

Obsessive-Compulsive Disorder and Gender Differences

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Introduction

Previously classified as an anxiety-related disorder, obsessive-compulsive disorder (OCD) was moved to a new "Obsessive-Compulsive and Related Disorders" section in the *Diagnostic and Statistical Manual of Mental Disorders* (5th ed.; *DSM-5*; American Psychiatric Association [APA], 2013). This section also includes body dysmorphic disorder (BDD), hoarding disorder (previously considered a subtype of OCD), trichotillomania (hair-pulling disorder), and excoriation (skin-picking disorder; APA, 2013) (see Chapter x). In *DSM-5*, OCD is characterized by the presence of obsessions and compulsions (Criterion A), which must be time-consuming or cause clinically significant distress or impairment (Criterion B; APA, 2013, p. 238). *Obsessions* are egodystonic "repetitive and persistent thoughts, images, or urges" (APA, 2013, p. 238), while *compulsions* are "repetitive behaviors ... that the individual feels driven to perform in response to an obsession or according to rules that must be applied rigidly" (APA, 2013, p. 237). Whereas obsessions are strictly mental activities, compulsions can be observable (e.g., checking locks or washing hands) or covert (e.g., counting or mentally repeating certain words or phrases).

Epidemiology

OCD is a relatively common disorder, affecting 1–3% of the general population in a given year (Apter et al., 1996; Ruscio, Stein, Chiu, & Kessler, 2010). Approximately half of all treatment-seeking adults with OCD are women (Rasmussen & Eisen, 1992). In community samples, women represent slightly more than half of all adults with OCD (Bebbington, 1998). In pediatric samples, the gender difference is skewed toward males, with an approximately 2:1 male to female ratio (e.g., Hanna, 1995). This difference may reflect the earlier modal age of onset for OCD in males (modal age 13 – 15) compared to females (20 – 24; Rasmussen & Eisen, 1990).

Several gender differences in OCD phenomenology have been identified. For example, women are more likely than men to report obsessions focusing on contamination (e.g., fears of spreading or contracting illness) and corresponding cleaning compulsions (e.g., excessive hand-washing and cleaning; de Mathis et al., 2011). This gender difference appears to be stable across cultures, indicating that biological factors or cross-cultural gender role norms may play a role in OCD presentation (de Mathis et al., 2011). Conversely, sexual obsessions (e.g., fears of pedophilia and homosexuality) are more frequently observed in men than women, as are ordering and symmetry obsessions (Lensi et al., 1996).

Gender differences in OCD-related impairment have also been identified. In a large Brazilian sample (Torresan et al., 2013), men with OCD were more likely than women to be single (61% of men vs. 47% of women), to be unemployed (20% vs. 14%), and to live with their family of origin or in assisted living facilities (50–66% vs. 20–40%). Although some studies have reported that OCD symptoms are more severe in women on average (Torresan et al., 2013), other studies have found no gender differences in OCD severity (Labad et al., 2008).

Subtypes

Perinatal OCD. Intrusive thoughts and compulsive behaviors similar to those that characterize OCD are common among new and expectant parents (Abramowitz, Schwartz, & Moore, 2003; Abramowitz, Schwartz, Moore, & Luenzmann, 2003; Fairbrother & Abramowitz, 2007; Zambaldi et al., 2009). Prevalence estimates of OCD during pregnancy range from 0.2% (Zar, Wijma, & Wijma, 2002) to 29% (Chaudron & Nirodi, 2010), with many studies reporting prevalence estimates in the range of 1–2% (Russell, Fawcett, & Mazmanian, 2013). Onset of OCD after the birth of a child (often called postpartum OCD) is more likely to occur in women than men (13% vs. 6.5% of individuals with OCD; Torresan et al., 2013). During the postpartum

period, prevalence estimates range from 0.7% (Navarro et al., 2008) to 9% (Zambaldi et al., 2009), with many estimates in the 2–4% range (Russell et al., 2013). A recent meta-analysis estimated the prevalence of OCD to be 2.1% during pregnancy and 2.4% during the first year postpartum; this review found that the perinatal period is associated with a 79% increase in risk for OCD compared to the general female population (Russell et al., 2013).

Among individuals with OCD, pregnancy and childbirth are commonly nominated as events precipitating the onset of symptoms (Maina, Albert, Bogetto, Vaschetto, & Ravizza, 1999). Among women with preexisting OCD, there does not seem to be a consistent relationship between pregnancy and OCD symptoms (Forray, Focseneanu, Pittman, McDougle, & Epperson, 2010; Williams & Koran, 1997). However, many women with OCD report that their symptoms worsen during the postpartum period (Labad et al., 2005; Williams & Koran, 1997).

