



# Interoception and Obsessive-Compulsive Disorder: A Review of Current Evidence and Future Directions

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Disrupted interoceptive processes are present in a range of psychiatric conditions, and there is a small but growing body of research on the role of interoception in obsessive-compulsive disorder (OCD). In this review, we outline dimensions of interoception and review current literature on the processing of internal bodily sensations within OCD. Investigations in OCD utilizing objective measures of interoception are limited and results mixed, however, the subjective experience of internal bodily sensations appears to be atypical and relate to specific patterns of symptom dimensions. Further, neuroimaging investigations suggest that interoception is related to core features of OCD, particularly sensory phenomena and disgust. Interoception is discussed in the context of treatment by presenting an overview of existing interventions and suggesting how modifications aimed at better targeting interoceptive processes could serve to optimize outcomes. Interoception represents a promising direction for multi-method research in OCD, which we expect, will prove useful for improving current interventions and identifying new treatment targets.

**Keywords:** obsessive-compulsive disorder, interoception, sensory phenomena, disgust, evidence-based treatment

## INTRODUCTION

OCD affects 1–3% of adults (1) and is associated with significant economic cost and a chronic course (2, 3). It is characterized by recurrent, intrusive thoughts, images, urges, and/or sensory-perceptual experiences that cause distress (obsessions) and repetitive behaviors performed to reduce this distress (compulsions). Clinical presentation and symptom content can vary greatly across individuals, with the most reliable dimensions including harm/checking, contamination/cleaning, and symmetry/ordering (4, 5). Though gold-standard treatments including serotonin reuptake inhibitors and cognitive behavioral therapy (CBT) work for many patients with OCD, a significant portion do not achieve meaningful symptom reduction (6, 7), which may be due to this heterogeneity.

Seminal conceptualizations of OCD that emphasize the role of cognitions and fear in the development and maintenance of symptoms are particularly relevant for obsessions and compulsions related to preventing or avoiding a feared outcome or bad event (e.g., “I check

my stove because I am afraid it has been left on and will burn down my house"). Indeed, traditional anxiety-based models form the foundation for evidence-based CBT interventions such as exposure and response prevention ExRP; (8–11). However, these models do not account as well for those symptoms of OCD that are less fear-driven, including behaviors that are more motivated by sensory or visceral sensations such as "not-just-right" experiences (NJREs; "I need to arrange objects until they look just right"), disgust, and physical urges ("I feel dirty or sticky so I have to wash my hands repeatedly"). These types of symptoms—frequently referred to as "sensory phenomena"—are prominent in ~50–80% of patients with OCD (12, 13) and have been the topic of an emerging body of work that aims to understand the psychological and neural correlates of these symptoms (14, 15) in an attempt to identify more targeted treatments.

A growing body of research has begun to investigate the role of sensory processing in OCD, including the processing of internal, or interoceptive stimuli (and the focus of this paper) and external (exteroceptive) stimuli [See Grimaldi and Stern (16) and Collins et al. (17) for more information on exteroception in OCD]. Interoception, defined as the detection, integration, and interpretation of internal bodily signals (18, 19). Body sensations provide important information necessary to maintain homeostasis, influence attentional, and emotional processes, impact decision-making, and motivate behavior (18–23). Indeed, interoception is posited to be a core facet of emotional, behavioral, and cognitive regulation (20, 23–27). Therefore, it is perhaps not surprising that disrupted interoceptive processes are present in a wide range of psychiatric conditions, including anxiety, depression, addiction, psychosis, and anorexia (18, 19, 22, 28, 29). With regard to OCD, there are several antecedents to compulsions that, in addition to being fear-based, could be driven at least in part by altered processing of body signals (such as NJREs and disgust). There are additional aspects of altered interoception in OCD that may not necessarily drive compulsive behavior in the traditional sense, but nonetheless can negatively impact disease course and treatment response in the disorder (such as anxiety sensitivity). An investigation into the behavioral and neural correlates of interoception in OCD has the potential to improve personalization of treatment and identify novel targets for intervention.

In this review, we discuss the existing literature examining the role of interoception in OCD with the goal of highlighting its relevance to clinical heterogeneity and the optimization of treatment outcomes. Extending prior work (30), we first provide an overview of the different aspects of interoception and their neural bases before discussing current research on interoception and related constructs in OCD. Then, we consider interoception in the context of clinical intervention and discuss implications for research and treatment.

## METHODS

A PubMed literature search was conducted in July 2021 to identify the existing investigations of interoception in

OCD or OC symptoms using the MeSH terms "obsessive compulsive OR obsessions OR compulsions" AND "interoception OR interoceptive OR body awareness." Reference lists of articles were also reviewed for additional relevant literature.

## RESULTS

The PubMed search resulted in 169 publications, of which 3 examined interoceptive accuracy (31–33) and 1 investigated interoceptive sensibility (34) in OCD. Review of reference lists yielded 1 additional article examining interoceptive accuracy in OCD (35) and 1 additional article examining interoceptive sensibility and OCD symptoms in an undergraduate sample.

## NEURAL BASIS OF INTEROCEPTION

The neurobiology underlying interoception has been fairly well-delineated. Ascending small-diameter primary fibers carry visceral (e.g., about heart, lungs, gastrointestinal, urogenital), somatic (e.g., muscles, joints, skin), and homeostatic information (e.g., about temperature, mechanical stress, cellular activity) from tissues in the body to brainstem nuclei e.g., parabrachial, nucleus of the solitary tract, periaqueductal gray (20, 21, 36). These afferents reach the thalamus and the hypothalamus (37), and primarily through the thalamus, project to other subcortical (insula, hippocampus, amygdala) and cortical (cingulate, somatosensory, orbitofrontal, and medial prefrontal) regions (20, 21, 38).

