REVIEW ARTICLE

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Obsessive-Compulsive Disorder

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UNLABELED USE OF PRODUCTS/INVESTIGATIONAL USE DISCLOSURE:
Drs Richter and Ramos discuss the unlabeled/investigational use of neuromodulation technology (deep brain stimulation, electroconvulsive therapy, and repetitive transcranial magnetic stimulation) and pharmacologic agents (citalopram, escitalopram, desvenlafaxine, duloxetine, mirtazapine, and venlafaxine) for the treatment of obsessive-compulsive disorder (some of which are approved for use in depression and psychosis).

ABSTRACT

PURPOSE OF REVIEW: This article reviews current knowledge regarding diagnosis, pathophysiology, and treatment trends in obsessive-compulsive disorder (OCD), a severe, underrecognized, and chronic condition frequently encountered in neurologic practice.

RECENT FINDINGS: With a lifetime prevalence estimated at 2.5%, OCD is a common condition that can also present comorbidly with neurologic disease. The core symptoms of OCD are obsessions and compulsions. Obsessions are intrusive repetitive thoughts, urges, images, or impulses that trigger anxiety and that the individual is not able to suppress. Compulsions are repetitive behaviors or mental acts occurring in response to an obsession with the intention of reducing the distress caused by obsessions. Neuroimaging, neuropsychological, and pharmacologic studies suggest that the expression of OCD symptoms is associated with dysfunction in a cortico-striato-thalamo-cortical circuit. Evidence-based treatments for OCD comprise pharmacotherapy and cognitive-behavioral therapy. Selective serotonin reuptake inhibitors (SSRIs) are the first-line drugs recommended for OCD, but significant differences exist in their use for OCD compared to their use for other mood and anxiety conditions, including the need for higher dosage, longer trials necessitated by a longer lag for therapeutic response, and typically lower response rates. Cognitive-behavioral therapy, based on the principles of exposure and response prevention, shows results superior to pharmacologic treatments with lower relapse rates on long-term follow-up and thus should be considered in the treatment plan of every patient with OCD.

SUMMARY: OCD and obsessive-compulsive symptoms are frequently encountered in the neurologic clinic setting and require a high index of suspicion to effectively screen for them and an illness-specific therapeutic approach.

INTRODUCTION

Obsessive-compulsive disorder (OCD) is a severe and relatively common psychiatric condition but still is underrecognized and undertreated.[1,2] The lifetime prevalence for OCD is estimated at 1% to 3% in adults[3,4] and adolescents,[5] but it is far more frequently encountered in general psychiatric and medical practice than these figures suggest because of its chronicity. The age of onset of OCD reported by patients shows a bimodal pattern, with symptoms appearing

during childhood/adolescence more frequently in males and in early adulthood in women.[6] It has been suggested that only 14% to 56% of patients seek treatment, and recognition and diagnosis is typically delayed by 8 to 10 years.[7] The diagnosis of OCD symptoms is frequently challenging, and management requires a unique approach, with specific adaptations in pharmacologic and psychotherapeutic treatments when compared to mood or other anxiety disorders.

DIAGNOSIS AND PSYCHIATRIC CLASSIFICATION

The cardinal features of OCD are obsessions and compulsions. Obsessions are defined as intrusive repetitive thoughts, urges, images, or impulses that trigger anxiety and that the individual is not able to suppress. Compulsions are repetitive behaviors or mental acts that occur in response to an obsession or must be done according to rigidly applied rules and are intended to reduce the distress caused by obsessions. However, OCD is heterogeneous, and its symptom profile may vary widely between patients who meet the diagnostic criteria. TABLE 8-1 describes examples of common obsessions and compulsions.[8] To make the diagnosis, the illness must be severe enough to cause significant distress, waste at least 1 hour of time per day, or cause significant interference in functioning.

Examples of Common Obsessions and Compulsions[a] TABLE 8-1

	Descriptions/Examples
Obsessions	
Contamination	Concerns about dirt, germs, body waste, illness
Symmetry	Needing things "just so," even, or lined up a certain arbitrary way
Aggressive	Most commonly focused on inadvertent harm, such as being responsible for a fire or break-in; also includes horrific thoughts or images of deliberately harming others, such as stabbing a loved one or pushing a stranger in front of a car
Sexual	Disturbing sexual thoughts that are not consistent with an individual's orientation or cultural norms, such as someone with a same-sex preference having unpleasant hetero-erotic thoughts or unwanted inappropriate sexual thoughts about children
Religious	Examples include thoughts about selling one's soul to the devil, deliberately thinking inappropriate thoughts about major religious figures, or committing mortal sins
Somatic	Exaggerated fears of contracting a serious illness such as hepatitis or a brain tumor in the absence of any identifiable high risk
Compulsions	
Washing	Excessive hand washing, showering, or cleaning activities
Checking	Repeatedly turning the stove on and off; rereading all emails to ensure content is appropriate; driving around the block to ensure did not hit someone; asking for repeated reassurance
Ordering	Folding clothes "just so" or arranging all cans in the cupboard so the labels are facing out
Counting	Performing actions a certain arbitrary number of times, such as tapping each foot 4 times when getting out of bed
Repeating	Repeatedly going up and down the stairs or flushing the toilet; typically done to cancel out a bad thought or until it feels "right"

[a] Reprinted with permission from Richter PM, Selchen S.[8] © 2018 Centre for Addiction and Mental Health.

