Meta-Analysis of Tourette Syndrome and Attention Deficit Hyperactivity Disorder Provides Support for a Shared Genetic Basis

Fotis Tsetsos, Shanmukha S. Padmanabhuni, John Alexander, Iordanis Karagiannidis, Margaritis Tsifintaris, Apostolia Topaloudi, Dimitrios Mantzaris, Marianthi Georgitsi, Petros Drineas, Peristera Paschou

DOI: http://dx.doi.org/10.3389/fnins.2016.00340

Gilles de la Tourette Syndrome (TS) is a childhood onset neurodevelopmental disorder, characterized phenotypically by the presence of multiple motor and vocal tics. It is often accompanied by multiple psychiatric comorbidities, with Attention Deficit/Hyperactivity Disorder (ADHD) among the most common. The extensive co-occurrence of the two disorders suggests a shared genetic background. A major step toward the elucidation of the genetic architecture of TS was undertaken by the first TS Genome-wide Association Study (GWAS) reporting 552 SNPs that were moderately associated with TS (p < 1E-3). Similarly, initial ADHD GWAS attempts and meta-analysis were not able to produce genome-wide significant findings, but have provided insight to the genetic basis of the disorder. Here, we examine the common genetic background of the two neuropsychiatric phenotypes, by meta-analyzing the 552 top hits in the TS GWAS with the results of ADHD first GWASs. We identify 19 significant SNPs, with the top four implicated genes being TBC1D7, GUCY1A3, RAP1GDS1, and CHST11. TBC1D7 harbors the top scoring SNP, rs1866863 (p:3.23E-07), located in a regulatory region downstream of the gene, and the third best-scoring SNP, rs2458304 (p:2.54E-06), located within an intron of the gene. Both variants were in linkage disequilibrium with eQTL rs499818, indicating a role in the expression levels of the gene. TBC1D7 is the third subunit of the TSC1/TSC2 complex, an inhibitor of the mTOR signaling pathway, with a central role in cell growth and autophagy. The top genes implicated by our study indicate a complex and intricate interplay between them, warranting further investigation into a possibly shared etiological mechanism for TS and ADHD.