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Genetic underpinnings of Tourette syndrome and obsessive-compulsive disorder

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Two papers reporting genetic factors associated with Tourette syndrome and obsessive-compulsive disorder are published in this week’s Molecular Psychiatry help provide a more complete understanding of the genetics behind these disorders. Although both neuropsychiatric disorders are highly heritable, definitive susceptibility genes have remained elusive. These are the first genome wide association studies (GWAS) performed for either disease.
Tourette syndrome is a chronic, childhood-onset neurodevelopmental disorder characterized by multiple motor tics and at least one vocal tic. Analyzing GWAS data for nearly 1500 TS cases and 5000 ancestry-matched controls, Jeremiah M. Scharf and colleagues identified a signal within the COL27A1 gene. This gene encodes a protein primarily expressed in cartilage, but also in the cerebellum, a brain region involved in motor control. The authors also observed an enrichment of genetic variants that regulate gene expression in the frontal cortex, consistent with the hypothesis that TS arises from developmental abnormalities in the circuitry of this region.

Obsessive-compulsive disorder (OCD) is defined by the presence of obsessions and compulsions that are distressing, time consuming or significantly impairing. In their search for genetic factors associated with OCD, S. Evelyn Stewart and colleagues found a strong signal close to the BTBD3 gene. BTBD3 is highly expressed in the brain during childhood and adolescence, when OCD frequently emerges. Interestingly, BTBD3 is related to a gene called BTBD9, which has been implicated in Tourette syndrome. Other top hits included several genes involved in glutamatergic signaling.

Although no genetic variant was found to be associated with either disease at a genome-wide significant level, the studies represent a major step in understanding the underlying genetic architecture of the two disorders. The current results will also facilitate studies of the genetic relationships between Tourette syndrome and OCD which often co-occur in patients, and contribute to the goal of identifying the biological pathways underlying these common neurodevelopmental conditions.

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