The *Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition* (*DSM-5*) also includes two important specifiers (extensions to the diagnostic criteria used to clarify important features of the diagnosis) for OCD.[9] First, individuals with OCD may present with a range of insight into their disorder-related beliefs, including good or fair insight, poor insight, and absent insight/delusional beliefs (complete conviction that OCD beliefs are true). The second specifier identifies the presence of tic-related symptoms and is justified by evidence that individuals with comorbid tic disorders differ from other patients with OCD in relation to comorbidities, course, pattern of familial transmission, treatment, and potentially etiology based on genetic studies.[10]

OCD was historically classified with the anxiety disorders, but in the *DSM-5*, it was moved to its own new category called "Obsessive-Compulsive and Related Disorders," which includes conditions characterized by specific types of preoccupations or repetitive behaviors.[9] This change reflects the observations that anxiety is not necessarily a core component of OCD and that, for many individuals, avoidant behavior can minimize anxiety and become a major driver of the illness.[10] While all of these disorders have some similarities in their clinical features, it is important to distinguish them from one another because of significant differences in treatment.

Hoarding disorder is characterized by the accumulation of excessive belongings unrelated to their value (ie, not exclusively related to their having perceived monetary worth) and difficulty discarding them because of associated anxiety and the need to save items. Many individuals affected by hoarding disorder also have difficulty with excessive acquisition of goods. Hoarding disorder is frequently associated with poor insight; accordingly, many individuals affected by this condition may deny any significant distress or impairment in functioning. However, the *DSM-5* criteria allow for diagnosis if the accumulation of belongings results in an unsafe environment for patients or those around them. Safety hazards resulting from hoarding disorder may include the risk of fires, infestations (ie, insects or rodents), mold and air quality issues (which can exacerbate lung disease), risk of falls, and inability for emergency services to access the patient's residence.[11] Although historically individuals presenting with hoarding difficulties were often given the diagnosis of OCD, hoarding disorder is now a separate formal diagnosis and should be distinguished from OCD as significant differences exist in terms of treatment approaches.

Other key disorders in the *DSM-5* group "Obsessive-Compulsive and Related Disorders" include body dysmorphic disorder, defined by the preoccupation with one or more perceived defects or flaws in physical appearance that are not observable by or appear slight to others; excoriation (skin-picking) disorder, defined by recurrent skin picking resulting in lesions; and trichotillomania (hair-pulling) disorder, defined by the recurrent pulling out of hair resulting in hair loss.[9] Both of these latter conditions (hairpulling/skin picking) are also associated with repeated attempts to reduce or stop the behavior. This diagnostic group also includes substance- and medication-induced obsessive-compulsive and related disorder and obsessive-compulsive and related disorder due to another medical condition.[12,13]

DIFFERENTIAL DIAGNOSIS

The variability of OCD symptoms can make it harder to differentiate OCD from other conditions. While most clinicians will readily recognize OCD in

individuals who check excessively for mistakes or who wash repeatedly because of contamination concerns, other patients may simply repeat actions over and over and not volunteer obsessional content, express excessive concern about contracting a serious illness, or relate obsessions with frankly bizarre content, such as a fear of losing a body part or being in another dimension. Thus, OCD may resemble a number of other psychiatric and neurologic conditions, such as psychosis, illness anxiety disorder, and stereotypic movement disorder.

Psychiatric Conditions

The differentiation between OCD and other OCD-related disorders is based on specific differences in content and character of thought processes and behaviors. In body dysmorphic disorder, the focus is exclusively on perceived defect(s) in the individual's appearance, both in terms of thoughts and any repetitive behaviors (eg, checking appearance in mirrors, seeking reassurance, or time-consuming grooming behaviors). Hoarding disorder is exclusively about difficulty with discarding and the accumulation of belongings that results from this. In trichotillomania and excoriation disorders, the focus is on repetitive hair pulling or skin picking, respectively, and not accompanied by triggering obsessions. It is important to distinguish between these conditions as significant differences exist in the treatment approach. They can also frequently occur comorbidly in individuals presenting with OCD.

Although individuals with anxiety disorders may report recurrent thoughts or worries, these are typically about readily understandable real-life concerns. For example, individuals with generalized anxiety disorder may express excessive worries about losing their job or about the health and welfare of their family members. In social phobia, the content is focused on exaggerated but understandable concerns about embarrassing themselves in social interactions. By contrast, obsessions are typically either very exaggerated or about unrealistic or irrational concerns and will usually be accompanied by compulsions. Depressed individuals may also express ruminations that are typically mood-congruent and not usually experienced as intrusive. These ruminations are thus not considered to be obsessions.