Interestingly, the content of obsessions and compulsions in this population appears to be influenced by the perinatal context. OCD with onset during pregnancy is commonly characterized by contamination obsessions and corresponding washing and cleaning compulsions, while OCD with onset during the postpartum period is commonly associated with harm obsessions and corresponding checking or avoidance compulsions (Buttolph & Holland, 1990; Sichel, Cohen, Dimmock, & Rosenbaum, 1993). Obsessions related to harming the infant can be distinguished from infanticidal ideation that may occur in severe postpartum depression or psychosis by the egodystonic nature of the obsessions; women with postpartum OCD often engage in extensive avoidance and rituals to address their fears of harming their infants (Abramowitz, Schwartz, Moore, & Luenzmann, 2003). To date, no cases of a woman with “pure” OCD causing harm to her infant have been documented (Ross & McLean, 2006).

H-OCD. One specific manifestation of OCD includes concerns related to sexual orientation, including doubts regarding one's sexual orientation and fears that one may be homosexual (H-OCD; Williams, 2008). These symptoms are often misdiagnosed; obsessions related to sexual orientation are commonly misattributed to "latent homosexuality" or interpreted as indicative that the patient is actually uncertain of his or her sexual orientation (Williams, 2008). In a sample of 409 patients in OCD specialty clinics, 8% of the sample reported current obsessions related to sexual orientation and 3.9% endorsed a lifetime history of these obsessions; men were twice as likely to endorse these obsessions (Williams & Farris, 2011).

Pediatric autoimmune neuropsychiatric disorder associated with streptococcal infections (PANDAS). PANDAS is a pediatric variant of OCD, the defining feature of which is a sudden onset of OCD following a Group A *streptococcus* infection (Giedd, Rapoport, Garvey, Perlmutter, & Swedo, 2000). OCD-related PANDAS symptoms are similar to those found in classic pediatric OCD. Mood lability, personality changes, hyperactivity, tics, decreased handwriting quality, and other symptoms are also frequently observed (Murphy, Storch, Lewin, Edge, & Goodman, 2012). To date, no large-scale epidemiological studies of PANDAS have been conducted. However, a recent study of 109 children ages 4–17 with OCD found that 41 of these children (68% male) met criteria for PANDAS, suggesting a higher prevalence in boys than girls (Murphy et al., 2012). In that study, children with PANDAS were more likely than those with non-PANDAS OCD to report an episodic course characterized by full remission and subsequent "flare-ups," to show symptom remission during antibiotic therapy, and to have elevated streptococcal titers.

Comorbidity

The majority of individuals who meet criteria for OCD also meet criteria for at least one additional psychiatric disorder (Rasmussen & Eisen, 1990; Steketee, Chambless, & Tran, 2001). In the National Comorbidity Survey – Replication study (NCS-R), 90% of adult respondents who met lifetime DSM-IV criteria for OCD also met criteria for another lifetime disorder (Ruscio et al., 2010). The most common comorbid conditions were anxiety disorders, followed by mood disorders, impulse control disorders, and substance use disorders (Ruscio et al., 2010). Comorbid obsessive-compulsive and related disorders are also common (Richter, Summerfeldt, Antony, & Swinson, 2003).

Gender differences in patterns of comorbidity appear to reflect overall gender differences in the prevalence of psychiatric disorders. Women with OCD are more likely to present with comorbid eating disorders (Bogetto, Venturello, Alert, Maina, & Ravizza, 1999; Lochner et al., 2004; Torresan et al., 2009; Torresan et al., 2013), major depression (Castle et al., 1995; Labad et al., 2008), and impulse control disorders (Bogetto et al., 1999; Torresan et al., 2009; Torresan et al., 2013). Conversely, men are more likely to present with comorbid social phobia (Bogetto et al., 1999; Jaisoorya, Reddy, Srinath, & Thennarasu, 2009; Torresan et al., 2013; Tükel, Polat, Genc, Bozkurt, & Atli, 2004), tic disorders (Jaisoorya et al., 2009; Torresan et al., 2009; Torresan et al., 2013), substance use disorders (Bogetto et al., 1999; Lochner et al., 2004; Torresan et al., 2013), and bipolar disorder (Bogetto et al., 1999; Lensi et al., 1996).

