



OBSESSIVE—COMPULSIVE

DISORDER AND ITS SPECTRUM

STORCH • MCKAY



OBSESSIVE—COMPULSIVE DISORDER AND ITS SPECTRUM

A LIFE-SPAN APPROACH

EDITED BY

ERIC A. STORCH AND DEAN MCKAY

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A LITERATURE

ERIC A. STORCH

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This practical
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framework.

Storch and McKay, two of the foremost experts on obsessive-compulsive disorder (OCD), have produced the ultimate authoritative text on the topic. This book is a masterful collection of skillfully written chapters authored by the Who's Who in OCD research and therapy. It is an essential resource for anybody interested in OCD—students, researchers, clinicians, psychologists, social workers, and psychiatrists.

—STEFAN G. HOFMANN, PHD, Professor of Psychology and author of *An Introduction to Modern CBT*

Effective treatment of the OCD spectrum requires in-depth knowledge and nuanced skill. Storch and McKay bring together a set of experts who provide a thoughtful mix of science with creative and proven therapeutic strategies. This is a "must-have" and "must-refer-to-often" resource for every clinician tackling this illness spectrum.

—ANNE MARIE ALBANO, PHD, ABPP, Associate Professor of Clinical Psychology in Psychiatry, Director, Columbia University Clinic for Anxiety and Related Disorders, New York, NY

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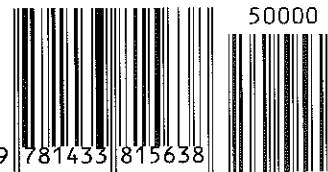
Written by prominent specialists, this volume provides practical, step-by-step descriptions of psychological approaches to treating OCD. Contributors describe evidence-based behavioral and cognitive approaches, such as exposure and ritual prevention and cognitive restructuring and discuss how to apply these strategies with particular presentations of OCD, including fears of contamination; doubting and checking; incompleteness concerns; religious, sexual, and aggressive obsessions; and compulsive hoarding.

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9 781433 815638
ISBN 13: 978-1-4338-1563-8
ISBN 10: 1-4338-1563-X

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Neuroscientific research now shows that obsessions and compulsions are a shared component of several mental health conditions. Linked by an underlying deficiency in behavioral inhibition, these conditions can be conceptualized as obsessive-compulsive spectrum disorders (OCSDs).

This practitioner-oriented book applies a life-span perspective to conceptual models for understanding OCSDs, with specific attention given to the unique clinical needs of children, adolescents, and older adults. Several conditions are examined, including obsessive-compulsive disorder (OCD), body dysmorphic disorder, Tourette's disorder, and hypochondriasis. Contributors discuss psychological and pharmacological treatments as well as comorbidities and other complications, and two chapters explore the neurobiological and behavioral-genetic support for the obsessive-compulsive spectrum. By bridging the psychological and biomedical perspectives on OCSDs, this book will appeal to a broad range of clinicians and researchers operating within this new diagnostic framework.

ABOUT THE EDITORS

ERIC A. STORCH, PHD, is a professor and All Children's Hospital Guild Endowed Chair in the Departments of Pediatrics, Psychiatry and Behavioral Neurosciences, and Psychology at the University of South Florida. He has published more than 325 peer-reviewed journal articles and book chapters, and has edited or coedited six books dealing with treatment of complex cases in children, obsessive-compulsive disorder (OCD), and childhood anxiety. He has received grant funding from the National Institutes of Health, Centers for Disease Control and Prevention, Agency for Healthcare Research and Quality, International OCD Foundation, Tourette Syndrome Association, and National Alliance for Research on Schizophrenia and Affective Disorders. He directs the cognitive-behavioral therapy component at the University of South Florida OCD Program and is highly regarded for his treatment of pediatric and adult OCD patients.

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ERIC A. STORCH
AND
DEAN MCKAY

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FOREWORD

GAIL STEKETEE

It is my pleasure to introduce you to this fine volume. As Drs. Eric Storch and Dean McKay rightly note in their introduction, although we have gained considerable knowledge about obsessive-compulsive spectrum disorders (OCSDs) and evidence-based treatments for these disorders, new research emerges at a regular rate, and much remains to be learned. Particularly interesting for the field as a whole are genetic studies and basic neuroscience and biological investigations that help us better understand brain dysfunction in OCSDs.

Although exposure and response prevention remains the gold standard behavioral treatment, cognitive therapies have added another tool set for resolving symptoms in OCSDs. Nonetheless, well-trained and accessible clinicians specializing in the treatment of these disorders are hard to find, perhaps especially for children with these conditions. Various medications, mainly the serotonin reuptake inhibitors, have been well studied and have positive outcomes for OCD patients, but recovery is often incomplete. Patients with other OCSDs may benefit from a variety of medications. The editors of this volume point to areas of study that are not yet well tapped, such as behavioral inhibition and reward processing. Certainly there is much

opportunity to expand our behavioral and cognitive processing treatment repertoire, as well as to search for biological interventions that improve outcomes, accessibility, and ease of application for clinicians and patients.

With 17 chapters (in four parts) written by top specialists in their fields, this volume provides a solid grounding in conceptual models for understanding OCSDs. Part I describes assessment and psychological treatments. Chapter 1 (Worden & Tolin) covers OCD in adults. Chapters 2 through 4 (Gryczkowski & Whiteside; Walther, Josyula, Freeman, & Garcia; Lewin) consider the unique treatment needs of children and adolescents with OCD, and Chapter 5 (Ayers & Najmi) considers the needs of older adults with OCSDs. Together with Chapter 1 on OCD in adults, these detailed reviews examine the cognitive, behavioral (including avoidance), and emotional symptoms and features across the developmental span, as well as assessment strategies and evidence-based behavioral and cognitive treatments. These chapters enable clinicians to consider special features of adult and child cases of OCD, including pediatric acute-onset neuropsychiatric syndrome, and help translate implementation of assessment and therapy methods, including family-based cognitive behavior therapy for children.

Chapter 6 (Muroff, Levis, & Bratiotis) closely examines hoarding disorder, an especially timely topic in view of the inclusion of this new diagnosis in the fifth edition of the *Diagnostic and Statistical Manual of Mental Disorders*. Chapter 7 (Hartmann, Blashill, Greenberg, & Wilhelm) focuses on body dysmorphic disorder, a particularly challenging problem with a significant risk of suicidality and a need to address low motivation for treatment. Using examples, the authors detail cognitive and behavioral methods for this disorder in adolescents and adults. Chapter 8 (Snorrason & Woods) addresses body-focused repetitive behavioral disorders such as trichotillomania, skin picking, and tic disorders, especially in children and young adults. Chapter 9 (Himle & Hayes) covers Tourette's syndrome. Finally, Chapter 10 (Hadjistavropoulos, Alberts, & Asmundson) examines hypochondriasis among youth, adults, and older adults.

Part II details co-occurring problems that may present together with OCSDs. Chapter 11 (Abramowitz & Blakey) addresses depression in OCSDs. Chapter 12 (Andover & Morris) examines similarities and distinctions between suicidal and nonsuicidal self-injury on the one hand and OCSDs on the other. Concluding Part II is Chapter 13 (Francis, Kim, & Jacob), which examines the possible link between autistic conditions and OCSDs. This chapter covers theoretical considerations, research findings, and treatment strategies and outcomes.