Other frequent differential psychiatric diagnoses include:

- **Eating disorders, in which preoccupations are exclusively focused on food, weight, or body image.**
- **Illness anxiety disorder, which is characterized by recurring thoughts that are exclusively related to fear of currently having a serious disease. By contrast, in individuals with somatic obsessions, the concern is typically about contracting the illness in the future, and other obsessional content will also be present.**
- **Tic disorders, which are characterized by sudden, rapid, recurrent, nonrhythmic behaviors (eg, blinking, touching, grimacing, or sniffing) that are not triggered by obsessions.**
- **Psychotic disorders, which must be differentiated from patients with OCD with poor insight or from patients with OCD who may be delusional regarding the obsessions but do not display hallucinations or formal thought disorder.**
- **Obsessive-compulsive personality disorder, which, despite the similarity in name, is not directly related to OCD. The personality disorder is characterized by a long-standing pattern of perfectionism and rigidity but will be perceived by the individual as appropriate, rather than reported as intrusive in the way that obsessions are experienced. These individuals will not have frank obsessions or compulsions.**

KEY POINTS

- **The lifetime prevalence for obsessive-compulsive disorder is estimated at 1% to 3%, with a bimodal pattern of onset; symptoms start during childhood/adolescence more frequently in males, while early adulthood onset is more common among women.**
- **Obsessions are intrusive repetitive thoughts, urges, images, or impulses that trigger anxiety and that the individual is not able to suppress.**
- **Compulsions are repetitive behaviors or mental acts occurring in response to an obsession that must be done according to rigid rules to reduce the distress caused by obsessions.**
- **Patients with obsessive-compulsive disorder can present with variable insight, ranging from good insight with full appreciation of the excessive/irrational nature of the symptoms to frankly delusional.**
- ***The Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition* (*DSM-5*) lists obsessive-compulsive disorder in the category "Obsessive-Compulsive and Related Disorders," which also includes hoarding disorder, body dysmorphic disorder, excoriation (skin-picking) disorder, and trichotillomania (hair-pulling) disorder.**
- **Individuals presenting exclusively with hoarding difficulties in the absence of frank obsessions or compulsions should not be diagnosed with obsessive-compulsive disorder but rather with hoarding disorder.**

KEY POINTS

- It is important to differentiate between obsessive-compulsive disorder and the obsessive-compulsive–related disorders as significant differences in the treatment approach are needed for each of these conditions.
- Obsessive-compulsive disorder is a frequent comorbid condition in Huntington disease, stroke, Parkinson disease, Sydenham chorea, traumatic brain injury, and Tourette syndrome.

Neurologic Conditions

Symptoms resembling OCD features can be found in some neurologic conditions. Huntington disease, an autosomal dominant neurodegenerative disease characterized by cognitive deterioration and progressive motor abnormalities, is associated with a higher occurrence of OCD symptoms that tend to become more severe with the progression of the disease.[14] Van Duijn and colleagues,[15] for example, found obsessive-compulsive behaviors in 13.2% of 1993 Huntington disease mutation carriers independent from the Huntington disease stage. Although obsessive-compulsive symptoms observed in Huntington disease will not necessarily be severe enough to fulfill *DSM-5* criteria for OCD, they may be incapacitating and poorly responsive to cognitive-behavioral therapy, leaving treatment with selective serotonin reuptake inhibitors (SSRIs) as the better therapeutic option.[16]

OCD, generalized anxiety disorder, and phobic disorders are among the most frequently observed psychiatric complications after stroke. In one of the few studies to specifically explore anxiety disorders poststroke, Cumming and colleagues[17] studied 149 stroke survivors assessed at 20 months poststroke and found symptoms compatible with the diagnosis of OCD in 9% of patients compared with a prevalence of 2% in a control group. OCD is also a frequent psychiatric complication of traumatic brain injuries, along with depression, substance abuse, and psychosis (CASE 8-1).[18]

Patients with Parkinson disease can show a peculiar behavior known as punding, which can be misidentified as an OCD feature.[19] Punding is described as a complex, prolonged, purposeless, and stereotyped behavior; it is usually experienced as comforting, but its interruption can result in anger. Punding is described as a symptom of Parkinson disease, but it can also be induced by antiparkinsonian medications and quetiapine.[20] It is important to be aware that atypical antipsychotics can also induce or exacerbate preexisting true OCD independently of the presence of punding symptoms. The most significant culprit is clozapine; however, problems can also arise reasonably frequently with olanzapine and, on occasion, other drugs in this category.[21] As neuroleptics are occasionally used in individuals with Parkinson disease, this will be seen not infrequently and may then warrant consideration of treatment targeting the comorbid OCD.

Sydenham chorea is particularly interesting as it was observed that virtually all patients will develop OCD symptoms early in the illness.[22,23] This close relationship is attributed to the underlying mechanism, which is an autoimmune response to streptococcal infection leading to inflammation in the basal ganglia, a brain region strongly implicated in the neurobiology of OCD.[24] This has also led to a proposed and somewhat controversial autoimmune syndrome underlying cases of early-onset OCD, termed *pediatric autoimmune neuropsychiatric disorders associated with streptococcal infections* (PANDAS). PANDAS criteria focus on the abrupt onset of OCD or tics and require demonstrable association with streptococcal infection, but the term has recently been broadened to *pediatric acute-onset neuropsychiatric syndrome* (PANS), which is similar but notes the illness may start with infectious triggers other than streptococcal. Both may be associated with neurologic changes, such as choreiform or other abnormal movements, behavioral regression, sensory or motor abnormalities, and somatic signs such as enuresis or sleep disturbance. In a 2017 large-scale population-based study of more than 1,000,000 children, Orlovska and colleagues[25] found that individuals with a streptococcal throat infection within the previous 17 years had

elevated risks of all mental disorders but particularly OCD and tic disorders (incidence rate ratios of 1.51 [95% confidence interval, 1.28 to 1.77] for OCD and 1.35 [95% confidence interval, 1.21 to 1.50] for tic disorders). However, they also found that children with a history of multiple nonstreptococcal infections showed increased risks for OCD and other psychiatric mental disorders as well, although less than in those who were streptococcal positive.