Many patients with OCD also meet criteria for at least one personality disorder (Baer & Jenike, 1992; Steketee et al., 2001). The most common comorbid *DSM-IV* Axis II disorders are those on Cluster C, the “anxious cluster” (Steketee et al., 2001). There is some evidence that men with OCD report higher levels of traits associated with the Cluster C personality disorders than do women (Castle et al., 1995; Lensi et al., 1996).

Psychobiology

Neuropsychology

Although a growing body of research has investigated neuropsychological performance in OCD, few studies have explicitly examined sex and gender differences in these domains. The existing studies suggest few, if any, consistent sex differences in executive functioning and neuropsychological performance. One of the largest such studies (Mataix-Cols et al., 2006) examined performance on a wide range of neuropsychological tests in a sample of 33 men and 23 women with OCD and 40 healthy controls (50% women, matched to the OCD sample on age, education level, and handedness). The study revealed a significant sex by group interaction for verbal fluency: women with OCD performed more poorly than healthy control women; no difference was found for men. No significant interactions were observed for any other domain, including general nonverbal intelligence, attention, working memory, set-shifting, or inhibition.

A subsequent study using a similar sample (31 men and 19 women with OCD and a healthy control group matched for sex, age, education, and handedness; Segalàs et al., 2010) did not replicate the previous finding of poorer verbal fluency among women with OCD. Instead, the study found poorer nonverbal memory performance in men with OCD compared to healthy control men. This difference was not observed for women. No interactions were found for verbal memory, general intelligence, attention, or working memory.

In several studies that did not explicitly examine gender, adults and children with OCD demonstrated deficits in response inhibition, defined as the ability to override a dominant or prepotent response (e.g., turning right to drive home) to make a less dominant, task-appropriate response (e.g., turning left to stop by the supermarket; Miyake et al., 2000). This finding does not appear to vary by sex (Kang et al., 2013). Impairments have also been observed in some studies

of planning and decision-making, although other studies have failed to replicate these findings (Menzies et al., 2008). Other studies have found few or no impairments on a range of executive functioning tasks in individuals with OCD (Abramovitch, Mittleman, Henin, & Geller, 2012).

Neurobiology

Neuroimaging research has revealed several brain regions and circuits that may play a role in the pathophysiology of OCD. Again, however, small sample sizes and a relative lack of research preclude strong conclusions about sex differences in these circuits. Leading neurobiological models of OCD focus on abnormalities in several interconnected brain regions, including the orbitofrontal cortex (OFC; particularly lateral and medial regions), anterior cingulate cortex (ACC, particularly dorsal regions), thalamus, and basal ganglia, which contains the striatum, nucleus accumbens, and other subregions (Graybiel & Rauch, 2000; Milad & Rauch, 2012).

The OFC is most commonly recognized for its role in emotional and motivational facets of behavior, including evaluating and monitoring changes in the reward value of a stimulus (Rolls, 2004). Findings from structural and functional neuroimaging studies suggest several OCD-related abnormalities in the OFC and its subregions. Compared to healthy controls, adults with OCD tend to show reduced OFC volume (Menzies et al., 2008; Rotge et al., 2009) but increased glucose metabolism at rest (Harrison et al., 2009) and in response to symptom-provocation paradigms, wherein OCD symptoms are elicited in the scanner (Rotge et al., 2009). Notably, this hypermetabolism in the OFC and in several other regions is normalized following effective cognitive-behavioral therapy or pharmacotherapy for OCD (see Abramovitch et al., 2012 for a review).

The OFC is strongly interconnected with the basal ganglia and its subregions, which play a strong role in selecting and initiating motor behaviors (Alexander & Crutcher, 1990). Basal ganglia abnormalities are often observed in patients with OCD and phenomenologically similar disorders, including PANDAS (Giedd et al., 2000) and Tourette's disorder (Mink, 2001). In adults with OCD, reduced striatal volumes have been observed in some studies but not others (Aylward et al., 1996; Rotge et al., 2009).

OCD-related hypermetabolism has also been found in the ACC, which plays a major role in error detection as well as the assessment and regulation of emotional information (Diler, Kibar, & Avci, 2004). This elevated activity may relate to the "not just right" feeling endorsed by many individuals with OCD (Aouizerate et al., 2004). OCD is also associated with increases in the volume of the thalamus, a midline structure that serves as a "switchboard" for several brain regions, among other functions (Gilbert, Moore, Keshavan et al., 2000; Rotge et al., 2009). In one pediatric OCD study, elevated thalamic volume was normalized following 12 weeks of effective treatment with paroxetine, a selective serotonin reuptake inhibitor (SSRI; Gilbert et al., 2000). These volumetric changes were associated with changes in OCD symptom severity.

