

Major genetic study confirms that many genes contribute to risk for Tourette's syndrome

March 1 2019



Credit: CC0 Public Domain

A meta-analysis of multiple studies into the genetic background of Tourette's syndrome (TS)—a neurodevelopmental disorder characterized by chronic involuntary motor and vocal tics—finds that variants in hundreds of genes, working in combination, contribute to the development of the syndrome and suggests that Tourette's is part of a continuous spectrum of tic disorders, ranging from mild, sometimes

transient tics to severe cases that can include psychiatric symptoms.

The report from an international team—led by investigators at Massachusetts General Hospital (MGH), the University of California at Los Angeles (UCLA), the University of Florida and Purdue University—also describes finding that individuals with more TS-associated variants are more severely affected, raising the possibility of predicting whether children with mild tic disorders will develop full-blown TS in the future.

"This study confirms that, for most patients, the underlying genetic basis of Tourette's syndrome is polygenic—that is, many [genes](#) working together to cause a disease," says Jeremiah Scharf, MD, Ph.D., of the Psychiatric & Neurodevelopmental Genetics Unit in the MGH Departments of Neurology and Psychiatry and the MGH Center for Genomic Medicine, co-senior and corresponding author of the report in the *American Journal of Psychiatry*. "This means that most people who have TS do not carry a single inactive gene but instead inherit hundreds of small DNA changes from both parents that combine to cause TS. This finding has multiple important implications, both scientifically as well as for patient advocacy and understanding of their symptoms."

While it is well known that most of the risk for TS is inherited, the few risk-associated gene variants that have been identified account for only a small percentage of cases. Many common gene variants acting in aggregate have been associated with increased disease risk, suggesting that large-scale, [genome-wide association studies](#) (GWAS) could clarify which potential risk genes do and which do not actually contribute the development of TS.

To achieve the largest possible data set, the investigators combined results from the only published GWAS study with new data from three international genetics consortia—the Tourette Association of America

International Consortium for Genetics, the Gilles de la Tourette GWAS Replication Initiative, and the Tourette International Collaborative Genetics Study—for a total of 4,819 individuals with TS and almost 9,500 unaffected control volunteers. A secondary analysis of data from the Iceland-based deCode genetics study compared more than 700 individuals with TS to more than 450 with other tic disorders and more than 6,000 controls.

The results of this analysis identified multiple gene variants—only one of which met genome-wide significance—associated with increased TS risk. Use of an aggregated polygenic risk score based on the identified risk variants to analyze every individual in the study—both with and without TS, as well as individuals with less severe tic disorders—confirmed that those inheriting more risk variants had more severe symptoms. However, the presence of TS-associated variants was not restricted to those with tic disorders.

"Every one of the variants that contribute to developing TS is present in a significant proportion of the general population, which means that most people with TS do not have 'broken' or 'mutated' genes," says Scharf. "The movements and thoughts that individuals with TS have are the same ones that all of us have, but just to a greater degree. As doctors and researchers, we know that there is nothing that separates those with TS from other children and adults, and now we've shown this is actually true on a genetic level."

The development of a polygenic risk score for TS raises the future possibility of predicting whether the symptoms of children who develop tics, which typically worsen in early adolescence, will continue to be severe or will resolve as the child matures, something that is not currently possible. Future studies enrolling even larger groups of participants should improve this potential predictive ability.

"This study is an example of the great impact of collaborative research in order to be able to finally understand the cause of complex disease" says Peristera Paschou, Ph.D., associate professor in the Department of Biological Sciences at Purdue University and one of the co-senior authors. "As a next step, we are now expanding analysis to an even larger sample of close to 12,000 patients with TS, again made possible thanks to widespread international collaboration. We hope that this will yield even higher power to further clarify the genetics of TS."

Co-lead author Jae Hoon Sul, Ph.D., of the Jane and Terry Semel Institute for Neuroscience and Human Behavior at UCLA, says, "We need larger sample sizes to pinpoint specific genes that cause TS, and there is an ongoing collaborative effort across the U.S., Canada and Europe to increase numbers to tens of thousands of individuals with TS, which will definitely improve our chance of finding more genes related to TS. Only by all of us working collaboratively can we reach that important goal."

Scharf, an assistant professor of Neurology at Harvard Medical School, notes that regions of the brain most likely to be affected by the risk-associated variants in the [polygenic risk score](#) are parts of a circuit involved in motor learning, planning and selection of appropriate movements or actions, areas previously suggested to contribute to TS and other tic disorders. "Studies of other polygenic disorders—both brain and non-brain based—have shown that even if a single gene variant plays only a small role in causing a disorder, every gene may be a candidate for understanding disease mechanisms and finding new treatments. We hope that by continuing to find new TS genes, we will be able to find new treatments that are more effective without causing the significant side effects associated with existing therapies."

More information: *American Journal of Psychiatry* (2019). [DOI: 10.1176/appi.ajp.2018.18070857](https://doi.org/10.1176/appi.ajp.2018.18070857)

Provided by Massachusetts General Hospital

Citation: Major genetic study confirms that many genes contribute to risk for Tourette's syndrome (2019, March 1) retrieved 17 April 2024 from <https://medicalxpress.com/news/2019-03-major-genetic-genes-contribute-tourette.html>

This document is subject to copyright. Apart from any fair dealing for the purpose of private study or research, no part may be reproduced without the written permission. The content is provided for information purposes only.