Tourette syndrome is a childhood-onset neurodevelopmental disorder that usually develops before 10 years of age and improves with age. The hallmarks of Tourette syndrome are motor tics such as blinking or grimacing, typically showing a rostral-caudal progression, and phonic tics such as grunting and throat clearing, but can include coprolalia (swearing tics). Complex tics and self-injurious behaviors can also be present. Tourette syndrome symptoms may resemble OCD rituals, especially "ticlike" compulsions such as touching, tapping, rubbing, and repeating routine activities. However, tics are not triggered by clear obsessions, are more severe, and frequently have a greater impact on social development.[26]

CASE 8-1

A 60-year-old man presented with an 8-year history of compulsive behaviors in the context of a variety of neurologic symptoms. He felt compelled to eliminate all rocks from his large 1-acre garden; in his effort to do this, he dug a trench 4 feet wide, 22 feet long, and 2 feet deep over a period of several years. He spent most of his waking hours on this project, describing any efforts to stop as anxiety provoking. He had started washing and waxing his car daily, including the motor. He also had random intrusive thoughts that he might have run someone over in his car. His obsessive-compulsive disorder symptoms started at the same time as marked memory difficulties, making it difficult for him to find his way home, and he reported chronologic confusion, interruptions in his speech, occasional clumsiness and difficulties buttoning his shirts, and an erratic sleep pattern of sleeping up to 20 hours a day for months on end, followed by prolonged periods of sleeping less than 5 hours a night. His medical history was significant for hypertension and hypercholesterolemia.

On examination, he was noted to have complex cognitive deficits and a dysexecutive syndrome. Serial MRIs over a period of several years had demonstrated diffuse cortical atrophy and a number of deep brain infarctions, and brain single-photon emission computed tomography (SPECT) showed mild to moderate decreased activity in the mesial temporal regions.

He was prescribed fluoxetine to a maximum of 80 mg/d, which resulted in significant improvement in his compulsive symptoms. Unfortunately, his neurocognitive decline continued, and he was eventually diagnosed with corticobasal syndrome and lost to follow-up.

COMMENT

This case illustrates how obsessive-compulsive disorder–like features may develop secondary to a neurodegenerative disease and may nonetheless respond to treatment with serotonergic antidepressants.

NEUROBIOLOGICAL BASIS

Current hypotheses concerning the neurobiological basis of OCD are derived from neuroimaging, neuropsychological, and pharmacologic research. The most influential model postulates that dysfunction in a cortico-striato-thalamo-cortical loop leads physiologically to expression of OCD behaviors and is based on imbalance between glutamatergically mediated excitatory and γ-aminobutyric acid-mediated (GABA-ergic) inhibitory control mechanisms in this frontostriatal circuit.[27,28] FIGURE 8-1 depicts this model, summarizing its anatomic and functional components. According to this hypothesis, OCD symptoms are not necessarily due to a dysfunction or lesion of a specific brain region but caused by imbalances in the interactions among these different structures, including links to the amygdala, which is involved in the affective modulation of OCD behaviors.

Neuroimaging Studies

Overall, studies with positron emission tomography (PET) and single-photon emission computed tomography (SPECT) show increased activity in the anterior cingulate cortices in patients with OCD[29–31] as well as different patterns of activation in the caudate.[31] These changes are frequently reduced or absent after treatment with drugs or cognitive-behavioral therapy, and evidence suggests that lower activity in the orbitofrontal cortex pretreatment predicts better response to serotonergic reuptake inhibitors.[32,33] Abnormalities in the posterior cingulate cortex also seem to correlate with a better response to treatment with fluvoxamine.[32]

In addition, symptom provocation studies show increased brain activity in the anterior/lateral orbitofrontal cortex and anterior cingulate cortex[34] and reduced recruiting of the striatum, usually involved in tasks such as serial reaction time tasks.[35] Functional studies also suggest that individuals with OCD rely on the