Inconsistencies in neuropsychological and neurobiological OCD research may be due to a number of factors, including small sample sizes, insufficiently sensitive tests, or heterogeneity of OCD symptoms (Abramovitch et al., 2012; Milad & Rauch, 2012). For example, compulsive hoarding was previously considered a subtype of OCD (APA, 1994) but has been reclassified as a distinct OC-spectrum disorder in *DSM-5* (APA, 2013). Individuals with hoarding disorder differ from those with OCD in terms of neural activity during some neuropsychological tasks (Tolin, Witt, & Stevens, in press) and in several other domains (Frost, Steketee, & Tolin 2012).

Thus, the inclusion of hoarding in previous OCD samples may have masked (or spuriously enhanced) true differences between individuals with OCD and healthy controls.

Genetics

OCD is a strongly heritable disorder, with strong concordance reported in monozygotic twins (Pauls, 2010). Stronger familial concordance has been observed for early-onset OCD (before 18 years; more commonly observed in males) than for later-onset OCD (Pauls, Alsobrook, Goodman, Rasmussen, & Leckman, 1995). Genetic linkage analyses suggest that a locus on chromosome 9 may contribute to OCD genetic vulnerability (Hanna et al., 2002), as may certain polymorphisms in the 5-HT_{2A} promoter gene, which plays a role in regulation of serotonin (Hu et al., 2006). However, other studies have failed to replicate these findings (Pauls, 2008). More recently, a genome-wide association study found evidence for enriched methylation of quantitative trait loci (QTLs) in the single-nucleotide polymorphisms (SNPs) that were most associated with OCD (Stewart et al., 2013). Taken together, these findings suggest that OCD is almost certainly the result of multiple genetic and environmental factors and that additional research is needed to elucidate the genetic underpinnings of OCD.

Some sex differences in the genetic diatheses for OCD have been identified. Women with OCD are more likely than men to possess a low activity-related allele of the monoamine oxidase A gene, whereas men are more likely to possess a low activity-related allele of the catechol-O-methyltransferase (COMT) gene (Lochner et al., 2004). Both genes are responsible for degrading a number of neurotransmitters, including serotonin, dopamine, and norepinephrine (Lochner et al., 2004). Additionally, some genetic polymorphisms (e.g., in the 5-HT_{2A} promoter gene) have been associated with OCD symptoms only in women (Enoch, Greenberg, Murphy, & Goldman, 2001), whereas other polymorphisms (e.g., SLC1A1, a polymorphism of the glutamate

transporter gene) have been linked to OCD only in men (Dickel et al., 2006; Arnold, Sicard, Burroughs, Richter, & Kennedy, 2006).

Diagnosis

Many individuals without OCD report some obsessions or compulsions (Rachman & De Silva, 1978; Salkovskis & Harrison, 1984); therefore, OCD is diagnosed only when symptoms reach clinically significant levels of interference or distress (APA, 2013). A wide variety of screening and diagnostic measures for OCD are available, including self-report measures and semi-structured diagnostic interviews. For an in-depth review of assessment measures for OCD, see Feske and Chambless (2000).

In primary care settings, the Primary Care Evaluation of Mental Disorders Patient Health Questionnaire (PHQ; Spitzer, Kroenke, & Williams, 1999) is often used. The PHQ is a brief self-report measure that screens for OCD as well as several mood, anxiety, and substance use disorders. It shows fair-to-good reliability with diagnoses assigned by mental health professionals (Spitzer et al., 1999). There are also several OCD-specific self-report measures that can be used with adults and older adolescents. The revised versions of the Obsessive Compulsive Inventory (OCI-R; Foa et al., 2002) and Padua Inventory (PI-R; Burns, Keortage, Formea, & Sternberger, 1996) contain symptom-specific subscales and have generally strong psychometric properties. Feske & Chambless (2000) note that the PI-R can be particularly useful for assessing treatment outcome.

Some of the most common clinical interviews for diagnosing OCD in adults are the Anxiety Disorders Interview Schedule-IV (ADIS-IV; Di Nardo, Brown, & Barlow, 1994) and the Structured Clinical Interview for DSM-IV Axis I Disorders (SCID; First, Spitzer, Gibbon, & Williams, 1997). These measures assess DSM-IV criteria for OCD; the ADIS-IV in particular

provides information regarding the type and severity of obsessions and compulsions, including their frequency and persistence (Di Nardo et al., 1994).

