The Psychobiology of Obsessive-compulsive Disorder: How Important is the Role of Disgust?

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Psychobiologic models of obsessive-compulsive disorder (OCD) have focused on cortico-striatal-thalamic-cortical (CTSC) circuits, noting normal function in cognitive and motoric procedural strategies. Such models have relied on the classification of OCD as an anxiety disorder, seldom exploring other relevant emotions. Based on the hypothesis that a central emotion in OCD is disgust, the authors review the literature on its psychobiology and its relevance to current models of OCD. There are important parallels between the psychobiology of OCD and that of disgust. Obsessive-compulsive disorder may be conceptualized in terms of a false contamination alarm in which disgust plays a crucial organizing or embodying role, not only at a basic brain level, but also in terms of the psychosocial aspects of the disorder. Just as psychobiologic models of panic disorder and post-traumatic stress disorder have been strengthened by the inclusion of preclinical work on amygdala-mediated fear conditioning, so findings on disgust and its mediating CSTC circuits may generate useful hypotheses for OCD research.

Introduction

Obsessive-compulsive disorder (OCD) is characterized by intrusive distressing thoughts (*eg,* about dirt or germs) and repetitive irrational rituals (*eg,* hand-washing or cleaning). For many years, OCD was viewed as an uncommon disorder, caused by unconscious conflict, and rather refractory to treatment. More recently, however, it has become clear that OCD is one of the most prevalent and disabling conditions, mediated by specific neurobiologic factors, and responsive to particular psychopharmacologic and psychotherapeutic interventions [1].

A growing body of research has contributed to this paradigm shift, and has allowed the development of a number of psychobiologic models of OCD. Much of the focus of such models has been on cortico-striatal-thalamic-cortical (CSTC) circuits. There are several good reasons for this focus, including the growing understanding of their normal anatomy and function in mediating cognitive and motoric procedural strategies, the range of evidence demonstrating CSTC dysfunction in OCD, and the availability of data addressing the underlying pathogenesis of such dysfunction [2].

Perhaps implicit in this work is the assumption that OCD is an anxiety disorder, with anxiety and fear as the predominant emotional symptoms and processes. Such an assumption is, however, arguably flawed for a number of reasons, including the considerable phenomenologic differences between OCD and disorders of fear (panic disorder and post-traumatic stress disorder), and the still unclear relevance of the growing body of preclinical work on amygdala-mediated fear conditioning to understanding OCD [3].

If fear is not the organizing emotion in OCD, what is? The authors' experience with researching and treating OCD has increasingly turned focus to the possible role of disgust in this disorder. Although recently labeled "the forgotten emotion of psychiatry" [4•], there is a growing literature on the phenomenology and psychobiology of this emotion [5,6], which prima facie appears relevant to OCD. The authors undertook a review of this literature with the aim of rethinking models of the psychobiology of OCD.

An initial broad search was undertaken of MedLine and PsychLit using the term *disgust*, for all articles published prior to the end of 2000. Reference lists of relevant articles were then examined for additional relevant studies. The authors present the findings in terms of a discussion of the nature of disgust and its psychobiology, before going on to explore the implications of this literature for models of the psychobiology of OCD.

The Nature of Disgust

Darwin [7] laid the foundation for current concepts of basic or primary emotions, hypothesizing that certain emotional displays, including those of disgust, represent evolutionarily conserved biologic mechanisms designed to enhance survival. More recent work using cross-cultural [8] and devel-

opmental [9] methodologies has consolidated the notion that there are distinct emotions with universal antecedent events and expressions, and with comparable cross-species expressions and specific neurophysiologic underpinnings.

Darwin [7] noted that disgust referred to "something revolting, primarily in relation to the sense of taste," and subsequent theorists have continued to define disgust (literal meaning is bad taste) in terms of revulsion at oral incorporation [10], particularly of contaminants [5]. The feeling of revulsion associated with disgust is reminiscent of nausea, and the somatic response (narrowing of the nostrils, raising of the upper lip, wrinkling of the brow, and even a shudder) can be seen as a vestigial component of rejecting bad tastes or smells. Indeed, disgust has similar expressions and elicitors in all cultures, these have clear homologues in human infants and nonhuman primates, as well as specific psychophysiologic correlates [5,11,12].