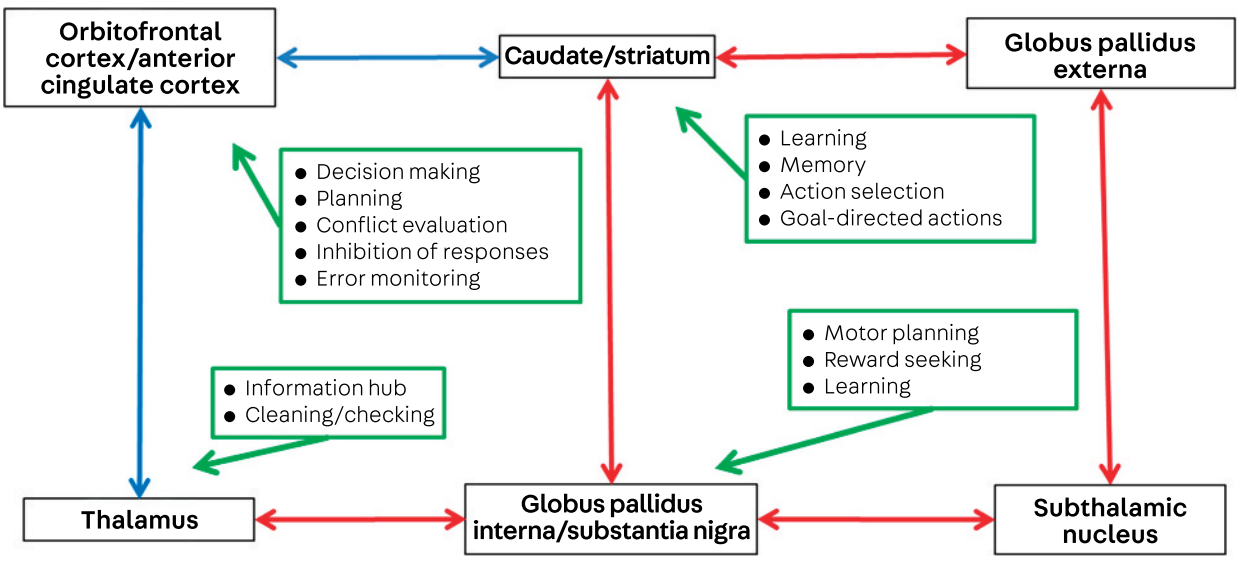

FIGURE 8-1

Schematic of the neurocircuitry of obsessive-compulsive disorder. *Blue arrows* depict glutamate (excitatory) and *red arrows* depict γ-aminobutyric acid–mediated (GABA-ergic) (inhibiting) pathways. *Green boxes* show neurocognitive functions ascribed to each brain structure that are relevant to obsessive-compulsive disorder.

frontotemporal circuits for explicit information-processing strategies to compensate for possible frontostriatal dysfunction associated with implicit information-processing deficits.[36]

Corticostriatal network dysfunction has been reported in children and adolescents with OCD. On inhibition tasks such as go/no-go tasks, adolescents with OCD show reduced activation in brain regions connected via the inferior and orbital fronto-striato-thalamic pathways compared to controls. The inhibition of response in the OCD group was also associated with reduction in activation of the mesial and dorsolateral prefrontal cortex, including the anterior cingulate gyrus. Besides confirming the involvement of a frontostriatal network during motor response inhibition, these studies suggest that tasks requiring more cognitive forms of inhibitory control, including selective and flexible use of attention, are associated with abnormalities in extrafrontal temporal, parietal, and cerebellar brain regions.[37,38]

Newer imaging techniques have corroborated the relevance of the fronto-striato-thalamic model for OCD. Using resting-state functional MRI (fMRI) to evaluate functional connectivity in unmedicated patients with OCD, Zhang and colleagues[39] found reduced functional connectivity between the rostral anterior cingulate cortex and the dorsolateral prefrontal cortex as well as increased connectivity between the dorsal anterior cingulate cortex and caudate. The magnitude of these alterations was shown to correlate with total scores on the Yale-Brown Obsessive Compulsive Scale (Y-BOCS),[40] the most widely used severity rating scale for OCD. Moreover, pretreatment resting-state fMRI may enable prediction of response to cognitive-behavioral therapy[41] and maintenance of gains 1 year later.[42]

It has been questioned if the heterogeneity of OCD symptoms may limit the applicability of general pathophysiologic models, and numerous authors have suggested these differences should be considered in the interpretation of functional studies. Factorial analysis supports a four-factor model of OCD symptoms, generating separate symptom dimensions of harm obsessions and checking, symmetry and ordering, cleanliness and washing, and hoarding.[43,44] These factors seem to be relatively stable over time,[29] have differential responses to treatment,[45] may differ in terms of genetics/heritability,[46,47] and are associated with different patterns of regional brain function in neuroimaging studies.[48] However, to date, relatively few OCD studies have incorporated testing of these dimensions.

In summary, substantial evidence exists for involvement of a cortico-striato-thalamo-cortical loop in OCD, whether through structural imaging studies or, more commonly, functional imaging using a variety of technologies. However, notwithstanding these findings as well as work suggesting that pretreatment imaging may correlate with response to treatment, routine imaging is not, as yet, recommended for evaluation of individuals with OCD as large interindividual variability limits current clinical utility.

Neuropsychology

Although the uncertainties, doubts, and ritualistic repetitions found in almost all patients suggest a common dysfunctional cognitive component in OCD, neuropsychological investigations frequently show inconsistent results.[49] Deficits in executive functions, processing speed, visuospatial abilities, nonverbal memory, and working memory have been reported in meta-analyses,[50,51] but

KEY POINTS

- **Neuroimaging and neuropsychological studies suggest that the expression of obsessive-compulsive disorder symptoms is associated with dysfunction in a cortico-striato-thalamo-cortical circuit.**
- **Neuroimaging is not currently recommended routinely for evaluation of individuals with obsessive-compulsive disorder.**

some of these findings may be secondary to deficits in spontaneously initiating verbal organization strategies during information-encoding processes and do not necessarily reflect other specific cognitive deficits.[52,53]

Attention is a key function involved in the modulation of other cognitive activities. In individuals with OCD, deficits in focused and sustained attention and trends toward deficits in selective and divided attention paradigms are frequently reported.[49] Repetitiveness and rigidity are characteristic of OCD and have led to the hypothesis that these individuals have reduced ability to change their behaviors following contextual changes. In fact, cognitive flexibility as measured by the Wisconsin Card Sorting Test seems to be reduced in OCD.[53] However, some new paradigms, such as reversal learning and task switching, suggest that the impaired performance in OCD may be due to differences in reaction times and not in response errors, a finding that correlates with symptom intensity and suggests a peculiar pattern of retardation in cognitive functioning in these patients.[49]

