evaluated via structured diagnostic interviews, including caregiver interviews, based on the Diagnostic and Statistical Manual of Mental Disorders, 4th edition, revised criteria (DSM-IV-R). The expression levels of risk genes DAT1, DRD4, DRD5, as well as their promoter methylation, were determined respectively, followed by the expression profiles of histone-modifying genes p300, MYST4, HDAC1, MeCP2. The multivariate logistic regressions were performed to establish ADHD prediction models. All of the seven genes tested were identified as risk factors for ADHD. The methylation of one critical CpG site located upstream of DRD4 was shown to affect its transcription, suggesting a role in ADHD’s development. Aberrant DNA methylation and histone acetylation were indicated in ADHD patients. In addition, a prediction model was established using the combination of p300, MYST4 and HDAC1, with the accuracy of 0.9338. This is, to our knowledge, the first study to clearly demonstrate the associations between epigenetic markers and ADHD, shedding light on the preliminary diagnosis and etiological studies of this widespread disorder.