The insula is considered a hub in this network (20, 39–41) and has been implicated in a wide variety of interoceptive processes including disgust (42), substance craving (43, 44), pain (45), and physical urges (46, 47). Converging evidence from several neuroimaging studies identify a tripartite functional parcellation of the insula into posterior, ventral anterior, and dorsal anterior subdivisions. The posterior insula is involved in sensory processing and has functional connections to the sensorimotor regions including somatosensory cortex (postcentral gyrus) and primary and secondary motor areas (precentral gyrus, supplementary motor area) (20, 48–50). The ventral and dorsal subdivisions of the anterior insula have different functional connectivity profiles (48). The ventral anterior insula is functionally connected to the limbic and paralimbic regions and is involved in emotion processing (48, 51, 52), whereas the dorsal anterior insula is functionally connected to regions involved in cognitive control and salience detection (53–55) including the dorsal anterior cingulate (ACC) and lateral prefrontal cortex (48, 51, 56). It has been proposed that different aspects of interoception follow this tripartite division of function of the insula: afferents carrying sensory signals from the body are first represented at the posterior insula before relaying information to the anterior insula, where interoceptive signals are re-represented with greater complexity through the integration of emotional (ventral) and cognitive (dorsal) information transmitted from connecting cortical and sub-cortical regions (30, 39, 40, 57, 58).

## DIMENSIONS OF INTEROCEPTION

Research has distinguished between separate facets of interoception, including the capacities to detect, discriminate, and evaluate the magnitude of different bodily signals [(59), see **Tables 1, 2**]. Garfinkel et al. (71), for instance, distinguished between the objective detection of bodily sensations (“interoceptive accuracy”), the subjective experience of bodily sensations (“interoceptive sensibility”) and the metacognitive awareness of interoceptive accuracy (e.g., whether a person believes they are accurately identifying bodily sensations, “interoceptive awareness”). Interoceptive accuracy and sensibility have been the focus of most research in healthy and clinical samples.

Interoceptive accuracy (IAcc) reflects the objective perceptual accuracy of interoceptive states. It is most commonly measured by a heartbeat detection task where individuals are asked to count the number of heartbeats occurring over a period of time, which is then compared to the actual number of heartbeats measured with pulse plethysmography (PPG) or electrocardiogram (ECG). IAcc has been found to be associated with emotional processing (91–93). Neuroimaging studies of heartbeat detection have linked individual differences in the functioning of several regions including the midbrain, ventral striatum, anterior cingulate cortex, somatosensory cortex, and the insula to greater interoceptive accuracy [e.g., (41, 63, 67, 94)]. From among these areas, the right dorsal anterior insula appears to be the most reliably positively associated with interoceptive accuracy across studies (41, 63, 95). It has been proposed that this insular subregion may contribute to instantaneous subjective feelings from the body that generate a sense of the present moment (40, 67).

Interoceptive sensibility (IS) relies on self-report and represents the subjective assessment of how internal body signals are appraised, regulated, and impact behavior (72, 73, 96, 97), and is frequently assessed using self-report questionnaires. Interoceptive sensibility is arguably the broadest of the three dimensions, encompassing several different aspects of subjective body processing. Commonly used scales include the Body Perception Questionnaire BPQ; (73), Body Awareness Questionnaire [BAQ; (74)], and the Multidimensional Assessment of Interoceptive Awareness [MAIA; (72)]. While both the BPQ and BAQ measure an individual’s general tendency to notice and be aware of their body sensations, the MAIA includes 8 subscales assessing different cognitive, emotional, and behavioral aspects and was designed to differentiate between “adaptive” and “maladaptive” forms of IS (98). Furthermore, the *emotional evaluation of interoceptive signals* [IE; (99, 100)] is a subcomponent of IS typically measured via self-report questions characterizing how an individual emotionally interprets bodily sensations. For example, IE is assessed by items in the MAIA “Not Worrying” subscale (e.g., “I start to worry that something is wrong if I feel any discomfort”). Existing literature suggests that IAcc and IS are often unrelated and emphasizes the utility in distinguishing between these two dimensions (30, 75). For example, IE has been shown to be unrelated to IAcc and more representative of top-down

processing (99). See **Table 2** for correlations among measures of interoceptive dimensions.

A number of neuroimaging studies have investigated IS, the majority of which utilized a single dimension measure such as the BPQ. Critchley et al. (41) for instance, found an association between self-reported awareness of body sensation assessed with the BPQ and gray matter volume in the insula. In a large sample of healthy adults, Wang et al. (76) found that IS was negatively correlated with functional connectivity between three pairs of brain regions: ventral anterior insula and superior temporal gyrus, dorsal anterior cingulate cortex and middle frontal cortex, and amygdala and medioventral occipital cortex. In clinical samples, IS has been linked to connectivity between the ACC and orbitofrontal cortex (OFC) (77) as well as between anterior insula and somatosensory regions (78). Only one study has examined the neural correlates of IS using a multidimensional measure. Using a dimensional reduction approach on the MAIA in a healthy sample, Stern et al. (75) reported a 3-factor solution, of which, one factor corresponded to reduced ability to regulate attention to body sensation, greater tendency to distract from uncomfortable body sensation, and greater worrying over body sensation. Scores on this component were related to increased BOLD activity in the anterior-mid insula, along with the cingulate cortex, and somatosensory/sensorimotor regions during interoceptive attention focusing. Compared to IAcc, the brain regions implicated in IS are less clear given fewer number of studies and differences in measures (i.e., MAIA vs. BPQ) and modalities (i.e., gray matter volume vs. functional connectivity). Whereas, literature most consistently implicates the involvement of the dorsal anterior insula in IAcc, findings in IS are less consistent. However, there does appear to be some overlap between neural correlates of these two facets, including the anterior cingulate (75, 76) and somatosensory areas (75).