A more precise OCD severity rating can be obtained using the Yale-Brown Obsessive-Compulsive Scale (Y-BOCS; Goodman et al., 1989). The Y-BOCS is a gold standard semi-structured interview that assesses current and lifetime presence of 36 types of obsessions and 23 types of compulsions. The Y-BOCS provides ratings for severity, time spent, interference, distress, resistance, and perceived control for the individual's primary obsessions and compulsions (Goodman et al., 1989). Administration of the Y-BOCS is generally preceded by assessment with the Y-BOCS Checklist (Steketee et al., 1996), which can be self- or clinician-administered. On the checklist, participants note the absence or presence of 58 obsessions and compulsions, identify the three main obsessions and compulsions, and rate the time spent, interference, distress, resistance and control for each on a Likert scale (Steketee et al., 1996).

When screening for OCD in younger children, an interviewer may phrase typical assessment questions more simply; for example, "do you do things over and over or have habits you can't stop?" (Geller et al., 2012, p. 102). The parent-report Child Behavior Checklist (Achenbach, 1991) shows good sensitivity and specificity in screening for pediatric OCD (Nelson et al., 2001).

Some of the most widely-used clinician-administered measures for diagnosing and evaluating OCD in pediatric samples include the Schedule for Affective Disorders and Schizophrenia for School-Age Children (K-SADS; Kaufman et al., 1997), and the Children's Y-BOCS (CY-BOCS, Scahill et al., 1997). The K-SADS covers a broad range of psychiatric disorders, including psychotic and externalizing disorders (see Lewin & Piacentini, 2010 for a review). The CY-BOCS is generally considered to be the gold standard interview for assessing

OCD in pediatric samples (Lewin & Piacentini, 2010). The CY-BOCS is structured similarly to the adult Y-BOCS and assesses the presence, frequency, interference, distress, resistance, and perceived control of obsessions and compulsions (Scahill et al., 1997). The symptom checklist of the Children's Y-BOCS (CY-BOCS; Scahill et al., 1997) can also be particularly informative when administered to both parents and children (Geller et al., 2012).

Evaluation

When evaluating OCD, several considerations are warranted. Independent of gender, individuals with OCD may be reluctant to describe their symptoms in detail. This hesitation may occur because the obsessions are embarrassing, alarming, or upsetting to the patient (e.g., in the case of sexual obsessions); because of the belief that describing the symptoms may cause the negative consequences that the person is trying to avoid via compulsions (a phenomenon called thought-action fusion, wherein the individual believes that having a thought is equivalent to acting on the thought; Shafran, Thordarson, & Rachman, 1996); or for fear that the patient will be misperceived as dangerous (e.g., in the case of harm obsessions) or psychotic.

In our clinical experience, underreporting is a particular risk for sexual and harm obsessions, often because of shame and fears of being misinterpreted or viewed as potentially dangerous. In the case of sexual obsessions, this apprehension may be increased when the interviewer is of a different gender than the patient (e.g., a male patient and a female interviewer). Therefore, it is important for the interviewer to normalize these symptoms. For example, an interviewer might state that individuals with OCD often experience unwanted, socially undesirable obsessions, such as obsessions related to harming oneself or someone else, of being a pedophile, of being gay, or of harming one's child. Such normalizing statements often

make patients more comfortable describing their symptoms and can increase “buy-in” for the treatment.

Independent of gender, it is critical to evaluate insight in patients with OCD. Most individuals with OCD recognize that their symptoms are unreasonable, unnecessary, or take up more time than is warranted (APA, 2013). However, a subset of individuals truly believe that their compulsions are necessary and appropriate. These individuals, who can be assigned the diagnostic specifier “with poor insight,” show poorer treatment response (Ravi Kishore, Samar, Janardhan Reddy, Chandrasekhar, & Thennarasu, 2004) and may require different or additional interventions (e.g., adjunctive antipsychotic pharmacotherapy; Ravi Kishore et al., 2004). The Brown Assessment of Beliefs Scale (BABS; Eisen et al., 1998) is a relatively brief, well-validated, clinician-administered measure that assesses patients’ insight into their symptoms (Eisen et al., 1998). When possible, formal assessment with the BABS or a similar standardized assessment method (e.g., item 11 from the Yale-Brown Obsessive Compulsive Scale; Y-BOCS; Goodman et al., 1989) is advisable.