Part III focuses on pharmacological treatment. It begins with Chapter 14 (Stewart & Stachon), a review of medications for children and adolescents with OCSDs, including the challenges of determining dosage,

monitoring for side effects, and combining treatments. Chapter 15 (Grant, Odlaug, & Schreiber) reviews pharmacological approaches for adults with OCSDs, especially monotherapies; augmentation strategies; and evidence supporting pharmacological approaches for OCD, body dysmorphic disorder, trichotillomania, and skin picking.

Part IV concludes the volume with a discussion of the biological bases of OCSDs from genetics and neuroscience research. Chapter 16 (Taylor) reviews the heritable features of OCD and indicates, in considerable detail, the extent to which genetics contributes to a variety of OCD features. The chapter also suggests future directions for the field of study. Finally, Chapter 17 (Lapidus, Stern, Berlin, & Goodman) examines the cognitive neuroscience of OCD with regard to behavioral inhibition, error monitoring, motor suppression, cognitive inflexibility, reward processing, and emotional processing. The chapter's focus on brain imaging and neurophysiology studies of disgust and neural fear circuits is particularly interesting, as is its review of neuropsychological factors for OCSDs, including trichotillomania, body dysmorphic disorder, and hoarding.

Researchers, clinicians, and students will appreciate the detailed information in this volume. It provides a strong basis for understanding the clinical features and underlying mechanisms for expression of OCSDs. Not surprisingly, many commonalities are evident in the types of evidence-based behavioral, cognitive, pharmacological, and family interventions across these disorders. There are also commonalities in the delivery methods for these interventions. This is a strength and also a concern for clinicians and researchers who struggle to achieve maximum benefit from interventions without prolonging their duration and cost. Accordingly, readers will appreciate the treatment findings and implementation strategies, at least so far as our understanding of these disorders permits.

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FUNCTIONAL NEUROIMAGING AND MODELS FOR OBSESSIVE–COMPULSIVE DISORDER AND OBSESSIVE– COMPULSIVE SPECTRUM DISORDERS

KYLE A.B. LAPIDUS, EMILY R. STERN, HEATHER A. BERLIN,
AND WAYNE K. GOODMAN

This chapter provides an overview of neuroimaging and cognitive neuroscience research on obsessive–compulsive disorder (OCD) and related disorders. We begin with a discussion of studies in OCD focusing on conflict and error monitoring, motor suppression, and task switching. We continue with a focus on reward and emotional processing in OCD. This is followed by consideration of the role of disgust and fear and the importance of these systems in OCD. Finally, we discuss data from imaging studies in OCD spectrum disorders, focusing on trichotillomania, body dysmorphic disorder, and hoarding.

COGNITIVE NEUROSCIENCE STUDIES IN OCD

For the past several decades, neuroimaging techniques such as functional magnetic resonance imaging (fMRI) and positron emission tomography (PET) have been used to investigate neurocircuit functioning in OCD. Numerous

<http://dx.doi.org/10.1037/14323-018>

Obsessive–Compulsive Disorder and Its Spectrum: A Life-Span Approach, Eric A. Storch and Dean McKay (Editors)

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studies have explored the neural correlates of cognitive and affective processes in OCD, with varying relevance for the symptoms of the disorder. On one end of the spectrum, tasks directly provoking symptoms are clearly relevant for the disorder, yet they do not address whether basic cognitive–affective mechanisms are impaired in the absence of symptom exacerbation. By contrast, the other end of the spectrum examines neural correlates of psychological processes whose impairment is likely secondary to the central dysfunction (or dysfunctions) driving the disorder. In this section, we selectively review neuroimaging studies using tasks that probe basic cognitive–affective processes potentially at the core of OCD, focusing on those constructs for which three or more studies have compared adults with OCD and a control group.

Conflict and Error Monitoring

Probably the most widespread investigation into the cognitive neuroscience of OCD has taken place in the field of conflict monitoring and error detection. This approach is based on the proposal that obsessions are caused by an overactive conflict or error signal, continually telling the patient that “something is wrong,” despite evidence to the contrary (Pitman, 1987). In this view, compulsions are behaviors that attempt to reduce this heightened conflict signal or to correct perceived errors. Cognitive conflict is typically studied in tasks in which there is a mismatch between what a subject would automatically do (i.e., a prepotent response) and what is required in the task. In the Stroop task, subjects must make a response according to the font color of a word, in which the word itself is the name of a color that is different from the font color (e.g., the word *blue* written in red font). In this case, the prepotent response is to read the name of the word, yet the task requires a response according to the color of the word, which creates conflict that significantly increases response times in comparison with trials in which the color and word name are the same (MacLeod, 1991). Conflict monitoring in healthy controls implicates dorsal medial frontal regions including anterior cingulate cortex (dACC) and supplemental motor area (SMA) (Botvinick, Braver, Barch, Carter, & Cohen, 2001; Garavan, Ross, Kaufman, & Stein, 2003; Hester, Fassbender, & Garavan, 2004; Ridderinkhof, Ullsperger, Crone, & Nieuwenhuis, 2004), yet results from the many neuroimaging studies investigating this process in OCD do not present a coherent picture. Although some investigations have found hyperactivity of dorsal medial frontal cortex during conflict in OCD (Ursu, Stenger, Shear, Jones, & Carter, 2003; Yücel et al., 2007), other studies have identified reduced activity in this region (K. D. Fitzgerald et al., 2005; Nakao et al., 2005) or no differences between patients and controls (Stern et al., 2011; Viard et al., 2005). Many studies have reported differences between patients and controls during

conflict monitoring in several other brain regions, including parietal cortex (Page et al., 2009; van den Heuvel et al., 2005), caudate nucleus (K. D. Fitzgerald et al., 2005; Nakao et al., 2005), ventral/rostral regions of medial frontal cortex (B. J. Harrison et al., 2006; Nabeyama et al., 2008; Yücel et al., 2007), and lateral (Nakao et al., 2005; Page et al., 2009) and medial (van den Heuvel et al., 2005) temporal cortex, but these results are often contradictory (i.e., some finding activations to be greater in OCD than controls, with others finding the opposite effect). At present it is unknown whether these inconsistencies are due to variability in task design and patient characteristics or whether brain mechanisms of conflict monitoring are simply not reliably altered in OCD.

Errors reflect a specific instance of conflict during which the intended or correct response does not match the actual response made by the subject. Similar to conflict monitoring, errors elicit activation in dorsal medial frontal regions including dACC and SMA. More than for conflict monitoring, errors tend to elicit an emotional/motivational reaction related to frustration, disappointment, or fear of punishment and elicit activation in a broad range of brain regions including anterior inferior medial frontal regions, including rostral ACC (rACC) and ventromedial prefrontal cortex (VMPFC) and, less consistently, in bilateral anterior inferior medial frontal regions, including dorsolateral prefrontal cortex (DLPFC), prefrontal cortex (PFC), ventrolateral prefrontal cortex/orbitofrontal cortex (OFC), and inferior parietal cortex (S. F. Taylor, Stern, & Gehring, 2007). Rostral ACC/VMPFC, aIns, and OFC have been associated with valuation and emotional/motivational responses (N. A. Harrison, Gray, Gianaros, & Critchley, 2010; Kober et al., 2008; Kringelbach & Rolls, 2004; Lebreton, Jorge, Michel, Thirion, & Pessiglione, 2009); as such, activation of these brain regions to errors may reflect the neural processing of the motivational significance of mistakes, whereas conflict associated with the mismatch between the actual and intended response may be processed in dorsal medial frontal cortex. Support for this notion comes from a study by S. F. Taylor et al. (2006), in which errors associated with a loss of money showed greater activation in rACC/VMPFC than did those involving no motivational consequences, with no effect of error consequence on activity in dorsal medial frontal regions.