Furthermore, it seems likely that disgust and fear evolved for different purposes; fear is crucial for responding to danger and threat, and disgust is important in the appraisal of contamination and disease and, particularly, of potentially harmful decayed food [5]. Although this does not rule out an intersecting role for fear and disgust in the development of various cognitive-affective symptoms, it does suggest the potential value of separating out these processes when developing and researching models of psychopathology.

Darwin [7] noted further that disgust occurred not only in relation to taste, but also "secondarily to anything that causes a similar feeling, through the sense of smell, touch or even eyesight." Certainly, disgust can be elicited by a range of sensory experiences [5,6,13]. Indeed, although disgust has been described as "the most embodied and visceral of emotions" [6], this extension of disgust goes even further, from disgust in taste aversion to disgust about other aspects of the body, through to disgust as a component of moral judgments [5,6,14].

This expansion of a concrete feeling through to more abstract concepts is certainly consistent with current understandings of how linguistic categorization operates [15]. Indeed, we can perhaps refer to the double embodiment of disgust, to its instantiation in the brain-body, and to its instantiation in social contexts and interactions. The authors tackle each of these subjects in more detail, before going on to consider parallel issues in the area of OCD.

Neuronal Correlates of Disgust

There is a limited database of neurophysiologic studies on disgust. Davidson *et al.* [16], for example, found right frontal and anterior temporal activation on exposure to disgusting stimuli, with activation of the left anterior temporal region by pleasant stimuli. Findings were notably consistent with an earlier electroencephalography (EEG) study that differentiated disgust (right-sided) from happiness (left-sided) [17], and with EEG activity in neonates responding to disgusting and pleasant tastes [18]. Also, in contrast to other expressions, disgust is selectively associated with alimentary automatisms and mesial temporal lobe seizures [19]. Finally, disgust and fear are distinguishable on a range of autonomic nervous system response patterns [20–23].

Lane *et al.* [24] found that during positron emission tomography (PET) scanning of healthy individuals, happiness, sadness, and disgust were all associated with increases in activity in the medial prefrontal cortex and thalamus, with some activation of anterior and posterior temporal structures. Disgust also activated the lateral cerebellum and some occipitotemporal areas. Subsequent studies by the same group [25] and others [26] confirm both overlap and distinctions in the functional neuroanatomy of pleasant and unpleasant emotional experience.

Reviewing such work, Reiman [25] suggested that although limbic (amygdala-hippocampal) regions are particularly involved in the emotional response to exteroceptive sensory stimuli, the anterior insula cortex is preferentially involved in the emotional response to potentially distressing cognitive stimuli, interoceptive sensory stimuli, and body sensations. This region serves as an internal alarm center, alerting the individual about dangers inside the body. The medial frontal cortex participates in the conscious experience of emotion, inhibition of excessive emotion, or monitoring one's own emotional state to make relevant decisions.

A particularly interesting set of recent research has focused on the role of brain circuits in perceiving facial expressions of disgust. There is growing understanding of the neural circuits involved in facial information processing; studies of patients with focal brain lesions, for example, demonstrate that different circuits are responsible for processing facial identity and for processing facial expressions of emotion [27]. Furthermore, although right hemisphere lesions are associated with impaired recognition of various negative facial expressions [28,29], bilateral lesions of the amygdala are associated with selective impairment in interpreting fearful expressions [30–33]. Similarly, functional imaging studies demonstrate that the right hemisphere has a particular role in the perception of negative expressions [34], and the amygdala are crucially involved in the recognition of fearful facial expressions [35,36].