Differential Diagnosis

OCD shares many clinical features with other emotional disorders. Individuals with body dysmorphic disorder (BDD) also report intrusive thoughts and engage in compulsive behaviors in an attempt to reduce the resulting anxiety. However, in BDD, individuals’ obsessions and compulsions are limited to concerns related to physical appearance (APA, 2013). If obsessions and compulsions are limited to concerns about weight or body shape, an eating disorder diagnosis should also be considered (APA, 2013). While impulse-control disorders (e.g., kleptomania) are characterized by behaviors that may be described as “compulsive,” these disorders can be distinguished from OCD by the absence of egodystonic obsessions (APA,

2013). Furthermore, the compulsive behaviors associated with these disorders are frequently egosyntonic, and the distress experienced by the individual results from the consequences of their compulsive behavior, rather than the behaviors themselves (Dell'Osso, Altamura, Allen, Marazziti, & Hollander, 2006).

Hoarding disorder is characterized by persistent difficulty discarding possessions due to a perceived need to save items, distress associated with discarding items, and problematic accumulation of possessions. In contrast to OCD, hoarding disorder is more likely to be egosyntonic and characterized by an absence of attempts to resist hoarding (Frost et al., 2012; Mataix-Cols et al., 2010).

Both mood and anxiety disorders may also be characterized by the experience of repetitive or intrusive thoughts. Of the anxiety disorders, generalized anxiety disorder (GAD) is most phenomenologically similar to OCD (Steketee & Barlow, 2002). GAD can be distinguished from OCD by the nature of the repetitive thoughts. In GAD, intrusive thoughts are characterized by excessive anxiety and worry about real-life concerns. In OCD, intrusive thoughts often have odd, irrational, or "magical" content (APA, 2013). GAD can also be distinguished from OCD by the absence of compulsions. Additionally, while individuals with major depressive disorder (MDD) may experience intrusive rumination, these thoughts are usually mood-congruent and somewhat egosyntonic. MDD can also be distinguished from OCD by the absence of compulsions (APA, 2013).

OCD can be distinguished from psychotic disorders by the absence of other characteristic features of these disorders, such as hallucinations and a formal thought disorder (APA, 2013). However, OCD can be characterized by delusional beliefs (O'Dwyer & Marks, 2000); these can be diagnosed using the "no insight" specifier in DSM-5.

Finally, despite the similarity in name, most individuals with OCD do not meet criteria for comorbid obsessive-compulsive personality disorder (OCPD; Steketee et al., 2001). Unlike OCD, which is characterized by intrusive thoughts and repetitive behaviors, OCPD is often characterized by rigidity and egosyntonic preoccupation with orderliness, perfectionism, and control (APA, 2013). Individuals exhibiting both obsessions/compulsions and pervasive, maladaptive perfectionism and rigidity may be diagnosed with both OCD and comorbid OCPD (Coles, Pinto, Mancebo, Rasmussen, & Eisen, 2008).

Pharmacotherapy

Meta-analyses suggest a significant benefit from several forms of pharmacotherapy for OCD, with relatively few studies noting sex or gender differences in treatment response. The most widely-investigated pharmacological treatments for OCD include clomipramine, a tricyclic antidepressant, and selective serotonin reuptake inhibitors (SSRIs; Foa & Kozak, 2008). Other biological interventions, which are typically used as an adjunct to conventional treatment or in the case of treatment-resistant OCD, include atypical antipsychotics, deep brain stimulation, transcranial magnetic stimulation (TMS), and d-cycloserine, among others.

Clomipramine, which inhibits the reuptake of serotonin and norepinephrine, was the first drug approved by the Food and Drug Administration (FDA) for the treatment of OCD. Several meta-analyses demonstrate that clomipramine is more effective than placebo in both adults (Ackerman et al., 2002; Greist, Jefferson, Kobak, Katzelnick, & Serlin, 1995) and children (Watson & Rees, 2008). Importantly, clomipramine can produce undesirable side effects, including dizziness, blurred vision, sedation, constipation, and weight gain. This problematic side effect profile has favored the increased use of SSRIs as a treatment for OCD.

SSRIs produce a clinically significant response in about 40 - 60% of OCD patients (Jenike, 2004). SSRIs are more effective than placebo even at low doses, but higher doses (e.g., 60 - 80mg of fluoxetine and its equivalents) produce greater reductions in symptoms (Bloch, McGuire, Landeros-Weisenberger, Leckman, & Pittenger, 2010). A Cochrane review comparing different types of SSRIs (fluoxetine, fluvoxamine, sertraline, paroxetine, and citalopram) found no significant differences in the effectiveness of each medication (Soomro, Altman, Rajagopal, and Oakley-Browne, 2008). Side effects of SSRIs can include dizziness, weight gain, decreased libido and anorgasmia, drowsiness, and insomnia; these and other side effects can be particularly pronounced at the higher doses required to treat OCD.