OCD patients show an increased neural response to errors in dACC (Maltby, Tolin, Worhunsky, O'Keefe, & Kiehl, 2005; Ursu et al., 2003), rACC (Maltby et al., 2005), and lateral frontal cortex, including OFC and DLPFC (Maltby et al., 2005). K. D. Fitzgerald et al. (2005) found hyperactivity in VMPFC in a small group of patients with OCD, a finding that was replicated in a larger study (E. R. Stern et al., 2011), which also identified hyperactivity of aIns. Despite some variation among the studies, overall these data suggest that OCD patients respond more strongly to

errors than do healthy individuals, particularly in ventral frontal and insula regions involved in processing the value or emotional importance of the error. However, it is important to note that these studies examined OCD patients' responses to actual errors (and conflict), whereas the phenotype of the disorder is more consistent with the detection of errors (or conflict) where there are none (or at least where their presence is uncertain). Thus, while hyperactive error responses in OCD may reflect an important characteristic of the disorder related to sensitivity to mistakes, these studies did not directly probe the neural mechanisms associated with the feeling or belief frequently expressed by patients that something is wrong even in the absence of overt errors.

Motor Output Suppression

Unlike conflict- or error-monitoring models of OCD, in which compulsions are often viewed as secondary responses to overactive conflict/error signals, experiments examining the suppression of motor output in OCD are directly relevant for repetitive motor compulsions. Inhibition of motoric output is commonly studied using a go/no-go task (or variant thereof, such as the stop-signal task) during which subjects make button-press responses to frequent stimuli (go trials) and are required to inhibit responses to infrequently presented stimuli (no-go trials). Even though this task inevitably involves conflict monitoring between the frequent go and infrequent no-go trials, these paradigms additionally involve a specific motor suppression component not present in conflict studies. Accordingly, although no-go trials are associated with activation of some of the same regions as for conflict monitoring including dACC and SMA (Aron & Poldrack, 2006; Buchsbaum, Greer, Chang, & Berman, 2005; Garavan, Hester, Murphy, Fassbender, & Kelly, 2006; Garavan, Ross, & Stein, 1999), they also elicit activation in subcortical structures, including thalamus and basal ganglia, as well as predominantly right-hemisphere lateral frontal and inferior parietal regions (Aron & Poldrack, 2006; Buchsbaum et al., 2005; Garavan et al., 1999, 2006; Robbins, 2007). In a meta-analysis, right inferior frontal (IFG) regions have been most consistently associated with no-go trials (Buchsbaum et al., 2005), which has been supported by lesion and brain stimulation studies showing impaired response inhibition after inactivation of this region (Aron, Fletcher, Bullmore, Sahakian, & Robbins, 2003; Chambers et al., 2006).

It may be hypothesized that an OCD deficit in suppressing motor output would be associated with aberrant recruitment of the response suppression network, which would lead to more failed inhibitions on no-go trials. Although this type of analysis has not as of yet been performed, prior studies

have compared OCD patients and controls during successful inhibition during which motor output is successfully suppressed on no-go trials. Reduced activity in SMA, right IFG, basal ganglia, and thalamus has been found in OCD patients during correct no-go trials (Page et al., 2009; Roth et al., 2007), which would suggest reduced recruitment of the response suppression network even during inhibition success. However, OCD hyperactivity in caudate nucleus and thalamus (Maltby et al., 2005; Roth et al., 2007)—as well as medial and lateral frontal regions, premotor cortex, middle temporal cortex, posterior cingulate cortex, and cerebellum (Maltby et al., 2005; Page et al., 2009)—has also been reported for successful inhibition, which has been interpreted as compensatory activation (Page et al., 2009). Given the variability of findings and the focus on neural differences during successful inhibitions (as opposed to inhibition failures), further research will be needed to determine whether dysfunction in a network for suppressing motor output is a core mechanism of OCD.

Switching and Cognitive Inflexibility

Another approach to investigating basic mechanisms of OCD has focused on how patients switch attention between two or more different tasks, stimuli, or rewards. Rather than hypothesizing an overactive conflict or error signal or a failure to suppress motor output, these studies are predicated on the notion that OCD patients exhibit an inflexibility that prevents them from shifting away from stimuli that may have at one time been correct or rewarding but are no longer so. As switching deficits need not be limited to the motor domain, impaired switching in OCD may be able to explain the presence of obsessions in addition to compulsions.

Many studies of switching have investigated neural activity associated with shifting attention between features or dimensions of stimuli (cognitive switching tasks). Not surprisingly, in a meta-analysis examining brain regions involved in cognitive switching and motor suppression, overlap between these processes was found in dACC/SMA, IFG, DLPFC, and inferior parietal cortex (Buchsbaum et al., 2005). However, frontoparietal activations were more widespread and bilateral for cognitive switching (Buchsbaum et al., 2005; Robbins, 2007), appearing very similar to a frontoparietal network often described as being involved in executive functions and task control (Bressler & Menon, 2010; J. D. Power et al., 2011). Studies looking at brain activity in OCD during cognitive switching have found reduced activation in patients in comparison with controls in this frontoparietal network as well as in OFC, caudate nucleus, temporal cortex, and medial parietal regions (Gu et al., 2008; Han et al., 2011; Page et al., 2009). Two studies reported widespread reductions across the cortex and basal ganglia (Gu et al., 2008;

Han et al., 2011), whereas one study found hypoactivations localized to a few regions of lateral frontal and medial parietal cortex (Page et al., 2009). Despite this difference, results were fairly consistent in pointing to cortical hypoactivation in OCD during cognitive switching.

Another type of switching that has been a topic of much research involves reversing stimulus–reward contingencies (so-called affective switching). In reversal tasks, the reward and punishment value of two stimuli switch so that the currently rewarded stimulus is punished and the previously punished stimulus is rewarded. Given the overall similarity between cognitive switching and reversal, it is surprising that evidence from human and animal studies indicates that lateral prefrontal regions involved in cognitive switching are not necessary for reversal of reward–punishment contingencies, which instead relies primarily on OFC (Dias, Robbins, & Roberts, 1996; Fellows & Farah, 2003; Hampshire & Owen, 2006; Robbins, 2007). Studies of reversal in OCD have examined neural activation on trials during which subjects made a reversal error that lead to a successful switch in comparison with errors that did not lead to a successful switch, thereby isolating activity associated with the moment that subjects learn that a switch is required (Chamberlain, Menzies, Hampshire, et al., 2008; Remijnse et al., 2006, 2009). For this comparison, OCD patients exhibit reduced activation in OFC, but similar to results from cognitive switching studies, reductions were also found throughout a frontoparietal network including DLPFC, bilateral insula, and lateral parietal cortex (Chamberlain, Menzies, Hampshire, et al., 2008; Remijnse et al., 2006, 2009). In one study, unaffected relatives of OCD also showed reduced activity in lateral OFC, DLPFC, and lateral parietal cortex during reversal (Chamberlain, Menzies, Hampshire, et al., 2008), suggesting that impaired frontal recruitment during reversal may be an endophenotype of the disorder.

