GAD1 gene polymorphisms are associated with hyperactivity in Attention-Deficit/Hyperactivity Disorder.


Abstract

Attention-Deficit/Hyperactivity Disorder (ADHD) is one of the most common neurodevelopmental disorders of childhood. Recent studies suggest a role for γ-aminobutyric acid (GABA) on ADHD hyperactive/impulsive symptoms due to behavioral disinhibition resulting from inappropriate modulation of both glutamatergic and GABAergic signaling. The glutamic acid decarboxylase (GAD1) gene encodes a key enzyme of GABA biosynthesis. The aim of the present study was to investigate the possible influence of GAD1 SNPs rs3749034 and rs11542313 on ADHD susceptibility. The clinical sample consisted of 547 families with ADHD probands recruited at the ADHD Outpatient Clinics from Hospital de Clínicas de Porto Alegre. Hyperactive/impulsive symptoms were evaluated based on parent reports from the Swanson, Nolan, and Pelham Scale-version IV (SNAP-IV). The C allele of rs11542313 was significantly overtransmitted from parents to ADHD probands (P = 0.02). Hyperactive/impulsive score was higher in rs3749034G allele (P = 0.005, Cohen's D = 0.19) and rs11542313C allele (P = 0.03; Cohen's D = 0.16) carriers. GAD1 haplotypes were also associated with higher hyperactive/impulsive scores in ADHD youths (global P-value = 0.01). In the specific haplotype test, the GC haplotype was the one with the highest hyperactive/impulsive scores (P = 0.03). Our results suggest that the GAD1 gene is associated with ADHD susceptibility, contributing particularly to the hyperactive/impulsive symptom domain.