Deficits in inhibitory mechanisms have also been investigated in a variety of ways. The cognitive component of behavioral inhibition as evaluated through the Stroop task (measuring interference in reaction time when naming the font color of color words printed in the same color as the word [such as the word *blue* printed in blue] as compared to a different or incongruent color [such as the word *blue* printed in green]) shows a trend for poorer performance in patients with OCD. These individuals also show impaired inhibitory capacity in motor responses as evaluated by the stop-signal task, in which subjects have to inhibit an already initiated response after the appearance of a stop cue.[54] Planning and decision making were studied in OCD because of the apparent reduced capacity for making choices and organizing new activities observed in these patients. Again, inconsistent results have been reported, probably because of the use of gambling experimental paradigms, such as the Iowa Gambling Task and the Cambridge Gambling Task, that may not be specific enough for evaluating cognitive processes specifically associated with OCD.[49]

In summary, a burgeoning literature is emerging around the patterns of neurocognitive deficits associated with OCD, including difficulties in set-shifting and response inhibition (both cognitive and motoric) and memory deficits. It has been suggested that these may represent helpful endophenotypes for etiologic research going forward. Despite the evidence supporting some degree of cognitive abnormalities in OCD, currently no clear indication exists for doing neuropsychological evaluations routinely as part of the assessment of these patients, although it will be interesting to see if specific targeted cognitive remediation strategies may prove helpful in the future.

TREATMENT

A number of published guidelines exist for OCD from organizations including the Canadian Psychiatric Association, American Psychiatric Association, and National Institute for Health and Care Excellence (UK).[55–57] The most recent at the time of this writing are the Canadian Clinical Practice Guidelines for OCD, published in 2014.[58] The recognized first-line options for OCD are pharmacotherapy with SSRIs and cognitive-behavioral therapy. While these modalities are used broadly for the treatment of mood and anxiety, a number of key differences should be kept in mind when applying them to individuals with OCD.

Psychoeducation

Psychoeducation is vital for patients with OCD and should ideally be provided before beginning any program of treatment. Individuals with OCD may often be laboring under the belief that they are alone in having "ridiculous" or "horrible" (eg, violent or sexual) thoughts. It is, therefore, very important to normalize and destigmatize from the beginning by explaining that we all have bizarre or inappropriate thoughts crossing our minds routinely and that no one can control their thoughts to prevent this.

Pharmacotherapy

Good Level 1 evidence exists for the use of all the SSRIs in the treatment of OCD.[55,59] Although citalopram and escitalopram are off-label for OCD in the United States, head-to-head trials do not demonstrate any significant differences between SSRIs, suggesting all are essentially equivalent in their efficacy.[60,61] These medications have the advantage of also working on mood and anxiety disorders, which are so often comorbid with OCD. Two major distinctions exist in the way these medications should be used for OCD as compared to depression. First, dosing is generally most effective at the upper end of the recommended range; as a result, the recommended target dose typically exceeds the dose used for depression.[62] Second, the therapeutic lag is longer before benefits are seen in OCD, generally 6 to 10 weeks.

For these reasons, it is generally best to discuss the treatment approach and target dose with patients, stressing that they are most likely to achieve the best response if they aim for the upper end of the dose range or until significant side effects occur, after which it will be important to allow at least a further 6 to 10 weeks to assess response. Using this approach, it is recommended that drug trials in OCD continue for 12 weeks or more before considering changing to another drug. Alternatively, lower doses in the typical depression range can be tried, but should this prove ineffective, it may necessitate a far lengthier trial as the dose will then need to be increased and require a further 2 to 3 months to assess therapeutic response.

The recommended maximum/target dose for citalopram in OCD is 60 mg/d to 80 mg/d. This exceeds both US Food and Drug Administration (FDA) and Health Canada recommendations not to exceed 40 mg/d because of the risk of cardiac QTc prolongation[63,64]; however, the impact of this medication on cardiac conduction is typically modest and can be managed easily with serial ECG monitoring. Escitalopram carries a similar warning in Canada[65] for doses exceeding 20 mg/d, notwithstanding evidence in OCD for best efficacy at doses up to 40 mg/d. Both carry recommendations regarding dosage in older populations; the maximum recommended dose of citalopram is 20 mg/d in those 65 years of age or older according to Health Canada or those older than 60 years of age according to the FDA.[63] For escitalopram, it is recommended not to exceed 10 mg/d in those 65 and older (Health Canada) or those older than 60 years of age in the United States (FDA) (TABLE 8-2).[66]

Most patients on SSRIs achieve modest improvement in OCD, with a reduction in severity of 25% to 35% considered a treatment response. Approximately 60% of patients will typically respond to the first medication tried, leaving many individuals unresponsive and requiring a trial of at least a second SSRI[67] and eventually consideration of second-line agents. If a second SSRI fails, most guidelines recommend moving on to a second-line option, such as clomipramine