Overall, these data do support the notion that OCD patients show hypoactivation in a variety of cortical regions both during cognitive switching and when reversing reward–punishment contingencies. Despite the dissociation of lateral and orbital frontal involvement in these processes, dysfunctional brain activity in OCD does not appear to be localized to one of these systems. Reduced recruitment of both DLPFC and OFC has been found when patients switch cognitive set as well as when they reverse reward contingencies. However, similar to the concerns discussed for the other approaches, interpretation of results from switching studies is complicated by the fact that neural differences between OCD patients and controls are examined during successful switches (either at the time of the correct switch response or at the time of the error right before a correct switch) rather than for unsuccessful switches, the latter of which would of course be most relevant for the OCD phenotype.

Reward Processing in OCD

It has been suggested that the difficulty exhibited by OCD patients in terminating inappropriate responses is related to a reduced signal of goal attainment or satiety (Szechtman & Woody, 2004). Within this framework, OCD patients continue to engage in compulsive behaviors such as checking, washing, or repeating/ordering because the normal reward signal associated with successfully completing these tasks is not attained. In healthy individuals, rewards elicit activation in a network of brain regions including ventral striatum, thalamus, putamen, hippocampus, anterior insula, medial frontal cortex, and parietal cortex (Liu, Hairston, Schrier, & Fan, 2011), and some studies in OCD have found reduced activation in patients in reward-related regions such as ventral medial frontal cortex during reward feedback in a reversal task (Remijnse et al., 2006, 2009). However, Jung et al. (2011) reported increased activity in cortical and subcortical regions, including putamen and dorsal medial frontal cortex, to monetary gain in OCD patients, with no regions showing reduced activity in patients in comparison with controls. In this same study, in comparison with controls, patients also showed increased activation of ventral striatum and temporal and parietal cortex in response to trials in which they avoided monetary loss. Finally, a recent study found no difference between OCD patients and controls during reward feedback (Figeo et al., 2011), although patients did show reduced activation in ventral striatum when anticipating an upcoming trial that could potentially provide reward. Overall, it is not yet clear whether dysfunctional brain responses to reward contribute to reduced feelings of goal attainment during compulsive behavior in OCD; future work may benefit from further investigation of brain responses in successfully avoiding a loss or bad event (as was done by Jung et al., 2011), which may be particularly important for OCD patients, as well as goal attainment or task completion unrelated to monetary outcomes.

Emotional Face Processing in OCD

Given the importance of negative emotion in OCD, it is somewhat surprising that so few studies have directly examined emotional processing in the disorder. It is possible that heightened neural activation in response to emotional stimuli in OCD could lead to the excessive fear and anxiety associated with obsessions. Experiments investigating the functional neuroanatomy of emotion often compare brain activity when viewing facial expressions of various emotions to activity elicited by neutral faces or nonface control tasks (see Phan, Wager, Taylor, & Liberzon, 2002). Studies examining the neural correlates of emotional face processing in OCD have yielded conflicting results. A recent study found hyperactivation in OCD in visual cortex,

DLPFC, posterior thalamus, and limbic regions including amygdala and parahippocampus when matching either happy or fearful facial expressions, in comparison with matching nonface shapes (Cardoner et al., 2011). There was also an effect of expression valence, such that OCD patients showed greater activation than did control patients in DLPFC and anterior insula for fearful in comparison with happy expressions. However, these findings contrast with an earlier report of reduced amygdala activation in OCD when observing fearful, happy, and neutral faces in comparison with a fixation condition (Cannistraro et al., 2004). Finally, when compared with neutral faces, facial expressions of disgust have been found to elicit greater activity in left OFC but reduced activity in thalamus in OCD, with no differences between patients and control subjects for fearful versus neutral faces (Lawrence et al., 2007). These discrepancies may be due to variability in task design and analyses, and further work is needed to determine whether OCD patients exhibit abnormality in response to other types of emotional stimuli.

Other Tasks and Conclusions

The above summary discusses a nonexhaustive selection of studies that focus on neuroimaging correlates of psychological processes that could potentially underlie the complex symptom presentation of patients with OCD. The most consistent findings from these studies were hyperactivation in response to errors and hypoactivation during switching tasks, with both effects occurring predominantly in the PFC. However, given the limitations concerning the applicability of analyses to the phenomenology of the disorder and inconsistency among studies using the same (or similar) tasks, it is clear that further investigation into the neurocircuitry underlying cognitive-affect dysfunction in OCD is needed. Other approaches investigating habit formation (Rauch et al., 1997; Rauch, Wedig, et al., 2007), loss expectancy (Jung et al., 2011; Ursu & Carter, 2009), decision uncertainty (Stern et al., 2012), image suppression (Koçak, Ozpolat, Atbasoglu, & Cicek, 2011), and working memory (Henseler et al., 2008; Koch et al., 2012; Nakao et al., 2009; van der Wee et al., 2003) have identified alterations in OCD that may also contribute to the phenomenology of the disorder.

OCD AND DISGUST

Contamination (intense, persistent feeling of having been polluted or infected; Rachman, 2004) concerns are the most common themes associated with OCD (Rasmussen & Tsuang, 1986), presenting in up to 50% of people with the disorder (Rachman & Hodgson, 1980; Rasmussen & Eisen,

1992). Intrusive contamination thoughts often lead to excessive sanitizing and disinfecting of the self and the environment, and to avoidance of situations and stimuli largely because of perceptions of being susceptible to disease and infection. Compulsive cleaning is the second most common compulsion of OCD (Rachman, 2004). Studies support the role of disgust in contamination-related OCD (Cisler, Olatunji, & Lohr, 2009; Mancini, Gragnani, & D'Olimpio, 2001; Olatunji, Forsyth, & Cherian, 2007; Olatunji & Sawchuk, 2005; Olatunji, Sawchuk, Arrindell, & Lohr, 2005; Thorpe, Patel, & Simonds, 2003; Tsao & McKay, 2004) and the notion that disgust is distinct from other negative affective states (e.g., anxiety, depression; Mancini et al., 2001; Olatunji, Sawchuk, Lohr, & de Jong, 2004; Tolin, Woods, & Abramowitz, 2006; Wood & Tolin, 2002).

Disgust is an emotion that likely evolved to provide protection, by way of avoidance, from contamination and disease (Izard, 1993); it involves the appraisal of objects and events for their potential role in contamination (Rozin & Fallon, 1987). Some forms of OCD conceivably involve a dysfunction of this appraisal process (Sprengelmeyer et al., 1997; S. R. Woody & Teachman, 2000; S. R. Woody & Tolin, 2002). Feelings of disgust may arise from sensory experiences (e.g., taste, smell) and from more abstract concerns (e.g., those related to aspects of the body or to moral judgments; Rozin, Lowery, Imada, & Haidt, 1999). Accordingly, OCD concerns may be quite concrete (e.g., about germs, bodily secretion, and illness) or more abstract (e.g., religious, ethical, and moral issues).

In terms of the psychosocial aspects of OCD, the disorder may involve a false contamination alarm in which disgust plays a crucial organizing or embodying role at a basic brain level (Stein, Liu, Shapira, & Goodman, 2001). Before the onset of contamination-related OCD, people who are high in disgust sensitivity may avoid objects (e.g., public toilets) and situations (e.g., public gatherings) associated with contamination. Because of limited exposure, those high in disgust sensitivity may be more prone to contamination obsessions and washing compulsions when they come into contact with perceived contaminants (Merckelbach, Dejong, Arntz, & Schouten, 1993). Disgust sensitivity has been shown to positively correlate with OCD and to predict contamination fear.