A seminal study by Sprengelmeyer *et al.* [37] suggested that CSTC circuits were particularly important in the recognition of disgust; patients with Huntington's disease, a disorder involving the striatum and other regions, demonstrated more severe impairment of recognition of facial and vocal expressions of disgust than of other emotions. This impairment was even more selective in subjects with presymptomatic Huntington's disease gene carriers, presumably reflecting restriction of the degeneration to the basal ganglia or caudate only [38]. Similarly, a recent report described a patient with insula-putamen lesions after stroke that had selective impairment in recognizing social signals of disgust

from multiple modalities [39]. Conversely, neuropsychiatric disorders with less specific pathology demonstrate some dissociation in the impairment of emotion recognition, but less selectively so [40,41].

Such data lead immediately to questions about the role of the striatum in disgust in normal individuals. Indeed, a study by Phillips *et al.* using functional MRI (fMRI) compared cerebral activation in response to facial expressions of disgust and of fear; although fear activated the amygdala, disgust activated anterior insular cortex as well as medial frontal cortex, right putamen, and thalamus [42]. Sprengelmeyer *et al.* [43•] similarly found that on fMRI perception of disgusted facial expressions activated the left insula cortex and right putamen; various expressions, including disgust, activated the inferior part of the left frontal cortex.

Another study by Phillips *et al.* [44•] found that although facial expressions of disgust activated the anterior insula as well as the caudate and putamen, vocal expressions of disgust did not. Instead, both facial and vocal expressions of disgust and fear activated the superior temporal gyrus. This finding differs somewhat from other data suggesting that the neural system for recognition of disgust can recognize signals of disgust from different modalities [37,40]. Nevertheless, it is striking that studies by different groups using different experimental paradigms all point toward the role of the insula and CSTC circuits in mediating the processing of disgust, and also suggest different neural systems for the processing of disgust and fear.

In line with the hypothesis that disgust evolved to lead to avoidance of potentially harmful decayed food [5], the anterior insula is part of gustatory cortex, containing neurons that respond to pleasant and unpleasant tastes [45]. Anterior insula activation on functional imaging has been demonstrated in response to taste [46], odor [47], and various aversive stimuli [25,48]. Ventral CSTC circuits may link medial temporal and orbitofrontal structures, so establishing associations to bad tastes and smells. The functional neuroanatomic findings suggest that appreciation of unpleasant taste and smell are linked to appreciation of visual expressions of disgust, consistent with such a process of associative learning [42].

Social Context of Disgust

The importance of observations of others about expression of disgust leads to questions about the social context of disgust. Anthropologists have long emphasized the role of taboos in constructing culture; societies sort experience into various categories, including the pure and impure, the clean and the contaminated, the "kosher" and the "untouchable" [49]. Indeed, few distinctions seem as pervasively important as this set of polarities in understanding social contexts and interactions.

Although at the core of such categorization may be concrete experiences of taste aversion and other sensorimotor experience, ultimately these distinctions become increasingly abstract and symbolic (disgust at violation of body borders, ideas of interpersonal contamination, and moral violations of purity-sanctity) [5,14]. The process of moving from concrete sensorimotor experience through to more abstract symbolic categories via processes of assimilation and accommodation is of course one that is central to human development and language [15].

From this perspective, disgust becomes an emotion that is central to the organization of a whole realm of sophisticated human thought and feeling. Neonates demonstrate rejection of food based on taste, and over time gradually learn to reject food based on the idea of what something is or where it comes from [50]. Furthermore, an association is gradually acquired between disgust and violations of purity-sanctity [14]. Moral, ethical, religious, and spiritual matters require not only the awareness of mankind's higher self, but by implication, and avoidance of baser, more disgusting, matters; disgust is socially constrained and socially constraining [6].

Phenomenology of OCD and Disgust

The symptoms of OCD commonly revolve around the issue of what is contaminated and what is not. Disgust involves the appraisal of objects and events for their potential role in contamination [5], and OCD conceivably involves a dysfunction of this appraisal process [51•]. Although smell is important in some OCD patients, other sensory modalities also come into play. Furthermore, although OCD concerns may be quite concrete (concerns about germs, bodily secretion, and illness), they are often more abstract (revolving around religious, ethical, and moral issues).