KEY POINTS

- **Obsessive-compulsive disorder is associated with a cluster of neurocognitive deficits, including difficulties in set-shifting and response inhibition.**
- **Psychoeducation is crucial in treating patients with obsessive-compulsive disorder because of the stigma associated with the illness and the general lack of knowledge in the community and because it will enhance treatment compliance.**
- **Selective serotonin reuptake inhibitors are the first-line pharmacologic treatment for obsessive-compulsive disorder. They are generally very safe and well tolerated and will also work for the mood and anxiety disorders frequently comorbid with obsessive-compulsive disorder.**
- **Pharmacologic treatment of obsessive-compulsive disorder distinctly differs from other mood and anxiety disorders, requiring a higher dose for the best likelihood of response and longer trials to accommodate the longer therapeutic lag (typically 6 to 10 weeks) in obsessive-compulsive disorder.**

or the serotonin norepinephrine reuptake inhibitor (SNRI) venlafaxine. Clomipramine has long been considered the gold-standard medication for OCD based on efficacy, but it is relegated to second line in treatment guidelines because of its more challenging side effect profile, impact on cardiac conduction and seizure threshold, and toxicity in case of overdose. However, it is still strongly recommended for patients for whom two or more SSRIs have failed.[60] Monitoring of blood levels may reduce these risks but has never been systematically evaluated. Clomipramine is also sometimes used as an augmentation agent in combination with SSRIs, typically starting at low doses and proceeding more cautiously to reduce risks, but, again, no controlled trials support this strategy.[10] Desvenlafaxine is the active metabolite of venlafaxine and, as such, would be expected to have efficacy similar to the parent compound, but as yet no controlled trials have been published in OCD. The SNRI duloxetine is similarly considered to be a second-line agent as several recent studies have supported its effectiveness.[68,69] Mirtazapine has also been listed as an alternative second-line treatment in US and Canadian (but not UK) treatment guidelines.

It is generally recommended that pharmacologic treatment be continued for at least 1 year, as a very significant relapse risk exists with early discontinuation. Most experts suggest referral for cognitive-behavioral therapy, if this is available, to reduce the risk of relapse for patients hoping to eventually come off medication.

TABLE 8-2

Medications Recommended for the Treatment of Obsessive-Compulsive Disorder

Medications	Recommended Starting Dose	Recommended Dose Range
First-line		
Fluoxetine	20 mg/d	20–80 mg/d
Fluvoxamine	50 mg/d	150–300 mg/d
Sertraline	50 mg/d	100–200 mg/d
Paroxetine	20 mg/d	20–60 mg/d
Citalopram	20 mg/d	20–80 mg/d[a]
Escitalopram	10 mg/d	10–40 mg/d[b]
Second-line		
Clomipramine	50 mg/d	150–250 mg/d
Venlafaxine	37.5 mg/d	75–325 mg/d
Venlafaxine ER	37.5 mg/d	75–225 mg/d
Desvenlafaxine	50 mg/d	100–200 mg/d
Mirtazapine	30 mg/d	30–45 mg/d
Duloxetine	60 mg/d	120 mg/d

[a] The US Food and Drug Administration (FDA) and Health Canada advise 40 mg/d or less.
[b] Health Canada advises 20 mg/d or less. For escitalopram, it is recommended not to exceed 10 mg/d in those 65 and older (Health Canada) or those older than 60 years of age in the United States (FDA).

In patients with very severe illness or for whom a number of medications have previously failed, many suggest long-term continuation of an effective medication for maintenance of stability.

Another frequently recommended option is augmentation with atypical antipsychotics. While Level 1 evidence exists for this, in a randomized controlled trial of SSRI partial responders, patients remaining on their SSRI did far better when randomly assigned to receive the addition of cognitive-behavioral therapy as compared to augmentation with an atypical antipsychotic or placebo, raising a question about the efficacy of this alternative in clinical practice. Furthermore, long-term use of many atypical antipsychotics is associated with significant weight gain and metabolic and cardiovascular consequences and therefore requires regular monitoring, which may limit enthusiasm for this alternative. Regarding other commonly used psychotropics, clear evidence exists that bupropion, clonazepam, and other benzodiazepines do not work in OCD and should be avoided for this indication.

Psychotherapy

Cognitive-behavioral therapy is the most effective treatment in OCD and the only form of psychotherapy for which robust evidence exists in OCD. Behavioral therapy is a core component of cognitive-behavioral therapy and has long been regarded as a gold-standard treatment for OCD. It is based on the principles of exposure to anxiety-provoking triggers without performance of rituals (often termed *exposure and response prevention*). This is now generally combined with cognitive approaches in which the patient identifies and learns to modify exaggerated or maladaptive thoughts and beliefs. Specific cognitive-behavioral therapy approaches targeting OCD have been developed; in contrast, general cognitive-behavioral therapy as is taught for depression tends to be quite ineffective for OCD. For this reason, if referring a patient for treatment, it is important to ascertain if the therapist has had specific training in cognitive-behavioral therapy for OCD (CASE 8-2).

In practice, a number of factors must be taken into consideration in determining if cognitive-behavioral therapy is the best option for a given patient. Insight (ie, recognition that the OCD is excessive or unreasonable) is important, as those with poor insight may be unwilling to challenge their rituals. The extent of comorbid conditions should be considered; for example, mild depression may not be a barrier, but more severe depression or active suicidal ideation generally would be. Similarly, personality disorders, if significant, may also complicate cognitive-behavioral therapy. Motivation is, in many ways, the single biggest factor to consider. For cognitive-behavioral therapy to succeed, patients must be committed and actively engaged in therapy. Regular practice of homework is a key requirement for success.

The interaction between patients and their families can serve to maintain or worsen OCD symptoms. *Family accommodation* refers to how the family adapts their routines to enable the individual with OCD to avoid triggers or minimize rituals. Often family members will try to help their loved one by providing regular reassurance or by accommodating (eg, locking the front door when leaving together or doing decontamination rituals to satisfy their relative). These behaviors, although well intended, will unfortunately serve to maintain the obsessional fears. Family-based psychoeducation and interventions to reduce accommodation have been shown to effectively reduce OCD and should be integrated into cognitive-behavioral therapy.