Intrusive thoughts and avoidance efforts may be associated with feelings of fear; however, disgust may also contribute to the etiology and phenomenology of OCD-related contamination obsessions and washing compulsions (Olatunji et al., 2007; M. L. Phillips, Senior, Fahy, & David, 1998; M. Power & Dalgleish, 1997). In fact, patients with contamination concerns often describe threat-relevant objects as "disgusting" rather than as "frightening" (Sieg & Scholz, 2001; Tolin, Worhunsky, & Maltby, 2004), and after exposure to a disgusting object, cleaning rituals are seen (Rozin & Fallon, 1987).

The distinction between fear/anxiety (i.e., sympathetic activation) and disgust (i.e., parasympathetic activation) in contamination-related OCD is not merely semantic: The two emotions may be represented by different neural circuits (Olatunji & Sawchuk, 2005). Disgust in OCD patients seems to be more resistant to extinction than is fear (Smits, Telch, & Randall, 2002), and functional imaging and patient-based studies have shown that the amygdala is involved in fear recognition (Calder, 2003), whereas the insular cortex and putamen appear to underlie disgust recognition (Calder, Keane, Manes, Antoun, & Young, 2000; Calder, Lawrence, & Young, 2001).

Although OCD is classified as an anxiety disorder, several lines of evidence suggest that the emotion of disgust plays an important role in its pathogenesis and maintenance (M. L. Phillips, Senior, et al., 1998; Schienle, Schafer, Stark, Walter, & Vaitl, 2005a; Stein et al., 2001). There is a strong relationship between the emotion of disgust/disgust sensitivity and obsessive-compulsive symptoms in both clinical and nonclinical populations (Mancini et al., 2001; Muris, Merckelbach, Schmidt, & Tierney, 1999; Olatunji & Sawchuk, 2005; Olatunji et al., 2004; Olatunji, Williams, Lohr, & Sawchuk, 2005; Schienle, Stark, Walter, & Vaitl, 2003; Thorpe et al., 2003; Tsao & McKay, 2004; S. R. Woody & Tolin, 2002). OCD patients have also shown deficits in identification of facial representations of disgust, in comparison with other anxiety disorders (Sprengelmeyer et al., 1997). Furthermore, OCD patients, especially those with contamination fears and washing compulsions, report experiencing intense disgust feelings during symptom provocation (M. L. Phillips et al., 2000; Sieg & Scholz, 2001). People with Huntington's disorder and OCD, both disorders with striatal dysfunction, have shown impairment in the recognition of disgust but not of other basic emotions (Sprengelmeyer et al., 1996).

One of the reasons the sense of taste exists is so that organisms can detect potential nutrients and toxins. The ability to distinguish between appetitive (e.g., sweet) and aversive (e.g., bitter) tastes is critical to survival because taste and expulsion are the last defenses against ingestion of toxins. Primary gustatory cortex includes anterior insula; therefore, it makes sense that the insula is involved in the disgust response. Disgust (measured by perception of and response to facial expressions of disgust and disgust-inducing stimuli) appears to be controlled most notably by the insular cortex and corticostriatothalamic circuitry (in particular, the striatum), according to lesion (Calder et al., 2000; Gray, Young, Barker, Curtis, & Gibson, 1997; Sprengelmeyer et al., 1996, 1997) and imaging data (Calder et al., 2001; Heining et al., 2003; Mataix-Cols et al., 2004, 2008; M. L. Phillips et al., 1997; Wicker et al., 2003; Wright, He, Shapira, Goodman, & Liu, 2004). The anterior insula and ventral striatum appear to be key structures in a system mediating the response to disgusting stimuli irrespective of sensory modality (Calder et al., 2001;

Heining et al., 2003; M. L. Phillips, Young, et al., 1998; M. L. Phillips et al., 1997; Shapira et al., 2003; Sprengelmeyer et al., 1996, 1997).

Functional brain imaging studies in healthy subjects show that the insula responds selectively to facial expressions of disgust (M. L. Phillips et al., 1997; Sprengelmeyer, Rausch, Eysel, & Przuntek, 1998) and that viewing disgust-eliciting pictures increases neural activity in the insula and basal ganglia (notably, the caudate and putamen) (Mataix-Cols et al., 2004, 2008; Phan et al., 2004; Shapira et al., 2003; Wicker et al., 2003). Imaging studies that expose subjects to unpleasant odors or tastes have also reported an association between the insula and ventral striatal activation and disgusting stimuli (Heining et al., 2003; Royet, Plailly, Delon-Martin, Kareken, & Segebarth, 2003; Small et al., 1999; Wicker et al., 2003; Zald & Pardo, 2000). In addition, an fMRI study of subjects asked to recall or reexperience an event that evoked disgust found increased activation of the insula and basal ganglia, indicating the involvement of these regions in the interoceptive experience of disgust (D. A. Fitzgerald et al., 2004).

Neuroimaging studies have shown that abnormalities of the same neural regions involved in disgust processing, in particular, the insula cortex and striatum, are also involved in OCD (Berle & Phillips, 2006; M. L. Phillips et al., 2000; Stein et al., 2001). Two recent structural MRI studies found that OCD patients have significantly larger anterior insular cortices bilaterally in comparison with healthy controls (HCs; Nishida et al., 2011; Song et al., 2011). Furthermore, functional imaging studies show that OCD patients with predominantly washing symptoms have increased neural responses to washing-related stimuli (Mataix-Cols et al., 2004; M. L. Phillips et al., 2000) and to disgusting pictures (Schienle et al., 2005a; Shapira et al., 2003) in brain regions implicated in disgust and autonomic response processing, including the anterior insula, ventrolateral PFC, and putamen/globus pallidus (Calder et al., 2001; Critchley, Wiens, Rotshtein, Ohman, & Dolan, 2004; M. L. Phillips et al., 1997, 2004; M. L. Phillips, Young, et al., 1998; Sprengelmeyer et al., 1998). Research has also found that there was greater activation of the insula to disgust-inducing images in OCD patients than in control patients but no difference in brain activation in response to threat-inducing images (Shapira et al., 2003). Furthermore, confrontation with disorder-relevant stimuli (vs. innocuous/disorder irrelevant stimuli) in OCD subjects has been shown to trigger activation of the anterior insula (Schienle et al., 2005a), as well as OFC, anterior cingulate, caudate nucleus, and amygdala (Breiter et al., 1996). Finally, OCD patients with contamination concerns demonstrate activation of the same neural regions with disgust-inducing pictures as with symptom relevant stimuli, most notably the insula (M. L. Phillips et al., 2000). Thus, the neurocircuits involved in disgust processing may be relevant to OCD and, in particular, the contamination subtype.