Randomized controlled trials and meta-analyses that have compared clomipramine and SSRIs have produced mixed results. Some meta-analyses suggest that clomipramine produces larger reductions in symptoms compared to SSRIs in both adults and children (Greist et al., 1995; Sánchez-Meca, Rosa-Alcázar, Iniesta-Sepúlveda, & Rosa-Alcázar, 2014). However, other meta-analyses have found no differences in efficacy between the treatments (Ackerman et al., 2002). Given the lower risk profile and potentially greater tolerability of SSRIs as compared to clomipramine, SSRIs are generally recommended as a first-line psychopharmacological treatment for both adults (Decloedt & Stein, 2010) and, in severe cases, children (Geller et al., 2012) with OCD.

In one study of gender differences in medication response (Mundo, Bareggi, Pirola, & Bellodi, 1999), men were more likely than women to experience a worsening of symptoms following administration of intravenous clomipramine (no patients improved following IV clomipramine administration). Following the IV administration, participants were randomly assigned to receive 10 weeks of standard oral treatment with clomipramine or fluvoxamine.

Women were more likely than men to experience a reduction in symptoms with clomipramine (94.1% of women improved relative to post-IV clomipramine treatment vs. 57.1% of men); no significant gender differences were found for fluvoxamine.

Atypical antipsychotics are sometimes used to augment clomipramine or SSRIs in individuals with treatment-resistant OCD. Risperidone and quetiapine show some promise as adjunctive treatments for treatment-resistant OCD (Fineberg, Gale, & Sivakumaran, 2006). However, as atypical antipsychotics can cause unpleasant and potentially dangerous side effects, careful consideration is warranted when considering their use (Fineberg et al., 2006).

Several studies have investigated the use of psychotropic medications in postpartum OCD. An open-label trial of fluoxetine for postpartum OCD found that the majority of patients experienced a positive response (Arnold, 1999). Another open trial found that augmentation with quetiapine was effective for postpartum women with OCD that had not responded to SSRI or SNRI monotherapy (Misri & Milis, 2004). Several case reports suggest that perinatal OCD can be effectively treated with clomipramine (Chelmow & Halfin, 1997), fluoxetine (Buttolph & Holland, 1990), and various other SSRIs (Sichel et al., 1993).

Importantly, although psychotropic medications are often effective for reducing OCD symptoms, the benefit is often lost when medication is discontinued (Fineberg, Reghunandanan, Brown, & Pampaloni, 2013). Given the short-lived treatment gains and the side effects associated with psychopharmacological treatment, cognitive-behavioral psychotherapy is recommended as a front-line treatment for OCD (NICE, 2005; see Psychotherapy below).

In the past decade, advances in neurotherapeutics have highlighted several promising adjunctive and alternative treatments for treatment-resistant OCD. In deep brain stimulation, an electrode is implanted in the brain (typically in the striatum) and electrical impulses are

transmitted to interfere with neuronal activity. This approach, although invasive, has been associated with positive short- and long-term results in individuals with chronic, intractable OCD (Greenberg et al., 2006). A newer approach is repetitive TMS (rTMS), wherein a non-invasive handheld device is used to alter magnetic activity in the brain. A recent meta-analysis suggests that rTMS produces a moderate improvement in OCD symptoms compared to placebo or "sham" stimulation (Berlim, Neufeld, & Van den Eyne, 2013).

Psychotherapy

Behavioral, cognitive, and combined cognitive-behavioral therapies have demonstrated efficacy in the treatment of OCD. Exposure and response (ritual) prevention (ERP) is a behavioral treatment in which patients are exposed to situations which normally elicit distress, while compulsions (rituals) are resisted or prevented (Abramowitz, 2006; Steketee & Barlow, 2002). In contemporary practice, ERP involves "therapist-guided, systematic, repeated, and prolonged exposure to situations that provoke obsessional fear, along with abstinence from compulsive behaviors" (Abramowitz, 2006, p. 409). Several meta-analyses have found that ERP produces large and significant reductions in OCD symptoms (Abramowitz, 1997; Abramowitz, Franklin, & Foa, 2002).