KEY POINTS

- A lack of response or partial response is more common in obsessive-compulsive disorder than in other psychiatric conditions. In individuals who are unresponsive, guidelines suggest trying two different selective serotonin reuptake inhibitors sequentially, then moving on to a second-line option, such as clomipramine or venlafaxine. Augmentation with atypical antipsychotics is also an option.
- It is generally recommended that patients continue on medication for a minimum of 1 year after achieving a good therapeutic response, as obsessive-compulsive disorder is associated with a very high relapse rate following medication discontinuation.
- Cognitive-behavioral therapy is the most effective treatment in obsessive-compulsive disorder. It is based on the principles of exposure to anxiety-provoking triggers without performance of rituals (often referred to as *exposure and response prevention*).

Neuromodulatory Treatments

As OCD can be severe and often refractory to standard first- and second-line treatments, considerable work has been done exploring alternative biological therapies. Referral should be made to a tertiary care center with specific expertise in OCD for individuals with very severe illness or those who have failed conventional treatment, as neuromodulatory treatments with varying degrees of invasiveness may be helpful.

Repetitive transcranial magnetic stimulation has shown promise in a number of sham-controlled trials and meta-analyses, although at this point it is still considered experimental for OCD as considerable work remains in terms of determining the best brain target and other treatment parameters.[70] Study of the

CASE 8-2

A 35-year-old man working in customer relations presented to a psychiatric outpatient clinic reporting that he felt unable to cope. He gave a history of minor contamination concerns since his teens that became problematic over the past 10 years. He also reported disturbing thoughts about harm befalling his family members. He was particularly concerned that he might cause family members to become ill and die by inadvertently contaminating them with germs or toxins. He washed his hands at least 20 times a day with soap or using a hand sanitizer he carried with him everywhere. He spent 2 hours per day cleaning his house after work, following a 1-hour shower and change of clothes. During his washing rituals, he repeated each step in multiples of three or until it "felt right." Over the past 2 years as his rituals became more time-consuming, he began to avoid shaking hands, sharing pens and other objects in the office, and any physical contact with colleagues. He had begun to limit visits with his parents for fear of making them ill. He recognized that his concerns were likely irrational but felt unable to change his behavior. He reported feeling increasingly depressed, exhausted, and hopeless regarding his diminished quality of life over the past 6 months.

The patient was diagnosed with obsessive-compulsive disorder (OCD), and, following psychoeducation, he refused cognitive-behavioral therapy as he did not feel able to challenge his fears but agreed to medication. He was started on escitalopram 10 mg/d and increased to 20 mg/d a week later. He reported some improvement in mood within 2 weeks and in OCD symptoms after 6 weeks. After 3 months of treatment, his hand washes were down to 6 to 10 times a day, and his showers were completed in 20 minutes. He then agreed to a course of cognitive-behavioral therapy, following which his OCD symptoms became minor, with rituals occupying a maximum of 20 minutes a day with almost no avoidance.

COMMENT

This case illustrates the tendency of OCD to worsen over time. Depressive symptoms are also frequently found in these patients. The case also illustrates how both medications and cognitive-behavioral therapy may be needed for optimal outcomes.

application of transcranial direct current stimulation[71] in OCD is in its infancy but has shown promise. By contrast, psychosurgery has been in use and well-studied in OCD for many decades. The most common procedures are anterior cingulotomy and anterior capsulotomy; while both brain targets improve OCD symptoms (response rates are 41% and 54%, respectively[72]), capsulotomy is far more frequently associated with severe adverse events, including personality change. Deep brain stimulation has been put forward as an alternative to ablative neurosurgery, and studies using a number of brain targets have generally shown positive results in OCD, with fewer and milder adverse events.[73] The utility of electroconvulsive therapy in OCD is unclear; no controlled trials have been published, but a 2015 systematic review provided some support for benefits in 60% of reported cases.[74]

KEY POINT

- **For extremely severe and refractory cases, neuromodulatory treatments with varying degrees of invasiveness can be helpful for obsessive-compulsive disorder. Referral to a tertiary care center with specific expertise in obsessive-compulsive disorder should be sought for these individuals.**

CONCLUSION

It is reasonable to expect the busy neurologist to be aware of OCD and the related disorders and to have a high index of suspicion for this disorder. Neurologists should feel comfortable routinely screening for OCD symptoms, discussing a probable diagnosis of OCD, providing basic psychoeducation and directing patients to published support and self-help materials, initiating referral to specialized treatment providers when possible, and providing first-line pharmacologic treatment while awaiting assistance from specialists with OCD expertise.

USEFUL WEBSITES

INTERNATIONAL OCD FOUNDATION
The International OCD Foundation website provides booklets and fact sheets about OCD and lists OCD programs available for both the public and professionals.
iocdf.org

ANXIETY AND DEPRESSION ASSOCIATION OF AMERICA
The Anxiety and Depression Association of America website provides resources for understanding depression, anxiety, and stress; information about suicide prevention; and links for treatment and support.
adaa.org

FREDERICK W. THOMPSON ANXIETY DISORDERS CENTRE, TORONTO, ONTARIO, CANADA
The Frederick W. Thompson Anxiety Disorders Centre website offers a downloadable patient handbook and links to other useful websites and resources for patients and clinicians.
sunnybrook.ca/thompsoncentre

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