Of relevance here, researchers interested in disgust [52,53] have emphasized that the classical laws of sympathetic magic [54–56] are useful in understanding this emotion. The law of contagion ("once in contact, always in contact") [56] refers to the tendency to act as if brief contact causes a permanent transfer of properties from one object to another (*eg*, people may decline to drink from a glass that once held dog feces, even though it has since been washed). The law of similarity ("the image equals the object") [54] refers to the tendency for attitudes to be based on physical similarities (*eg*, a piece of chocolate fudge is less desirable when shaped like a piece of dog feces).

Furthermore, after exposure to a disgusting object, cleaning rituals are seen [52]. Although such cleaning may be argued to be hygienic, it is likely that conventional recognition of the disgusting predates what is later viewed as wise hygiene [6]. Taken together, these phenomena are certainly reminiscent of OCD, and raise the question of whether OCD is an extreme presentation of this universal emotion, or whether it represents a dysfunction in the appraisal and processing of disgust. Certainly, both the

concrete contamination concerns of children and mentally retarded patients with OCD, as well as the more abstract and symbolic symptoms of some older patients, demonstrate a pattern of "magical" thought and behavior.

Conversely, although OCD is classified as an anxiety disorder, and although there is certainly an element of anxiety in the condition, it is not clear that this is the most powerful emotional process and symptom in OCD [3]. Early behavioral explanations of OCD as based on conditioned fear [57], have received little contemporary empirical support. Indeed, a number of cognitive-behavioral theorists have begun to move towards a theoretic position, which emphasizes the importance of disgust in OCD [58,59].

Psychobiology of OCD and Disgust

There appear to be a number of convergences between the psychobiology of disgust and OCD. As described earlier, fMRI studies have demonstrated activation of the anterior insula cortex and CSTC circuits in the perception of disgust expressions [43,44]. Although CSTC activation is the more commonly emphasized finding in OCD, a number of studies have also noted anterior insula activation. Conversely, it is notable that in OCD the amygdala, which has been so closely linked to fear responses, is not activated in provocation paradigms.

The insula is part of gustatory cortex and is connected to ventro-posterior-medial thalamic nucleus [45]. In addition, the insula is closely connected to orbitofrontal cortex, which plays an important role in integrating information about rewards and punishments in planning future behavior [59], and to frontal-subcortical circuits, which may underpin evolved response patterns involving cleaning, checking, and similar procedural strategies.

Indeed, an important study by Sprengelmeyer *et al.* [51•] demonstrated that those patients with OCD, but not Tourette's disorder patients without OCD or anxiety disorder control patients, demonstrated impaired recognition of facial expressions of disgust. OCD subjects had no difficulties in assigning words to basic emotional categories; the problem, however, was one of perception.

The authors suggested that a dysfunction in the appraisal of disgust in OCD would result in childhood failure to learn to recognize facial expressions of disgust [51•]. However, Huntington's disease, where onset is much later than OCD, is also associated with impairment in recognition of disgust [37]. An alternative hypothesis would view the impairment of expressed and perceived disgust in OCD as primary, so that patients are less sensitive to socially observed disgust associations, and more sensitive to internally generated disgust associations. Most recently, functional MRI of OCD patients during exposure to disgusting photographs demonstrated activation of similar regions, including anterior insula. During exposure to washer-relevant stimuli, similar regions were again activated in washers, although CSTC circuits were activated in checkers, and frontal regions were activated in normal patients [60]. Additional work is needed to expand on these interesting data. There is preliminary evidence of an association between disgust sensitivity and obsessive-compulsive personality [61]. Also, in a nonclinical sample of obsessive-compulsive and control students, obsessive-compulsive men tended to produce more negative emotional facial expressions, including fear and disgust, than control patients in response to a frightening film clip [62].

An Integrated Approach

Although most medical research addresses the proximal mechanisms involved in disease pathogenesis, there is also a growing literature on the distal mechanisms responsible for disease—the way in which evolutionary processes have contributed to the pathogenesis of illness [63]. Applied to the anxiety disorders, an evolutionary framework asks questions about the function of fear and disgust circuits, and the role of "false alarms" in disorders of fear and disgust [64]. Panic disorder, for example, has been conceptualized in terms of a false suffocation alarm and dysfunction of an amygdala circuit that mediates fear conditioning.