## INTEROCEPTIVE DIMENSIONS AND OCD

Few studies have directly examined interoceptive dimensions in OCD utilizing the measures discussed above. Interoceptive accuracy has been examined in two studies using the heartbeat detection task with mixed results. Yoris et al. (70) reported increased accuracy in OCD patients compared to controls when counting heartbeats, whereas Schultchen et al. (32) and DeMartini et al. (31) found decreased accuracy (31, 32, 70). It is possible that variation in counting procedure [e.g., tapping hand in Yoris et al. (70) vs. silent counting in Schultchen et al. (32) and DeMartini et al. (31)] contributed to inconsistent findings. Though heartbeat detection tasks are the most commonly used measure of IAcc, the role of the cardiovascular system is not as clearly relevant for OCD as it is for other psychiatric conditions like panic disorder. In a study utilizing a different approach to measuring the processing of internal sensation in OCD, Lazarov et al. (35) used a muscle tension task and found that individuals with OCD were less accurate than healthy controls and individuals diagnosed with other anxiety disorders in their ability to produce specific muscle tensions when feedback was not given (35). Although these few studies represent important

**TABLE 1** | Interoceptive dimensions.

Interoceptive Component	Definition	Method of Assessment	Neural correlates	Findings in OCD
Attention	Observation of internal body sensations	Focusing task: Attend to sensations in specific organ (e.g., Simmons et al. (60); Farb et al. (61))	Right dorsal middle anterior insula (60), posterior insula (61)	N/A
Detection	Presence/absence of conscious report	Example: Subjects judge whether external tones occur simultaneous to pulse/heartbeat (e.g., Khalsa et al. (62))	Anterior insula (63)	N/A
Magnitude	Intensity of body sensations	Example: Dial ratings of internal sensation intensity [e.g. Khalsa et al. (64)]	N/A	N/A
Discrimination	Localization of sensation to a specific system, and differentiation from other sensations	Organ specific ratings, heartbeat discrimination task [e.g., Aziz et al. (65); Khalsa et al. (64)]	Anterior cingulate (65)	N/A
Interoceptive accuracy (IAcc)	Objective accuracy of interoceptive states	Examples: Heartbeat detection Task: Comparison of subjective heartbeat count to actual heartbeats measured with EEG [e.g., Schandry et al. (66)]	Subcortical: Insula and right dorsal anterior insula in particular, midbrain, ventral striatum Cortical anterior cingulate, orbitofrontal somatosensory (41, 63, 67–69)	<ul style="list-style-type: none"> <li>Decreased IAcc: <ul style="list-style-type: none"> <li>Heartbeat counting task (32)</li> <li>Muscle tension task (35)</li> </ul> </li> <li>Increased IAcc (70)</li> </ul>
Interoceptive Awareness (IA)	Meta-cognitive awareness of interoceptive accuracy	Agreement between objective and subjective report: Subjective confidence ratings during heartbeat detection task compared to IAcc [e.g., Garfinkel et al. (71)]	N/A	N/A
Interoceptive Sensibility (IS)	Subjective assessment of how internal body signals are appraised, regulated, and impact behavior	Self-report, for example: MAIA (72), BPQ (73) BAQ (74) Confidence ratings	Anterior-mid insula, cingulate cortex, orbitofrontal cortex, somatosensory and sensorimotor regions (75–78)	<ul style="list-style-type: none"> <li>Compared to healthy controls, OCD demonstrated higher noticing, distracting, worrying, emotional awareness, listening but lower trusting on MAIA</li> <li>Higher noticing related to responsibility/harm, symmetry/ordering symptoms</li> <li>Higher distracting related to unacceptable/taboo thoughts (34)</li> </ul>
Emotional Evaluation of Interoceptive Signals (IE)	Emotional appraisal of internal bodily signals	MAIA Not Worrying Subscale (72), ASI Physical Subscale (79)	Posterior, dorsal, and anterior insula, dorsal anterior cingulate (75)	<ul style="list-style-type: none"> <li>OCD appraises internal physical sensations more negatively than controls (34, 80)</li> <li>Negative appraisal of internal sensations correlated with responsibility/harm, contamination/washing, symmetry/ordering, certainty/doubting (34, 81, 82)</li> </ul>

ASI, Anxiety Sensitivity Index; BPQ, Body Perception Questionnaire; BAQ, Body Awareness Questionnaire; EEG, electroencephalogram; MAIA, Multidimensional Assessment of Interoceptive Awareness; OCD, obsessive-compulsive disorder.

