**////Title: Obsessive-compulsive Disorder: The Genetic Links Between Traits and Clinical Diagnosis**

**////Stand-first**: Although obsessive-compulsive disorder (OCD) is a commonly occurring psychiatric disorder, the underlying genetic basis has until recently, remained poorly defined. Drs Christie Burton, Jennifer Crosbie, and Russell Schachar at The Hospital for Sick Children (SickKids) in Toronto, Canada, and Dr Paul Arnold at the University of Calgary in Calgary, Canada and their extensive network of collaborators conducted a genome-wide association study to address this key gap. These researchers are the first to empirically demonstrate that OCD and obsessive-compulsive traits have a shared genetic risk, and start to pinpoint the genetic basis of this.

**////Body text:**

Obsessive-compulsive disorder (OCD) is a common psychiatric disorder characterised by intrusive, recurrent thoughts and repeated, ritualised behaviours. For example, an extreme, deeply rooted fear of germs may be associated with an individual experiencing persistent and distressing thoughts about contamination and engaging in compulsive hand washing to try to avoid this.

Between 1 and 2% of the population are diagnosed with OCD. Up to half of all cases start before adulthood (i.e., before an individual reaches the age of 18 years). OCD that begins in childhood is thought to have a greater inherited (that is, genetic) risk than OCD that has begun only in adulthood.

The clinical diagnosis of OCD requires that the symptoms meet specific criteria, such as being time-consuming (for example, taking up more than 1 hour per day) and resulting in clinically significant distress in social, occupational, or other important areas of functioning for the individual. The behaviours and thoughts found in OCD (i.e., OCD traits) are thought to occur on a spectrum with people being more or less obsessive and compulsive. People who meet the criteria for an OCD diagnosis would be on the extreme of this spectrum.

The genome-wide association study (GWAS) approach is an important methodology used in genetics research to associate specific genetic variations commonly found in the population (usually, in at least 5% of people)with a particular disorder. By examining the genetic variations across the genomes of large groups of people, researchers can identify specific genetic markers that can be used to predict the presence of a disease.

However, until recently, researchers have been unable to confirm the genetic variants linked to OCD due to conflicting and inconsistent findings from under-powered studies (i.e., studies without sufficient numbers of participants such that we can have confidence in the conclusions). Some researchers believe that focusing on OCD traits, rather than just patients with an OCD diagnosis, will be a faster and more powerful way to understand the genetics of OCD. The question remains is that true and can OCD traits tell us something about the genetics of OCD as a disorder?

Drs Christie Burton, Jennifer Crosbie, and Russell Schachar at The Hospital for Sick Children (SickKids) in Toronto, Canada, and Dr Paul Arnold at the University of Calgary in Calgary, Canada, and their extensive network of collaborators sought to resolve this gap in the literature by conducting a GWAS of OCD traits in a large group of children and youth to identify novel genetic variants and explore the genetic links between OCD traits and diagnosis of OCD.

Participants were part of a wider research programme called ‘Spit for Science’ at the Ontario Science Centre. Approximately half the sample were female and the average age was 11 years old. Children, youth and parents completed a measure of the child or youth’s OCD traits over the past six months using a questionnaire known as the Toronto Obsessive-Compulsive Scale developed by the authors. Genetic information on each participant was obtained via their spit.

Dr Burton and her colleagues wanted to test whether genetic variants associated with OCD traits in their Spit for Science participants would also be associated with those found in patients with a clinical diagnosis of OCD. To answer this question, they obtained genetic information about patients with OCD diagnoses from independent clinical studies, and used sophisticated statistical techniques to compare this with the genetic information they obtained about their own participants.

Critically, the researchers were able to clearly establish a genetic variant associated with both OCD traits and diagnosis. This variant is known as rs7856850 and is located in the gene *PTPRD*, a type of protein-coding gene known as a protein tyrosine phosphatase receptor type d.

Furthermore, Dr Burton and her colleagues established that the genetic risk for having OCD traits in their Spit for Science participants was shared with that identified in individuals with a clinical diagnosis of OCD.

The extent of the shared risk of having OCD and displaying OCD traits strongly supports the notion that a spectrum exists for OCD, with those at the more severe end of the scale receiving a clinical diagnosis of the disorder but that within the general population, there exist many individuals with less frequent or severe symptoms that present in the form of OCD traits.

Dr Burton and her colleagues note that the magnitude of the shared risk of OCD and OCD traits is broadly comparable with that found for other disorders that are also considered to exist on a spectrum. These include autistic spectrum disorder (as the name suggests) and mood instability.

An important implication arising from this work is that the overall approach of examining trait characteristics of individuals in the general population provides a powerful complementary approach to studies in patients, which are often more difficult, expensive and slow to conduct for a range of reasons.

In summary, Dr Burton and her colleagues have provided the first demonstration that OCD and OCD traits have a shared genetic risk, and they have successfully pinpointed the genetic basis of this. The researchers note that future research will require even larger groups of participants to understand more fully the genetic contribution to OCD and it will also be important to look at how symptoms of OCD fluctuate over time in patients.

The findings and methodological advances reported by Dr Burton and her colleagues represent a significant step forward not only in understanding OCD but also in accelerating gene discovery in the fascinating field of psychiatric genetics.

This SciPod is a summary of the open access paper ‘[Genome-wide association study of pediatric obsessive-compulsive traits: shared genetic risk between traits and disorder](https://www.nature.com/articles/s41398-020-01121-9)’, published in the journal Translational Psychiatry. https://doi.org/10.1038/s41398-020-01121-9

For further information, you can connect with Christie Burton at christie.burton@sickkids.ca