Disgust Versus Fear-Related Neural Circuits

Disgust and fear are basic emotions that have different elicitors and expressions, and they appear to be mediated by different neurocircuits (Miller, 1997; M. L. Phillips et al., 1997, 2004; M. L. Phillips, Young, et al., 1998; Stein et al., 2001). Studies in healthy people show that insular cortex and the basal ganglia are more frequently activated during disgust processing than during fear processing, and amygdala is more frequently activated in fear processing (Calder et al., 2001; Murphy, Nimmo-Smith, & Lawrence, 2003). Functional MRI experiments (M. L. Phillips et al., 1997, 2004; M. L. Phillips, Young, et al., 1998) support a double dissociation in healthy subjects for whom fearful faces activate the amygdala (confirming other reports; Breiter et al., 1996; Morris et al., 1996) but not the insula, whereas disgust faces activate the anterior insular cortex, medial frontal cortex, right putamen, and thalamus, but not the amygdala (confirmed by others; Anderson, Christoff, Panitz, De Rosa, & Gabrieli, 2003; Sprengelmeyer et al., 1998). However, these differential patterns of activation only occur when the participants are fully aware of the stimuli presented (M. L. Phillips et al., 2004).

Stark et al. (2007) also found that insula activation was associated with disgust ratings and the processing of disgusting scenes, but not fear ratings or the processing of fearful scenes. But both fear- and disgust-inducing scenes activated the amygdala, occipital cortex, and PFC. Disgust-related amygdala activation has repeatedly been found (Britton et al., 2006; D. A. Fitzgerald, Angstadt, Jelsone, Nathan, & Phan, 2006; Schienle et al., 2002, 2006; Schienle, Schafer, Stark, Walter, & Vaitl, 2005b; Stark et al., 2003, 2005, 2007). Furthermore, people with lesions that include the amygdala show reduced startle potentiation to disgust and fearful pictures (Buchanan, Tranel, & Adolphs, 2004). However, Sprengelmeyer et al. (1999) described a patient with bilateral amygdala damage, whose ability to recognize and experience fear was reduced while recognition and experience of disgust were intact. Some of these inconsistencies could be due to interindividual differences in the experience of emotional stimuli and difference in experimental design (Stark et al., 2007). Further research is needed to clarify the role of the amygdala in disgust processing.

Disgust Versus Fear-Related Neural Circuits in OCD Patients

The basic emotions of fear and disgust have clear relevance to the anxiety disorders in general and to OCD in particular (McKay, 2002; M. L. Phillips, Senior, et al., 1998). The amygdala plays a key role in mediating fear and anxiety (Davis, 1997; LeDoux, 1998) and has been implicated in anxiety disorders (Davis & Whalen, 2001; Gorman, Kent, Sullivan, & Coplan,

2000). In contrast, disgust appears to be mediated primarily by the insula and striatum (Adolphs, Tranel, & Damasio, 2003; M. L. Phillips, Senior, et al., 1998; Sprengelmeyer et al., 1998), which have been implicated in OCD in particular (Kim et al., 2001; Rauch & Baxter, 1998; Rauch, Shin, Whalen, & Pitman, 1998; Stein, Arya, Pietrini, Rapoport, & Swedo, 2006).

Using PET, Stein et al. (2006) found that in comparison with controls, OCD had greater activation of the left insula during the disgust-inducing tasks than during the resting tasks. OCD patients, but not control patients, showed greater right lateral OFC activation than rest during the disgust-inducing task. Neural activity of OCD subjects did not differ from controls in the anticipatory anxiety versus resting state, and anxiety ratings, heart rate, and electrodermal activity increased during an anticipatory anxiety task in both groups. Using fMRI, Shapira et al. (2003) found that activation patterns in response to threat-inducing stimuli were similar in OCD and control subjects, but OCD patients had greater activation in the insula and inferior frontal regions in response to disgust-inducing stimuli. Various findings also suggest a role for the ventrolateral PFC in mediating enhanced responses to disgust-related visual stimuli in OCD patients than in control patients (Lawrence et al., 2007; Mataix-Cols et al., 2004; Schienle et al., 2005a; Shapira et al., 2003; Sprengelmeyer et al., 1998).

In contrast to the findings of increased insula activation to disgusting stimuli in OCD patients in comparison with HCs, most findings to date suggest that there is no difference in neural activation between OCD patients and HCs during the processing of threatening/fearful stimuli (Shapira et al., 2003; Stein et al., 2006). However, one study did report increased insula responses in OCD patients to pictures of fearful, as well as disgusting and disorder-relevant, scenes (Schienle et al., 2005a). The increased insular reactivity of OCD patients during all aversive picture conditions might reflect their susceptibility/proneness to experience negative somatic states, which might be a vulnerability factor for OCD.

The profile of amygdala activation in response to facial expressions in OCD distinguishes it from other anxiety disorders, which show exaggerated amygdala activation to threatening faces (Britton et al., 2010). Although exaggerated amygdala activation has been shown in response to OCD-specific stimuli (e.g., disgusting toilets) in some studies of adults with OCD (Adler et al., 2000; Breiter et al., 1996; van den Heuvel et al., 2004), less amygdala activation in response to happy, fearful, and neutral faces (in relation to fixation) has been found in adult (Cannistraro et al., 2004) and pediatric (Britton et al., 2010) OCD subjects, in comparison with HCs. Britton et al. (2010) also found reduced amygdala activation in pediatric OCD patients in response to disgusted faces. So although OCD may be similar to other anxiety disorders with respect to greater amygdala activation during symptom

provocation (Breiter et al., 1996), the finding of less amygdala activation to emotional stimuli (facial expressions) may distinguish OCD from other anxiety disorders. Reduced amygdala activation may predict disease onset or be an endophenotype of OCD.

In line with this, in a recent, thorough review of the literature, Fiddick (2011) argued for a distinction between fear-provoking immediate threats and anxiety-provoking potential threats, with the amygdala processing immediate threats and the cingulate cortex (and insular) processing potential threats. This provides support for recent models proposing the existence of a separate potential threat system that is dysfunctional in OCD (Szechtman & Woody, 2004; E. Z. Woody & Szechtman, 2011). However, S. Taylor, McKay, and Abramowitz (2005) pointed out some limitations of this model. In particular, they claimed that proposing a single dysfunctional mechanism to explain OCD is limited and does not account for the heterogeneity and complexity of the disorder.

In summary, findings in OCD patients, particularly those with contamination preoccupation, suggest a specific enhancement in insula and ventrolateral PFC activation in response to symptom-related and disgusting pictures (and some suggest reduced amygdala activation) but no difference in brain activation or decreased amygdala activation (Britton et al., 2010; Cannistraro et al., 2004) or increased insula activation to fearful stimuli, in comparison with HCs (Schielenle et al., 2005a).

FUNCTIONAL IMAGING STUDIES IN OCD SPECTRUM DISORDERS

Neuroimaging techniques have also been used to investigate neurocircuit functioning in related OCD spectrum disorders. Unfortunately, many fewer studies have been published involving these disorders. Among these few studies, small sample sizes and failure to correct for multiple comparisons complicate interpretation of the data. In this section, we review the available data from neuroimaging studies probing disorders from the OCD spectrum, including trichotillomania (TTM), body dysmorphic disorder (BDD), and hoarding. Additional putative members of the OCD spectrum such as dermatillomania (skin picking) and onychophagia (nail biting) lack published data and are excluded, as are impulse control disorders, of which only pathological gambling has been explored in published imaging studies.

Trichotillomania

Classified in the *Diagnostic and Statistical Manual of Mental Disorders* (4th ed., text rev.; DSM-IV-TR; American Psychiatric Association, 2000)

as an impulse control disorder, TTM involves the pathological pulling out of the affected person's own hair. Similar pathological grooming behavior is seen in other related disorders: skin picking (dermatillomania) and nail biting (onychophagia) disorders. Excessive grooming behavior is a salient feature of some putative animal models of OCD (Welch et al., 2007).

