Abstract

The dopamine D4 receptor (DRD4) gene is implicated in the etiology of attention-deficit/ hyperactivity disorder (ADHD). The most established association is the 7-repeat (7R) allele of the variable number tandem repeat (VNTR) polymorphism on exon III of the DRD4 gene. Yet, this finding has not been replicated in the Chinese population given low prevalence of 7R allele in this population. Instead, the 2-repeat (2R) allele is found to be of high prevalence. Research suggests the 2R allele as an evolutionary derivative of the 7R allele, which shows similar blunted responses to dopamine. In a case-control study, Leung and colleagues (2005) found a 1.65 increase in prevalence of 2R alleles among Chinese ADHD children, suggesting its possible role in ADHD. Extending from these results, this study used a family-based approach to test the association and preferential transmission of the 2R allele and all non-4R alleles. Thirty-three Han Chinese boys with confirmed ADHD diagnosis and their biological parents were genotyped. Results show a significant association between the 2R and all non-4R alleles with ADHD (Haplotype Relative Risk (HRR): χ^2 (1, N=132) = 3.15, $p_{\text{one-tailed}}$ = .038, OR = 2.04 for 2R, and χ^2 (1, N=132) = 3.59, *df* =1, $p_{\text{one-tailed}}$ = .029, OR = 2.07 for non-4R). There is also a preferential transmission of the 2R allele and all non-4R alleles from parents to ADHD probands (Transmission Disequilibrium Test (TDT): McNemar's χ^2 (1, N=66) = 2.78, *df* =1, $p_{\text{one-tailed}}$ = 0.048, OR = 2.29 for 2R, McNemar's χ^2 (1, N=66) = 3.38, $p_{\text{one-tailed}}$ = 0.032, OR = 2.43 for non-4R). These findings support that the 2R allele plays a role in ADHD in Chinese population, and the hypothesis that any variants differing from the conserved ancestral 4R allele, which may potentially alter biochemistry/phenotype of the receptor, are associated with ADHD. The present findings, obtained from a small sample size, should be replicated. Further

research that focuses on potential biochemical impact of rare genetic variants among VNTR alleles should be explored.