**TABLE 2** | Reliability and validity of select interoceptive assessments.

Interoceptive Dimension	Assessment	Reliability	Correlations Between Interoceptive Constructs		
			Interoceptive Awareness (IA)	Interoceptive Sensibility (IS)	Emotional Evaluation of Interoceptive Signals (IE)
Interoceptive accuracy (IAcc)	Heartbeat detection (counting) task	Retest reliability (2 months) = 0.60 (83) $\alpha$ = 0.89 (84)	$r = 0.16, p = 0.17$ (85)	MAIA (84): Noticing $r = -0.05, ns$ Not Distracting $r = -0.06, ns$ Not Worrying $r = 0.08, ns$ Attention Regulation $r = 0.20, p = 0.02$ Emotional Awareness $r = -0.05, ns$ Self-Regulation $r = -0.03, ns$ Body Listening $r = 0.00, ns$ Trusting $r = 0.08, ns$ BPQ: $r = 0.06, ns$ (71) BAQ: $r = 0.18, p < 0.05$ (86) Confidence rating: $r = 0.28, p < 0.05$ (71)	MAIA Not Worrying: $r = 0.08, ns$ (84)
Interoceptive Awareness (IA)	Agreement between objective and subjective report: Subjective confidence ratings during heartbeat detection task compared to IAcc			Confidence rating: $r = -0.02, p = 0.84$ (85)	
Interoceptive Sensibility (IS)	Self-report, e.g., MAIA, BPQ, BAQ, confidence ratings	MAIA (72), $\alpha = 0.66-0.87$ (72), retest reliability (M days = 113, SD = 4.3) = 0.66-0.79 (87) BPQ (73) BPQ-SF $\omega = 0.83-0.91$ , retest reliability (1 week) = 0.91-0.96 (88), Confidence ratings			
Emotional Evaluation of Interoceptive Signals (IE)	Self-report, e.g., MAIA Not Worrying subscale, ASI Physical subscale	MAIA Not Worrying: $\alpha = 0.67$ (72); retest reliability (M days = 113, SD = 4.3) = 0.76 (87) ASI Physical: $\alpha = 0.76-0.89$ (89); ASI-3 retest reliability (3 months) = 0.70 (90) <sup>a</sup>			

Samples are non-clinical unless otherwise noted.

MAIA, Multidimensional Assessment of Interoceptive Awareness; BPQ, Body Perception Questionnaire; BPQ-SF, Body Perception Questionnaire-Short Form; BAQ, Body Awareness Questionnaire; ASI, Anxiety Sensitivity Index; ASI-3, Anxiety Sensitivity Index-3  $\alpha$ , Cronbach's alpha (internal consistency);  $\omega$ , Categorical Omega (internal consistency);  $r$ , Pearson correlation coefficient.

<sup>a</sup>Sample of treatment seeking smokers.

first steps investigating interoceptive accuracy in OCD, given the limited number of studies, task variability, and mixed findings, more research is needed before conclusions can be drawn. It has been recommended that tasks assess IAcc across organ different systems (e.g., cardiovascular, respiratory, gastrointestinal, etc.) to create a more reliable and comprehensive “interoceptive profile” (59). Indeed, future investigations may benefit from including multisystem tasks to clarify IAcc in OCD.

Our group has examined interoceptive sensibility in OCD utilizing the MAIA (34). In our investigation, compared to healthy controls, individuals with OCD reported hyperawareness of bodily sensations. Further, the OCD group demonstrated a more maladaptive profile of IS including increased distraction from and worry about uncomfortable sensations. Within OCD, different dimensions of IS also related to clinical heterogeneity. For example, increased tendency to notice bodily sensations



correlated with higher severity of symmetry/ordering (e.g., “feelings that something is not just right and behaviors designed to achieve order, symmetry, or balance”) and responsibility for harm (e.g., “thoughts and behaviors related to harm and disasters”) symptoms. Greater worry about body sensations, which corresponds to the IE sub-dimension of interoceptive sensibility, was related to increased severity of both the responsibility for harm and contamination symptom dimensions. In an undergraduate sample, Jokić and Purić (101) found that a similar pattern of MAIA subscales demonstrated significant (albeit small) correlations with overall OC symptoms (101). Therefore, existing findings suggest that obsessive-compulsive symptoms may relate to a profile of interoceptive sensibility characterized by awareness of bodily sensations, reliance on sensations for information, appraisal of sensations as threatening, and the tendency to respond to aversive sensations with cognitive avoidance.

Anxiety sensitivity (AS) is a construct related to interoceptive sensibility that has been more frequently researched in OCD patients. Anxiety sensitivity reflects fear of anxiety-related body sensations (79). AS is most commonly assessed utilizing self-report methods, specifically by the 16-item Anxiety Sensitivity Index (ASI), which allows calculation of a total score in addition to subscale scores measuring fear of social evaluation (ASI-Social), cognitive (ASI-Cognitive), and physical symptoms ASI-Physical; e.g., “When my stomach is upset, I worry that I might be seriously ill” (102). Greater fear of physical anxiety symptoms, as measured by ASI-physical, is correlated with increased worrying about body sensations and a greater tendency to regulate emotional states through attention to body sensation as measured by the MAIA (72), and thus corresponds to the interoceptive sensibility subconstruct of *emotional evaluation of interoceptive signals*. AS is considered to be a transdiagnostic construct and is known to be broadly related to a range of psychopathology including panic disorder, posttraumatic stress disorder (PTSD), generalized anxiety disorder (GAD), substance-use disorders, and suicidal ideation (103–107). OCD samples demonstrate higher levels of physical anxiety sensitivity compared to healthy controls and comparable levels to anxiety disorder samples (80). Greater fear of physical symptoms is not only associated with overall OCD symptom severity, but also has been related to increased contamination, symmetry/ordering, and certainty/doubting symptoms (81, 82, 108). A recent longitudinal study in adolescents found a bidirectional association between AS and OC symptoms suggesting that not only is AS a risk factor for developing OC symptoms, but experiencing symptoms also increases the prospective risk of elevated AS over a 2-year period (109).