There is significant comorbidity between TTM and OCD (Lochner & Stein, 2010; Richter, Summerfeldt, Antony, & Swinson, 2003). Additionally, relatives of OCD patients show high levels of pathological grooming behaviors such as TTM (Bienvenu et al., 2012). Comorbidity, familial commonalities, and phenomenological relationships, including difficulty in suppressing behaviors, have led some to suggest that TTM may be part of the OCD spectrum. Structural imaging studies have yielded inconsistent results, though some have indicated that as with OCD, TTM is associated with alterations in frontostriatal volumes and density (Chamberlain, Menzies, Fineberg, et al., 2008; Keuthen et al., 2007; O'Sullivan et al., 1997; Stein, Coetzer, Lee, Davids, & Bouwer, 1997).

Diffusion tensor imaging has been used to assess connectivity in these circuits. Eighteen subjects with TTM—but without comorbid OCD, other impulse control disorders, or depression—were compared with 19 HCs using MRI (Chamberlain et al., 2010). In this study, the TTM group displayed abnormal reductions in fractional anisotropy (FA) in white matter tracts connecting bilateral anterior cingulate and orbitofrontal cortices. Fractional anisotropy decreases were also noted in presupplementary and left primary somatosensory cortices along with left temporal lobe. Changes in FA did not correlate with disease severity and were independent of prior treatment.

Global brain metabolic rate was found to be increased using PET and 18-F-fluorodeoxyglucose in 10 TTM patients versus 20 HCs (Swedo et al., 1991). In TTM subjects, metabolic rates were significantly elevated in every brain region analyzed. Normalizing each region to total brain metabolic rate identified regions with locally increased metabolism in TTM subjects: right superior parietal and bilateral cerebellum. Additionally, ratios of left caudate to global metabolic activity and right cerebellum to global activity correlated negatively with measures of TTM symptom severity. Cerebellar and left ACC activation correlated with chronic, though not acute, anxiety severity. Although only some regions were found to be important in similar studies in OCD, this study found that clomipramine-related improvement in symptoms was associated with similar changes in TTM subjects, as has been reported in OCD subjects (Swedo et al., 1991). Anterior cingulate and orbitofrontal activity was negatively correlated with symptomatic improvement in response to 5 weeks of clomipramine treatment.

Treatment response to 12 weeks of citalopram was studied in 10 women with TTM (Stein et al., 2002). These subjects underwent single photon

emission computed tomography (SPECT) scans before and after treatment while being asked to try to experience hair-pulling urges and were allowed to pull out hair if they wanted. Findings suggested that citalopram treatment leads to decreases in regional brain activity in relation to whole brain activity in posterior–inferior and anterior–superior frontal regions as well as in the right anterior temporal area and left putamen. At baseline, hair-pulling severity correlated negatively with bilateral frontal, left parietal, and left putamen activity. After pharmacotherapy, symptom severity correlated with increases in left frontal, right medial–temporal, and right putamen activity.

Brain activation during implicit sequence learning using the serial reaction time was assessed in 10 TTM and 12 HC female subjects (Rauch, Wright, et al., 2007). No significant differences in reaction time were identified between groups, and both groups were able to learn in this paradigm. Also, activations of right dorsal caudate and left ventral striatum were similar between groups. No between-groups differences were found in any brain region analyzed.

In combination with fMRI, symptom provocation (exposing subjects to imagery and tactile stimuli of hair vs. neutral stimuli of a ball) was used to identify differences in brain activation between children and adolescents with TTM and HC. In a study of seven female subjects with TTM and nine female HCs, both groups showed activation of the inferior temporal and middle occipital gyri and inferior parietal lobule with visual symptom provoking stimuli only (Lee et al., 2010). In contrast to HCs, TTM subjects also displayed activation in the superior temporal gyrus, posterior cingulate, cerebellum, putamen, and insula. When exposed to both visual and tactile symptom provoking stimuli, HC and TTM groups both exhibited activation of the middle occipital gyrus, though HCs displayed further activation of inferior parietal lobule, cuneus, inferior temporal, lingual, and postcentral gyri along with cerebellar activation. The middle temporal gyrus was activated in TTM but not HCs under these conditions.

These studies of TTM suggest structural and functional brain abnormalities that partially resemble those identified in subjects with OCD. Regions frequently identified as important include striatum, particularly putamen, along with insula, orbitotemporal, and cingulate cortex. Interestingly, cerebellar abnormalities have also been identified in several TTM studies.

Body Dysmorphic Disorder

BDD involves a preoccupation with imagined or trivial appearance defects (American Psychiatric Association, 2000). Partly because of phenomenological similarities (e.g., recurrent disturbing thoughts accompanied by repetitive behaviors) between BDD and OCD, they have been viewed

as along the so-called OCD spectrum. BDD, along with TTM and hoarding disorder, are listed in the *Diagnostic and Statistical Manual of Mental Disorders* (5th ed.; DSM-5; American Psychiatric Association, 2013) in a new category of obsessive-compulsive and related disorders. BDD also shares comorbidities, familial loading, and treatment-response similarities with OCD (K. A. Phillips & Kaye, 2007).

Morphometric comparison between eight BDD and eight HC women indicated increased total cerebral volume, accounted for by an increase in white matter in the BDD group (Rauch et al., 2003). Although no other between-groups volumetric differences were found, the BDD group displayed abnormally left-shifted caudate asymmetry. These results were interpreted as further support for BDD being part of this group of OCD spectrum disorders. Another morphometric study in men found reduced OFC and ACC volumes in BDD in relation to HC subjects (Atmaca et al., 2010). This study failed to find between-groups differences in caudate, but reported data consistent with leftward shift of caudate asymmetry, without reporting laterality. Additionally, this study confirmed the finding of increased white matter in the BDD group. In contrast, a study of both sexes found no difference between BDD and HC subjects in total white matter and caudate laterality (Feusner et al., 2009). Subgroup analysis of only women and subjects without comorbid MDD also failed to replicate the prior findings. Instead, this group found a correlation of BDD symptom severity with left inferior frontal gyrus and right amygdala volumes. Perfusion deficits in parietal and occipital areas of six BDD subjects were suggested by SPECT data from an uncontrolled case series (Carey, Seedat, Warwick, van Heerden, & Stein, 2004). This study did not detect consistent abnormalities in other regions, though increases in basal ganglia perfusion were seen in two of the subjects; the study's findings have not been replicated.

Visual information processing has been examined using fMRI in several studies of BDD. The first published study included 12 BDD and 13 HC subjects (Feusner, Townsend, Bystritsky, & Bookheimer, 2007). In this study of face matching, both groups activated extrastriate visual cortex and fusiform gyrus. In addition, the BDD group showed significantly greater activation of left middle and inferior temporal gyri when high-pass-filtered faces were presented. With low-pass faces, the BDD group activated left infraparietal sulcus and left inferior and superior frontal gyri, along with right precentral and postcentral gyri, right superior and middle frontal gyri, and bilateral dorsal ACC. Without filtering, the BDD group displayed significantly greater activation of left superior temporal gyrus, left inferior frontal gyrus, and left insula. The HC group exhibited no significantly greater activation when given filtered faces, but in the task with unfiltered faces had significantly greater activation of bilateral cuneus and left middle occipital gyrus.

