Genetics of Obsessive-Compulsive Disorder and Related Disorders

Heidi A. Browne, BSc[a,b], Shannon L. Gair, BA[a], Jeremiah M. Scharf, MD, PhD[c,d,*], Dorothy E. Grice, MD[a,b,*]

KEYWORDS

• OCD • Genetics • Heritability • Twin study • Familial recurrence • GWAS • Candidate gene • Model system

KEY POINTS

- Although most genetic studies focus primarily on obsessive-compulsive disorder (OCD) and Tourette Syndrome (TS), twin and family studies support a significant genetic contribution to OCD and also to related disorders (eg, Tourette syndrome), including chronic tic disorders, trichotillomania, skin-picking disorder, body dysmorphic disorder, and hoarding disorder.
- Recently, population-based studies and novel laboratory-based methods have confirmed substantial heritability in OCD and TS.
- Genomewide association studies and candidate gene studies have provided information on specific genes that may be involved in the pathobiology of OCD and related disorders, and for some genes studies using model systems have supported a likely role in OCD.
- A substantial portion of the genetic contribution to OCD is still unknown.

Disclosures: J.M. Scharf has received research support from the National Institutes of Health, grants U01 NS40024 and K02 NS085048 and the Tourette Syndrome Association (TSA) and serves on the TSA Scientific Advisory Board. He has received travel support from the TSA and from the European Commission (COST Action BM0905). D. E. Grice has received research support from the National Institutes of Health, grant R01 MH092516, the Tourette Syndrome Association (TSA), and the Tourette Syndrome Association of New Jersey. The other authors have no relevant financial or nonfinancial disclosures.

[a] OCD and Related Disorders Program, Division of Tics, OCD, and Related Disorders, Department of Psychiatry, Icahn School of Medicine at Mount Sinai, One Gustave L. Levy Place, Box 1230, New York, NY 10029, USA; [b] Friedman Brain Institute, Icahn School of Medicine at Mount Sinai, One Gustave L. Levy Place, New York, NY 10029, USA; [c] Movement Disorders Unit, Department of Neurology, Massachusetts General Hospital, Harvard Medical School, 185 Cambridge Street, 6254, Boston, MA 02114, USA; [d] Psychiatric and Neurodevelopmental Genetics Unit, Department of Psychiatry, Massachusetts General Hospital, Harvard Medical School, 185 Cambridge Street, 6254, Boston, MA 02114, USA
* Corresponding authors.
E-mail addresses: jscharf@partners.org; dorothy.grice@mssm.edu

Psychiatr Clin N Am 37 (2014) 319–335
http://dx.doi.org/10.1016/j.psc.2014.06.002 **psych.theclinics.com**
0193-953X/14/$ – see front matter

Abbreviations	
BDD	Body dysmorphic disorder
CI	Confidence interval
CNVs	Copy number variants
COMT	Catechol-*O*-methyltransferase
CT	Chronic tic disorder
DD	Developmental delay
GCTA	Genome wide complex trait analysis
GWAS	Genome wide association study
ID	Intellectual disability
IOCDFGC	International OCD Foundation Genetics Consortium
OC	Obsessive-compulsive
OCD	Obsessive-compulsive disorder
OCGAS	OCD Collaborative Genetic Association Study
RRR	Relative recurrence risk
SNP	Single nucleotide polymorphism
TS	Tourette syndrome
TTM	Trichotillomania

OVERVIEW

Obsessive-compulsive disorder (OCD) is a disorder that can onset during childhood or during adult life. As a result, OCD is a disorder of interest to both child and adult psychiatrists. There are several other disorders that either commonly co-occur with OCD or have overlapping or similar features and symptoms. Tourette syndrome (TS) is characterized the presence of both motor and vocal tics that onset in childhood and last at least 12 months. A related condition, chronic tic disorder (CT), (CT; defined by the presence of motor tics or vocal tics, but not both and also lasting more than one year) is thought to be an alternate phenotype to TS and shares genetic and biological underpinnings with TS. There is a substantial body of literature focused on the twin, familial, and genetic aspects of TS and CT, a summary of which is presented elsewhere in this issue in the article, "Tics and Tourette's Disorder" by Shaw and Coffey. Of relevance here is that chronic tic disorders (TS and CT) are often seen in conjunction with childhood-onset OCD, reflected in the recent addition of a *tic-related* specifier for OCD in DSM-5. Other OCD-related disorders beyond TS and CT, namely trichotillomania (TTM), skin picking disorder, body dysmorphic disorder (BDD), and hoarding disorder, occur across the lifespan. Although compared with TS and CT there is less specific genetic evidence that these other related disorders share pathobiology with OCD, there is growing evidence that overlapping genetic risk factors may exist across OCD, TTM, skin picking disorder, BDD, and hoarding disorder.

The earliest studies to support a role for genetic factors in OCD demonstrated a higher concordance rate for OCD among monozygotic twins compared with dizygotic twins. Although fewer studies have focused on TTM, skin picking disorder, BDD, and hoarding disorder, there is emergent evidence that some portion of risk for these related disorders is also rooted in genetic factors. These twin studies and subsequent family studies provide estimates of heritability in OCD and related disorders as high as 50%. Recently, powerful population-based epidemiologic studies and new molecular methods have confirmed significant heritability, indicating that genetics contribute substantially to risk for these disorders. Because OCD and related disorders show substantial heritability, familial recurrence risk is high. Over the past several years,