To the best of our knowledge, no study has yet evaluated AS in individuals with OCD using neuroimaging but existing literature on AS in individuals and subthreshold anxiety symptoms seems to consistently implicate the anterior insula. Higher ASI-total score was associated with neural activity in the insula (posterior and dorsal anterior) and dorsal anterior cingulate (dACC) in individuals with panic disorder with agoraphobia when viewing fearful and angry emotional faces (110). Additionally, dorsal anterior insula and amygdala activity was found to be higher

among individuals with subthreshold anxiety symptoms in a face viewing task (111). Using the 36-item Anxiety Sensitivity Index (Revised; ASI-R) in a sample of individuals with panic disorder, Kim et al. (112) reported that total ASI-R score was associated with greater functional anisotropy (i.e., indicator of white matter integrity) in the white matter regions near the insula, corpus callosum, posterior limb, retrolenticular parts of the internal capsule, posterior thalamic radiata, posterior corona radiata, and sagittal striatum (112). These white matter findings were consistent with a previous report stating that AS is associated with functional connectivity between the insula and other neural regions (including the thalamus and amygdala) that are known to modulate interoceptive processing (113–115).

Of the three dimensions proposed by Garfinkel et al. (71, 96), interoceptive sensibility, or the self-reported assessment of interoceptive ability, appears to be most consistently abnormal in OCD. Specifically, studies using the MAIA and ASI-physical subscale indicate that OC symptoms may relate to an attentiveness to internal sensations and a reliance on sensations to clarify emotional states and inform behavior (34, 101). Further, and perhaps most consistent with the subdimension of emotional evaluation of interoceptive signals, studies demonstrate that individuals with OCD appraise internal bodily sensations as threatening and respond to aversive sensations with cognitive avoidance (34, 80, 101). These findings are somewhat consistent with CBT models, which emphasize the role of appraisal and avoidance in maintaining symptoms e.g. (9, 116). Studies also demonstrate associations between facets of IS and specific OC symptom dimensions, suggesting that interoception might be particularly relevant for certain presentations (34, 81, 82, 108). For example, the positive associations of the symmetry/ordering dimension with self-reported awareness of sensations (34) and negative appraisal of internal sensations (81, 82, 108) could suggest that interoceptive dysfunction is more relevant to this clinical presentation. Given the significant clinical heterogeneity within OCD, such findings are particularly meaningful as they could lead to better treatment matching and more targeted interventions.

## INTEROCEPTION AND CORE OCD PHENOMENA

### Sensory Phenomena

Sensory phenomena (SP) are uncomfortable or aversive sensations that motivate repetitive behaviors. As opposed to compulsions driven by an effort to reduce anxiety or avoid harm, individuals with SP report engaging in repetitive behaviors aimed at reducing discomfort elicited by an inner feeling of incompleteness (INC) or “not just right” experience (NJRE) (117). Sensory phenomena are most commonly assessed via self-report [e.g., Obsessive-Compulsive Trait Core Domains Questionnaire; Not Just Right Experiences Questionnaire-Revised; Symmetry/NJRE subscale on the Dimensional Obsessive-Compulsive Scale (118–120)], or clinical interview [University of São Paulo Sensory Phenomena Scale (121)]. As many as 60–70% of individuals diagnosed with OCD

experience some form of sensory symptom in the absence of a specific feared outcome (12, 13, 117, 121–123). Further, studies in both clinical and non-clinical samples have found sensory phenomena to be uniquely associated with OC severity even after controlling for harm avoidance and OC-specific beliefs (122, 124–126). Research suggests sensory phenomena are associated with a number of specific and important clinical characteristics, for example, symmetry, ordering, and arranging symptoms (12, 127, 128). Our group identified a relationship between symmetry/ordering/NJRE symptoms and the tendency to notice and be aware of internal sensation as measured by the MAIA, suggesting that increased IS may contribute to these types of symptoms in OCD (34). There is some evidence to suggest that sensory phenomena may also relate to onset and course of OC symptoms (129). For example, one study found that individuals diagnosed with OCD retrospectively perceived increases in NJRE-related urges as one of the top two clinical characteristics (after stress) that played a role in the transition from sub-threshold symptoms to clinical OCD suggesting the potential role of interoceptive processes in the etiology of the disorder (130).

Findings from two neuroimaging studies in individuals with OCD suggest a relationship between SP and neural regions associated with interoception including the insula, sensorimotor, and somatosensory regions (14, 15). Higher SP severity was associated with greater activity of the mid-posterior insula, as well as somatosensory cortex, orbitofrontal cortex, and lateral prefrontal cortex when individuals with OCD viewed “body-focused” videos (15). Interestingly, greater gray matter volumes in sensorimotor regions were also observed in patients with OCD who reported experiencing SP compared to those who did not (14).

### Premonitory Urge and “Urges-for-Action”

Premonitory urges (PU) are uncomfortable or aversive sensations preceding movements or vocalizations in individuals with tic disorders. Often described as a building up of inner tension or an “itching” or “tingling” in the area of the body that has the tic, PUs are most commonly measured using the self-report Premonitory Urge for Tics Scale [PUTS; (131)]. In TS, PU are related to specific OC symptoms including the symmetry and aggression dimensions (132) and several studies have highlighted the similarity between premonitory urges in TS and sensory phenomena preceding compulsive behavior in OCD (121, 133). Indeed, Brandt et al. (134) found a temporal relationship between premonitory urges and compulsions in patients with OCD, characterized by increasing urge intensity until execution of compulsion, followed by immediate, temporary urge decrease (134).