Post hoc analysis revealed significantly greater right amygdala activation in the BDD group when filtered faces were presented. These differences were interpreted to suggest greater and focused attention on details of faces in the BDD group. These face-matching tasks were used in another study that included images of the subjects' own faces. This study included 17 BDD and 16 HC subjects (Feusner et al., 2010). This confirmed the previous finding of extrastriate visual cortex and fusiform gyrus activation in both groups. It also found greater activation of left OFC and bilateral caudate for subjects' own unfiltered faces in the BDD group. When these faces were low-pass filtered, HCs displayed greater left occipital cortex activation. Also, BDD symptom severity correlated with own-face-induced activation of right OFC, right head of caudate, right precentral and postcentral gyri, and right dorsal occipital cortex. In total, these findings suggest frontostriatal hyperactivity in BDD. To assess brain activation with stimuli that do not pertain to symptoms, we used a similar task involving pictures of unfiltered and filtered houses rather than faces. A study using this task in 14 BDD and 14 HC subjects again found similar activations of visual cortex and fusiform areas (Feusner, Hembacher, Moller, & Moody, 2011). No significant activation differences were found between groups with unfiltered images. However, for low-pass-filtered images, the BDD group displayed lower activation of left parahippocampal cortex, left hippocampus, left lingual gyrus, left posterior cingulate, and bilateral precuneus, whereas with high-pass-filtered images, the BDD group displayed greater activation of bilateral frontal pole, left superior frontal gyrus, right anterior cingulate gyrus, and right paracingulate gyrus. These data suggest abnormalities in generalized visual processing in BDD. In addition to these visual processing abnormalities, many of the BDD imaging findings suggest that it may be part of this spectrum. These include cortical striatal and limbic anomalies.

Hoarding

Historically seen strictly as a subtype or symptom dimension of OCD, hoarding—the acquisition of and inability to discard objects seen by others as having little or no value—appears as a distinct disorder in *DSM-5* (Pertusa et al., 2010). This history may have led some previous imaging studies to mix cases of OCD and hoarding disorder. A few have performed analyses on the basis of symptom dimensions, and others have focused explicitly on hoarding.

The only structural study of hoarding found a trend-level association of symptoms with reduced volumes in Brodmann Area 6, including premotor cortex and supplementary motor cortex (Gilbert et al., 2008). The analysis of symptom dimensions was post hoc and included only a few patients, given the total population of OCD subjects ($n = 25$). In a PET study of 45 OCD

subjects, 12 of whom had hoarding as their most prominent symptom, and 17 HC subjects, nonhoarding OCD subjects had significantly greater bilateral thalamic metabolism than did either of the other groups (Saxena et al., 2004). Hoarders had significantly lower metabolism in the posterior cingulate gyrus than did HCs. In comparison with OCD subjects without hoarding disorder, hoarders had lower bilateral dACC metabolism, and hoarding severity negatively correlated with metabolism in dACC across all OCD subjects. Yet hoarders displayed higher metabolism in part of the right SMA than did nonhoarders, and activity in this region correlated with hoarding severity.

A symptom provocation study in 17 OCD subjects with mixed symptoms and 17 HCs showed that hoarding provocation induced greater activation of left precentral/superior frontal gyrus, left fusiform gyrus, and right OFC in OCD subjects than in HCs, and HCs displayed greater activation of bilateral visual areas (Mataix-Cols et al., 2004). Hoarding-related anxiety also correlated with activation of left precentral/superior frontal gyrus. Another symptom provocation study in 13 OCD subjects with and 16 without prominent hoarding symptoms along with 21 HCs found that hoarders uniquely activated frontal pole, anterior OFC, and medial frontal gyrus, whereas nonhoarders activated putamen and caudate, and controls activated striatum, left thalamus, and VMPFC, including OFC and anterior ACC (An et al., 2009). The hoarding group exhibited significantly greater activation of the anterior VMPFC and cerebellum than did HCs. The correlation of hoarding-related anxiety with pre- and postcentral gyri activations confirmed findings from prior studies (Mataix-Cols et al., 2004; Saxena et al., 2004). This anxiety inversely correlated with activity in bilateral dorsal prefrontal regions, basal ganglia, temporal cortex, and parieto-occipital regions, further implicating emotional regulation and planning deficits in these patients.

Another study focused on decision making in subjects with hoarding (Tolin, Kiehl, Worhunsky, Book, & Maltby, 2009). Here, 12 subjects with hoarding were compared with 12 HCs while making decisions about whether to keep or discard items that did or did not belong to them. Of note, only two of the hoarding subjects had comorbid OCD. When deciding to discard personal items, hoarders exhibited greater activation of left lateral OFC, left amygdala, left parahippocampal gyrus, and left cerebellum. The increased cingulate activity noted in this study contrasts with earlier reports of decreased cingulate activity in this population, suggesting that decreased activity at rest may be accompanied by excessive activation with provocation.

OFC and ACC abnormalities have been noted in multiple hoarding studies. In addition, as with BDD, pre- and postcentral gyrus abnormalities have been identified. Finally, amygdala and other limbic and prefrontal activation abnormalities have been noted.

In total, these studies suggest partly overlapping but distinct patterns of functional changes in OCD and related spectrum disorders. These illnesses require further study, including replication and evaluation of commonalities and differences. Future research will benefit from focused studies that limit inclusion of comorbidity along with increased diagnostic specificity.

OVERALL CONCLUSIONS

In this chapter, we present a summary of neuroimaging studies in OCD and OC spectrum disorders including TTM, BDD, and hoarding. A review of the cognitive neuroscientific literature to date yields contradictory findings in a variety of studies examining cognitive, motor, and emotional functioning, with the most consistent effects pointing to prefrontal hyperactivation and to errors or hypoactivation during switching in OCD. Some of the difficulty in identifying consistent areas of dysfunction could be due to the wide variety of tasks used in these investigations. The majority of studies focus on cognitive or motor functioning without addressing the importance of anxiety and emotional discomfort in the disorder. However, studies of emotional face processing do not capture the characteristic cognitive and motoric inflexibility shown by patients. It is clear that no one paradigm or approach is likely to explain all the clinical phenomena of this heterogeneous disorder, and future work would benefit from combining the strengths of these many approaches to explore the cognitive neuroscientific study of OCD and its spectrum from a variety of perspectives.

The study of OC spectrum disorders reveals both commonalities and differences between OCD and TTM, BDD, and hoarding. Limited data are currently available on the OC spectrum, and future studies will clarify the neurobiological abnormalities along this putative spectrum. Investigation of this spectrum is likely to prove useful in that it may also provide endophenotypes or specific mechanistic targets for future treatment development.

The neurocircuitry involved in disgust processing has been shown to be relevant to OCD, in particular, contamination-type OCD. More research is needed to better understand the neural mechanisms underlying disgust and the role disgust plays in the pathophysiology of OCD, which will have important implications for rehabilitation. For example, exposure-response therapy could be aimed at desensitizing OCD patients to disgusting stimuli rather than targeting their specific cognitive symptoms. Or deep transcranial magnetic stimulation therapy could be used to modulate OCD patients' increased insula activation to disgusting stimuli. Targeting the neurocircuitry related to disgust processing via pharmacological, cognitive, behavioral, or brain stimulation techniques may produce more effective and rapid treatment results.

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