Abstract

Frequent non-pathogenic genetic variants may act as moderators of phenotypic severity for complex disorders such as autism spectrum disorder (ASD). We previously identified polymorphisms affecting mRNA expression of candidate genes, including tryptophan hydroxylase 2 (TPH2), dopamine beta hydroxylase (DBH), and dopamine transporter (DAT, SLC6A3). We compare genotypes and (1) clinical response to atomoxetine, (2) scores from the Autism Diagnostic Interview-Revised (ADI-R), and (3) severity of Attention Deficit Hyperactivity Disorder (ADHD) symptoms in a cohort of patients with ASD from multiple study sites. There was no association between CYP2D6 metabolizer status and atomoxetine response. TPH2 rs7305115 genotype was associated with ADI-R Restrictive/Repetitive Behavior score (p = 0.03). DBH rs1611115 genotype was associated with ADI-R Social score (p = 0.002), and Restrictive/Repetitive Behavior score (p = 0.04). The DAT intron 8 5/6 repeat was associated with ADHD symptoms (ABC Hyperactivity p = 0.01 and SNAP ADHD p = 0.03), replicating a previous finding. We find associations between ASD phenotypes and regulatory variants in catecholamine biosynthesis genes. This work may help guide future genetics studies related to ASD.