Limited research demonstrates that interoceptive processes may relate to premonitory urges in adults with Tourette Syndrome. Rae et al. (135) found that interoceptive sensibility (as measured by the BPQ) predicted PU severity. Interoceptive accuracy has been examined in relation to PU in two studies: Ganos et al. (136) reported that IAcc predicted PU severity, whereas Rae et al. (135) did not find a significant correlation. The relatively small sample sizes in both of these investigations

( $n = 19–21$ ) combined with slight differences in task design (e.g., length and timing of individual trials) could have contributed to inconsistent findings.

It has been suggested that urges preceding repetitive behaviors in OCD and TD may be phenomenologically similar to “urges-for-action,” which are everyday sensations that motivate behaviors such as blinking or scratching (137, 138). A core feature of “urges-for-action” is the need to suppress or delay a behavior which builds up over time the longer the behavior is suppressed (139), differentiating these pre-movement experiences from those associated with more intentional and goal-directed behaviors (138). Prior work has indicated that every-day “urges-for-action” activate a network of brain regions including the insula and sensorimotor cortical regions (137, 138, 140–142). Using eyeblink suppression as a model to investigate sensory-based urges in OCD, we observed greater eyeblink suppression failures in patients with OCD compared to controls when asked to suppress eye blinking for a period of 60 s (46). OCD patients showed greater neural activity during blink suppression in a network of regions including the anterior insula, cingulate, striatum, superior/inferior parietal cortex, precuneus, and the lateral occipital cortex (46). Interestingly, many of these brain regions overlapped with those found in studies of everyday “urges-for-action” (138).

### Disgust Proneness

Disgust is a basic emotion that functions to motivate avoidance of potentially harmful stimuli that could cause disease (143, 144). It is associated with a visceral response and physiological signs involving interoceptive processes such as nausea (145). Indeed, interoceptive functioning may contribute to disgust proneness, or the extent to which one not only experiences disgust but also finds it to be aversive (146). Disgust proneness can be further divided into two specific dimensions: Disgust Propensity, the frequency of feeling disgusted, and Disgust Sensitivity, how negatively these experiences are appraised (146). Two common assessments of disgust proneness include The Disgust Propensity and Sensitivity Scale-Revised (147) and The Disgust Scale-Revised (148).

Not surprisingly, in both non-clinical and OCD samples, evidence reliably demonstrates a connection involving disgust-proneness with contamination symptoms and behavioral avoidance (149–157). Further, studies have shown disgust proneness to mediate the relation between OC symptoms and behavioral avoidance (158, 159). The construct of contamination includes both physical and mental contamination. While physical contamination involves the presence of a contact contaminant, mental contamination refers to the internal sensation of “dirtiness” in absence of a contact contamination (e.g., dirt, germs) (157, 160, 161). Mental and contact contamination are closely related, yet diverge not only in terms of antecedents but also differ in regards to the efficacy of washing in relieving these feelings (with washing theorized to alleviate physical contamination more than mental) (156, 157, 161). Although disgust proneness has not been investigated in relation to interoceptive accuracy or sensibility, functional neuroimaging

studies identify an association between insula activation and disgust (162, 163).

Compared to controls, individuals with OCD showed greater activity in left and right insula when viewing disgust-inducing images, but did not show different patterns of neural activity when viewing fear/threat-inducing images (164–166). As disgust proneness may also be related to negative affect (155), further neuroimaging studies are required to clarify the neural correlates of the association between disgust and OCD symptoms with measures of affect included as covariates in the model.

## INTEROCEPTION AND OCD TREATMENT

To date, self-report and neuroimaging investigations provide the most compelling evidence for interoceptive differences in patients with OCD. Further, interoception may be more relevant to specific clinical presentations, including individuals with symptoms of symmetry/ordering motivated by sensory phenomena or contamination/washing driven by visceral feelings of disgust. Beyond self-report data, neuroimaging investigations demonstrate the involvement of key interoceptive regions like the insula in the pathophysiology of sensory phenomena, urges-for-action, and disgust. Given this, looking at interoception and related core OCD phenomena in the context of treatment could provide valuable insights necessary for improving therapeutic outcomes.

### Psychotherapy

Cognitive behavioral therapy (CBT) with exposure and response prevention (ExRP) is the gold standard treatment intervention for OCD (167). Response prevention is the elimination of compulsive/avoidance behaviors and exposure entails repeated, systematic confrontation with distress-inducing stimuli. ExRP is theorized to work through various mechanisms such as habituation (i.e., distress decreases naturally during and between exposure sessions) and expectancy violation [i.e., by approaching a feared situation, one learns that it can be tolerated and rarely leads to a feared outcome (168–170)]. Interestingly, studies investigating ExRP treatment response in individuals with OCD have observed associations between insula activations and treatment response, suggesting that interoceptive mechanisms subserved by the insula may have roles in the therapeutic process of ExRP. A recent investigation using whole-brain network-based statistics in unmedicated individuals with OCD found network alterations involving the anterior insula significantly predicted response to exposure therapy (171). Norman et al. (172) found a trend association between greater baseline anterior insula BOLD activity during cognitive control and better ExRP treatment response. Separately, Nakao et al. found that individuals with OCD who showed improvement following either 12 weeks of fluvoxamine or exposure therapy showed increased BOLD activity in the bilateral insula during a Stroop task and reduced activity in the left posterior insula during symptom provocation compared to baseline neural activity (173). Consistently, reduced BOLD activity in regions including the bilateral insula were also observed during individualized symptom-provocation OCD following ExRP treatment (174).

