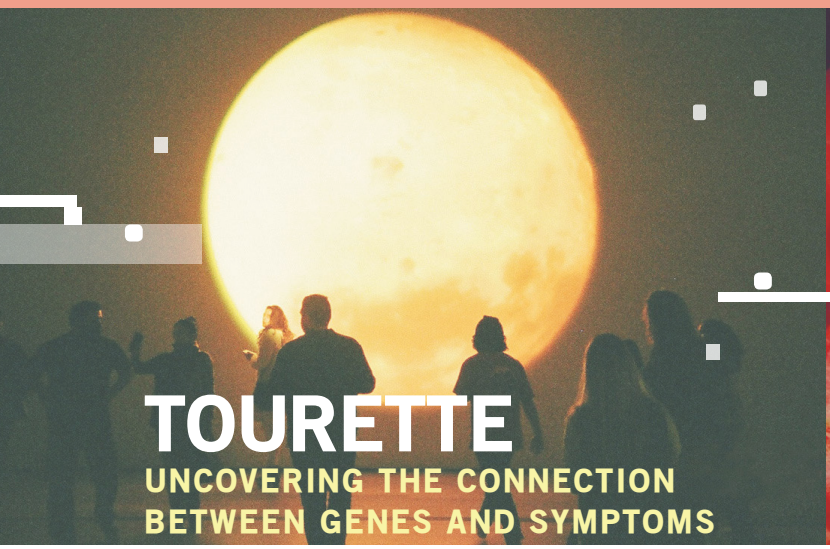

TOURETTE

UNCOVERING THE CONNECTION BETWEEN GENES AND SYMPTOMS

DANIEL RAYNER

Tourette Syndrome (TS) is a common behavioural and neurological disorder characterized by involuntary phonic and motor tics, onsetting primarily between early childhood to adolescence.[1] One common problem facing TS diagnosis is the comorbidity of the syndrome, where similar symptoms are shared amongst different diseases. Comorbidity is prevalent in those affected, with approximately 85% of individuals experiencing additional neuropsychiatric disorders.[1] Common comorbidities include: attention-deficit/hyperactivity disorder, obsessive-compulsive disorder, and autism spectrum disorders.[1,2,3] As a result, TS is considered a model neuropsychiatric disorder and discovery of its etiology may present findings applicable to other psychiatric disorders.[3]

Although there is an association between environmental factors and a greater risk of developing TS, it is primarily a genetic disorder. In fact, Davis and colleagues estimated that heritability for TS is 58%, making it one of the most heritable complex neuropsychiatric disorders.[3,4] Past studies have suggested that dysregulated development and/or the maintenance of parallel cortico-striatal-thalamo-cortical circuits are the main cause of TS and its comorbidities. Despite this lead, identification of TS susceptibility genes has proven to be difficult, with minimal consensus across studies.[3]

In an analysis of genotypes with potential influence on comorbidity, both copy number variations (CNVs) and gene deletions in specific gene loci were found to increase the risk of TS. Genetic and CNV analysis conducted by Huang and colleagues identified two individual, genome-wide, significant loci: CNTN6 duplications and NRXN1 deletions. These genetic variations substantially increased TS risk and were found in approximately 1% of TS patients in the study.[3] In analyzing the genetic etiology of TS, new treatments may be developed for this disorder. Given its many comorbidities, this research also has the potential to improve our understanding of other neuropsychiatric syndromes.

1. Thenganatt MA, Jankovic, J. Recent advancements in understanding and managing tourette syndrome. *F1000Research.* 2016;5:1-10. Available from: doi:10.12688/f1000research.7424.1.
2. Robertson MM. The gilles de la tourette syndrome: The current status. *Arch Dis Child Educ Pract Ed.* 2012; 97(5):166-175. Available from: doi:10.1136/archdischild-2011-300585.
3. Huang AY, Yu D, Davis LK, Sul JH, Tsetsos F, Ramensky V, et al. Rare copy number variants in NRXN1 and CNTN6 increase risk for Tourette syndrome. *Neuron.* 2017;94(6):1101-11. Available from: doi:10.1016/j.neuron.2017.06.010.
4. Davis LK, Yu D, Keenan CL, Gamazon ER, Konkashbaev AI, Derks EM, et al. Partitioning the heritability of Tourette syndrome and obsessive compulsive disorder reveals differences in genetic architecture. *PLOS Gene.* 2013; 9(10). Available from: doi:10.1371/journal.pgen.1003864.
5. Thapar A, Cooper M. Copy number variation: What it is and what has it told us about child psychiatric disorders?. *J Am Acad Child Adolesc Psychiatry.* 2013; 52(8): 772-4. Available from: doi:10.1016/j.jaac.2013.05.013.

ROSEHIP NEURON

DISCOVERING LIMITATIONS IN CURRENT NEUROLOGICAL RESEARCH

AARON WEN

In 2013, Barack Obama announced the federal BRAIN initiative in partnership with the National Institute of Health.[1] The goal was simple: identify every type of cell found in the brains of mice, monkeys, and humans. Amongst the 100 billion neurons in the human brain, 60 types had been identified and categorized to date.[2] In August of 2018, scientists identified yet another type of neuron with perplexing features. Researchers at the Allen Institute of Brain Science and University of Szeged have discovered a new neuron that is present in humans, but not rodents. The rosehip neuron, named after its striking resemblance to a rose and its petals, inhibits neuronal functioning through the repression of other neurons.[3] Although these neurons are few in number, their strategic locations have made scientists hypothesize that they function in regulating the complex circuitry that comes with human consciousness.[4]

While further research is being conducted to examine the specific role of rosehip neurons, lead researchers Ed Lein and Gabor Tamas are concerned with the implications of this discovery. Lein stated, "[Rosehip neurons] throw some doubt on the ability to use [murine models] to study certain elements of human function and disease."[5] However, researchers are unsure if rosehip neurons are truly unique to humans. Hence, more research is needed to evaluate the use of animal systems as models for human disease.

Additionally, rosehip neurons are a type of inhibitory neuron for which several highly selective markers have been implicated as risk factors for neuropsychiatric disorders.[5] A better understanding of this neuron and its connection to the overlying neuronal circuitry may lead to the development of more promising treatments against human neurological pathologies.

1. National Institutes of Health. *What is the National Brain Initiative?* [Internet]. 2018 [Accessed 2018 Sep 12]. Available from: https://www.braininitiative.nih.gov/
2. Houzel S. The human brain in numbers: A linearly scaled-up primate brain. *Front Hum Neurosci.* 2009;3:31. Available from: doi:10.3389/neuro.09.031.2009
3. Eyal G, Verhoog M, Testa-Silva G, Deitcher Y, Lodder J, Benavides-Piccione R, et al. Unique membrane properties and enhanced signal processing in human neocortical neurons. *eLife.* 2016;5:e16553. Available from: doi:10.7554/eLife.16553
4. Boldog E, Bakken TE, Hodge RD, Novotny M, Aevermann BD, Baka J, et al. Transcriptomic and morphophysiological evidence for a specialized human cortical GABAergic cell type. *Nat Neurosci.* 2018;21(9):1185-95. Available from: doi:10.1038/s41593-018-0205-2.
5. Hamilton J. *What makes a human brain unique? A newly discovered neuron may be a clue* [Internet]. 2018 [Accessed 2018 Sep 9]. Available from: https://www.npr.org/sections/health-shots/2018/08/27/642255886/a-new-discovery-may-explain-what-makes-the-human-brain-unique.