Glutamatergic copy number variants and their role in attention-deficit/hyperactivity disorder.


Abstract
Attention-Deficit/Hyperactivity Disorder (ADHD) is a common neurodevelopmental disorder with a strong genetic component. The glutamate metabotropic receptor genes (GRMs) have been considered potential candidates for ADHD susceptibility. The aim of the present study was to investigate if copy number variants (CNVs) in GRM1, GRM5, and GRM8 genes are overrepresented in ADHD subjects. A total of 1038 individuals with ADHD and 1057 subjects without this disorder were investigated. No significant difference in the total number of CNVs was found comparing the entire ADHD sample and the population sample without ADHD (P = 0.326, OR = 1.112, 95% CI = 0.762-1.624). The presence of CNVs was associated with lower intelligence quotient (IQ) scores in ADHD samples (P = 0.026, OR = 1.824, 95% CI = 1.066-3.121) but not in the sample of individuals without ADHD. CNVs in GRM5 were associated with presence of anxiety disorders in ADHD cases (P = 0.002, OR = 3.915, 95% CI = 1.631-9.402), but not in individuals without ADHD. Taken together, our results suggest a role for glutamate in ADHD as CNVs in the glutamatergic genes investigated herein were associated with cognitive and clinical characteristics of ADHD individuals.