Although one cannot infer a psychological process from neural data alone (175), such findings do suggest that insula function may impact the efficacy of traditional exposure exercises in OCD even though they tend to focus on situations (*in vivo*) or mental stimuli (imaginal) that elicit fear, rather than target sensory-based symptoms. Still, there is evidence suggesting that patients experiencing sensory phenomena derive greater clinical benefit from ExRP when it is optimized to specifically target those symptoms (176). A recent meta-analysis found that though incompleteness improves moderately during CBT, only a minority (18%) of studies tailored treatment to address sensory-related symptoms. Importantly, moderator analyses showed that when treatment was modified to target incompleteness, there was a greater reduction in incompleteness scores (176). Further, some laboratory and outcome research suggests that learned disgust responses are more resistant to extinction and slower to habituate than fear (177–183). Therefore, individuals with OCD with predominant sensory phenomena or disgust may benefit from therapeutic processes that aim to reduce or ameliorate aspects of interoception. Recently, there has been increasing interest in using exposures to specifically target internal sensations (interoceptive exposure) in OCD (103, 170). In one investigation of transdiagnostic CBT, patients with OCD demonstrated the greatest decreases in physical anxiety sensitivity following the introduction of interoceptive exposures (184). Though more published studies are needed, these findings provide preliminary data to suggest that interoceptive exposures may reduce negative appraisal of physical sensations in OCD (103, 184). Khalsa et al. suggested that creating an “interoceptive profile” of patients through assessment of several organ systems (e.g., cardiovascular, gastrointestinal, etc.) could assist clinicians with personalizing and calibrating “dose” of exposures (59). OCD clinicians must also be familiar with the nature of interoceptive-related features such as sensory phenomena, disgust, anxiety sensitivity, and how they differ from fear in treatment. Interestingly, clinician surveys indicate that only a minority report utilizing interoceptive exposure, suggesting that treatment delivery may be suboptimal for many patients with OCD (185, 186).

### Pharmacotherapy

Serotonin reuptake inhibitors (SRIs) including the tricyclic antidepressant clomipramine, and selective SRIs are considered a first line treatment for OCD (167, 187). However, many patients don't respond to an adequate trial and relapse is common after discontinuation (167). Therefore, examining moderators of response to these medications is necessary. Unfortunately, very little has been published on interoception in OCD and treatment response to SRIs. One open trial found that patients reporting sensory phenomena responded better to clomipramine than patients without sensory phenomena (188). Separately, Nakao et al. found that individuals with OCD who showed improvement following 12 weeks of fluvoxamine pharmacotherapy showed increased BOLD activity in the bilateral insula during a cognitive inhibition task (Stroop) and reduced activity in the left posterior insula during symptom provocation compared to baseline neural activity (173). Given the scarcity of research, looking to novel pharmacological treatments that specifically target



interoceptive dysfunction may hold promise. Ondansetron, a 5-HT<sub>3</sub> antagonist that is FDA-approved for the treatment of nausea and vomiting, demonstrates efficacy in the treatment of sensory symptoms related to pruritus (189). We have found that single high doses of ondansetron reduce activation in the insula, sensorimotor regions, and cingulate cortex in healthy individuals (190). Dopaminergic agents may also hold promise for modulating interoception. Domperidone, a D<sub>2</sub> receptor antagonist, was recently found to influence oculomotor avoidance of disgusting visual stimuli (191). Given the research suggesting disgust may be more resistant to habituation than fear, domperidone could hold potential for augmenting ExRP (191). Botulinum toxin is a protein that acts to block presynaptic release of the neurotransmitter acetylcholine from motor neurons. Though not yet investigated in OCD, it has been shown to reduce premonitory urge and premonitory sensations (generalized urges, tingling sensations) in Tourette's Syndrome (192). To our knowledge, no work-to-date has investigated glutamate-modulating-agents such as N-acetylcysteine (NAC) on interoception in OCD. However, a prior study reporting no significant effect of NAC on overall OCD symptom severity proposed that this agent might be particularly efficacious for patients with urges and sensory phenomena (193) based on prior work revealing NAC efficacy in reducing urges in trichotillomania and excoriation disorder (194, 195).

## Brain Stimulation/Neuromodulation

Deep brain stimulation (DBS) involves the electrical stimulation of specific brain areas through implantation of electrodes. Most commonly used in the treatment of movement disorders such as Parkinson's disease, DBS is a FDA-approved intervention for treatment-refractory OCD (196, 197). Electrodes are most commonly implanted in striatal areas or the subthalamic nucleus (STN) and OCD symptom improvement has been associated with normalization of frontostriatal activity (197–199). Although no studies have directly examined the impact of DBS on interoceptive processing in OCD, neuroimaging findings demonstrate effects of DBS on the functioning of key interoceptive regions. Indeed, resting state functional connectivity with insular and sensorimotor regions at baseline has shown to predict optimal DBS outcome, regardless of target placement (200). Further, DBS of the ventral anterior limb of the internal capsule in patients with treatment-refractory OCD has been found to lead to decreased latero-basal amygdala-insula connectivity (201). Despite these neuroimaging findings, there is a paucity of data investigating the impact of DBS on interoception.