Cognitive therapies for OCD focus on identifying and challenging the beliefs that support patients' OCD behaviors and correcting problematic beliefs (Steketee & Barlow, 2002; Wilhelm & Steketee, 2006). An early meta-analysis of cognitive-behavioral interventions for OCD found that the effect of cognitive interventions was not reliably different from zero, but this null finding was attributed this to the small number of studies directly assessing cognitive interventions (Abramowitz et al., 2002). More recently, a meta-analysis of 16 randomized controlled trials of cognitive-behavioral interventions for OCD found no difference in efficacy between

interventions using ERP and those using primarily cognitive interventions; both interventions produced clinically significant reductions in OCD symptoms (Olatunji, Davis, Powers, & Smits, 2013). Thus, ERP has been classified as a “well-established treatment” for OCD, while cognitive therapy has been classified as a “probably efficacious treatment” (Chambless et al., 1998; DeRubeis & Crits-Cristoph, 1998). ERP is generally considered the first-line treatment for adults (NICE, 2005) and children (Geller et al., 2012) with OCD. In the case of severe, treatment-refractory pediatric OCD, concurrent psychopharmacological treatment with SSRIs is also recommended (Geller et al., 2012).

D-cycloserine (DCS), an antibiotic that operates on a specific glutamate receptor, has been used to augment CBT for OCD and several anxiety disorders. Preliminary evidence suggests that, although DCS does not appear to alter long-term outcomes, it may reduce the number of sessions required for successful extinction learning and, correspondingly, symptom reduction (Abramowitz, Taylor, & McKay, 2009; Wilhelm et al., 2008).

Surprisingly, we found only a single study that directly investigated gender differences in treatment response for OCD, although a number of studies have examined gender as a moderator of treatment response. In a study of predictors of response to intense residential treatment for individuals with severe OCD, Stewart and colleagues (2006) found that men were significantly less likely to be classified as treatment responders than women. A meta-analysis of 16 studies of CBT for OCD found that the percentage of females in each study was not significantly associated with effect size (Olatunji et al., 2013). As psychotherapy outcome studies are often underpowered to detect gender differences in treatment response, it is currently unclear whether there are gender differences in the efficacy of ERP for OCD.

Although few studies have investigated treatments specific to perinatal populations with OCD, there is no theoretical basis to believe that OCD in perinatal samples should respond differently to established treatments for OCD (Abramowitz, Schwartz, & Moore, 2003). In the only existing randomized controlled trial in this population, Timpano and colleagues (2011) found that a cognitive-behavioral prevention program for pregnant women at-risk for OCD resulted in significant reductions in obsessions and compulsions during the first 6 months postpartum. Case studies have also demonstrated successful treatment of perinatal OCD with CBT, either as a standalone treatment (Christian & Storch, 2009) or with adjunctive pharmacotherapy (Flosnik & Khin, 2012).

Several studies and meta-analyses have evaluated the utility of combined treatment (i.e., ERP plus pharmacotherapy) for OCD. A recent meta-analysis suggests that ERP alone is as effective as ERP plus pharmacotherapy for the treatment of pediatric OCD; both approaches were superior to pharmacotherapy alone (Sánchez-Meca et al., 2014). In adults, a meta-analysis of four studies comparing combined ERP and serotonergic pharmacotherapy to pharmacotherapy alone suggested a small but significant benefit of combined treatment over ERP alone, while ERP alone and combined treatment were both superior to pharmacotherapy alone (Tolin, 2012). These results suggest that, when available, ERP should be the front-line treatment for OCD, but that the addition of SSRIs or other serotonergic medications may also be of some benefit.

Conclusions

A small but growing body of research suggests several differences in the prevalence, clinical features, and genetic underpinnings of OCD. In pediatric samples, OCD is twice as common in males than females, corresponding to an earlier age of onset in males than females. In adult community samples, the gender distribution is roughly equal, whereas treatment-seeking

samples are characterized by a slightly higher percentage of women. Phenomenologically, women are more likely than men to report cleaning and contamination obsessions, particularly in the context of perinatal OCD, whereas men are more likely to report sexual and symmetry-related obsessions. Patterns of comorbidity correspond to commonly-observed gender differences in other disorders; for example, men with OCD are more likely to experience comorbid substance-related disorders, whereas women more commonly experience comorbid mood and anxiety disorders. Corresponding to these epidemiological and phenomenological differences, genetic research hints at sex differences in the genetic underpinnings of OCD. Few gender-related differences in OCD treatment responsivity have been identified. As such, cognitive-behavioral therapy and pharmacotherapy with SSRIs are considered front-line treatments for OCD irrespective of gender.

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