Transcranial magnetic stimulation (TMS) is a non-invasive neuromodulation technique that involves placing a magnetic coil on the scalp that generates a brief and high-intensity magnetic field that excites or inhibits a part of the brain under the coil (202, 203). TMS is FDA-approved for therapeutic applications in several psychiatric conditions such as depression and OCD, although its therapeutic effects on symptoms relating to interoception remain relatively under-investigated. Prior studies have applied inhibitory TMS targeting neural regions known to be involved in interoception, including the anterior

insula, somatosensory cortex, and supplementary motor area. In a sample of healthy individuals, inhibitory stimulation using a figure-of-eight coil applied separately over the right anterior insula and right somatosensory area led to reduced interoceptive accuracy and increased interoceptive sensibility (100). These results must be interpreted with caution, as the insula is located approximately 5 cm under the skull, and the standard stimulation protocol used by the authors may not have reached the depth of insula (204). Direct stimulation of the insula may be achieved using different coil configurations, such as H-coils, that can deliver deeper but broader stimulation to the brain (205–207). Existing studies that applied H-coils targeting the insula for addiction (208), severe and enduring anorexia nervosa (209), and eyeblink suppression (210) have reported mixed therapeutic effects of insula stimulation. A recent transcranial direct current stimulation (tDCS) study found that sham, but not anodal stimulation targeting the insula, was related to IAcc improvement (211). Further studies are required to evaluate the clinical efficacy of tDCS and deep TMS.

Although studies targeting the insula with TMS are somewhat difficult to conduct, a body of research has pointed to the potential utility of targeting sensorimotor areas closer to the surface of the brain such as the supplementary motor area (SMA). An investigation applying inhibitory repetitive TMS over the bilateral SMA area for 10 daily sessions in a small sample of individuals with treatment-resistant OCD ( $n = 5$ ) or Tourette syndrome ( $n = 3$ ) (212) found that patients with OCD showed symptom reduction, and two out of three patients with Tourette syndrome showed complete remission of tics at the end of 2 weeks. Significant reductions in anxiety and depressive symptoms were also observed in this study. Subsequent investigations involving the supplementary motor area (SMA) also reported reduction in OCD severity (213–215), with benefits persisting at 6–12 weeks after treatment (214). A recent investigation, also involving inhibitory repetitive TMS of the SMA in individuals with OCD, showed symptom reduction that persists up to 3 months post TMS (216). In this study, both baseline and post-TMS symptom scores predicted post-TMS reduction in functional connectivity of the supplementary motor area with regions including the orbitofrontal cortex, anterior cingulate, and insula (216).

Even though the bulk of existing studies using TMS in OCD did not specifically evaluate changes in interoceptive processes, existing findings indicate that regions that are important in interoception could be indirectly (in the case of insula) or directly (in the case of sensorimotor regions) modulated by TMS (216). A recent randomized-controlled investigation using tDCS found that anodal stimulation of the SMA resulted in superior reductions in OCD symptoms compared to sham in a treatment-resistant sample (217). Despite preliminary evidence that non-invasive neurostimulation techniques like tDCS and transcutaneous electrical nerve stimulation (TENS) may provide therapeutic benefits (218), their application to modulate interoceptive processes is currently lacking.

## Biofeedback and Real-Time fMRI Neurofeedback

Biofeedback generally involves measuring one's own physiological state and feeding the information back in real-time via visual or auditory or tactile feedback so that the individual can learn to modulate the physiological processes that are usually otherwise involuntary (219, 220). Biofeedback has shown promise in ameliorating stress and anxiety symptoms (221–224), and studies also reported improvements in interoceptive accuracy following biofeedback training (225, 226). For example, Meyerholz et al. (225) examined the effect of true cardiac feedback, false-feedback, mindfulness practice, or a waiting control condition on cardiac IAcc. IAcc only improved significantly in the feedback condition, and this change was significantly greater than the three other conditions, suggesting that biofeedback holds promise for modifying interoceptive accuracy (225).

Real-time fMRI neurofeedback, another personalized approach, involves analyzing BOLD activity in real time as fMRI data is collected, and presenting information about neural activity in specific regions to the individual to guide modulation or self-regulation (227). Neurofeedback studies have shown that training can be effective for both modulating anterior insula activity (228–231). In a sample of 3 individuals with OCD with contamination-related obsessions and compulsions, Buyuturkoglu et al. (232) showed that active down-regulation of the insula led to reduced disgust levels and anxiety in response to viewing disgust-inducing images in 2 out of 3 patients. Although further research is required in larger samples, early evidence indicates that real-time fMRI neurofeedback may be beneficial in modulating interoceptive processes by actively regulating neural activity.

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## CONCLUSION

Despite increased understanding in the pathophysiology of OCD, current mainstay treatments have largely remained unchanged over the past 30 years. The clinical heterogeneity of a significant number of patients has not been fully accounted for by traditional anxiety-based models, thus prompting more research into the processing of internal sensations. Interoception presents itself as a promising target for OCD research given the established theoretical framework and measurable behavioral and biological correlates (59). Indeed, a growing body of behavioral and neurobiological literature provides evidence for the role of interoception in OCD. We expect that continuing this line of research will prove useful for both improving personalization of existing treatments like ExRP and identifying new targets for intervention.

## AUTHOR CONTRIBUTIONS

LB, ES, and GE contributed to the conception of the review. LB and AB searched and reviewed relevant literature. LB wrote the first draft of the manuscript. GE, ES, and KC wrote sections of the manuscript. All authors contributed to manuscript revision, read, and approved the submitted version.

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