Several authors have suggested that in OCD there may be a false contamination alarm [64]. Although the normal function of the contamination alarm circuit is to provide warning about potentially dangerous stimuli, in OCD this circuit becomes triggered autonomously and excessively. Striatal dysfunction caused by neurogenetic and neuroimmunologic factors, among others, have been hypothesized to mediate this contamination false alarm (although on occasion, frontal or temporal lobe damage is associated with OCD [65,66]).

More generally, however, OCD has been characterized in terms of dysfunction of CSTC–mediated implicit cognitive-affective processing [67]. Specific contamination concerns and impairment of disgust perception may be a frequent consequence of such dysfunction, with other symptom profiles and processes also a possible outcome. Given the close relationships between insula and ventral CSTC circuits, dysfunction of the latter pathways may be associated particularly strongly with autonomous thoughts and feelings regarding contamination. CSTC dysfunction may, however, also be associated with other autonomous strategic procedures such as stereotypes, hoarding, and so forth.

Certainly, OCD is a heterogeneous disorder [68]. Only one of the factors yielded in factor analysis of OCD symptoms revolves around contamination. Other symptom factors appear rather different in nature; symmetry and hoarding, in particular, have unique phenomenologic correlates (symmetry concerns are, for example, more commonly seen in Tourette's syndrome) and psychobiologic underpinnings (hoarding is associated with relatively poor response to serotonin reuptake inhibitors). Indeed, patients with Tourette's syndrome (but not OCD) did not demonstrate impaired perception of disgust expression [51•].

Furthermore, anxiety and depression, although not specific to OCD, may play an important role in the pathogenesis of the disorder. In addition to disgust about potential contamination, patients may also develop fear of future contamination and demoralization about past contamination. Indeed, on functional brain imaging of patients with OCD and other anxiety disorders, in addition to specific patterns of activation in each of the various disorders, they each demonstrate nonspecific activation of paralimbic circuitry [69,70].

Conversely, disgust or its dysfunction may play some role in various disorders other than OCD [4•], although perhaps not a particularly large one. Disgust sensitivity is particularly relevant to animal phobias where the animal is associated with disease carrying (*eg*, rats), dirty places (*eg*, spiders), or disgust stimuli such as mucus (*eg*, snakes) [71], although even here not all data is consistent [72]. Blood–injury phobia is unusual to the extent that as it is involves a parasympathetic response and faintness, and this too may be elicited by both disgust and fear [73,74] (a combination that may be particularly important in horror [6]). Once trait anxiety is controlled, disgust sensitivity appears less relevant to most anxiety symptoms [75]. Patients with depression have subtle changes in disgust expression [76], although eating disorder patients differ from normal control individuals on only some measures of disgust sensitivity [77].

Avenues for Further Research

If a psychobiologic model of OCD emphasizing the role of disgust is to be consolidated, several avenues of future research need to be explored.

First, patients with OCD should differ from normal individuals during studies of disgust processing. Patients with OCD may be more sensitive to internally generated disgust associations, but less sensitive to socially generated associations. Differences in the experience and perception of disgust may be observable on cognitive tasks or on brain imaging.

Second, following the successful treatment of OCD patients, whether using pharmacotherapy or psychotherapy, there should be normalization of the cognitive-affective processes involving disgust experience and perception. This should be observable via specific changes in relevant measures and tasks [13,78].

Selective serotonin reuptake inhibitors are useful in a spectrum of different mood and anxiety disorders, and have a broad range of effects in patients with mood or other anxiety disorders other than OCD. Therefore, as a third avenue of research, treatment with selective serotonin reuptake inhibitors should lead not only to decrease in mood and anxiety symptoms in general, but also to reduction in disgust sensitivity.

Fourth, it may ultimately be possible to delineate the pharmacology of disgust in more detail. Certain agents ought to be able to provoke fear but not disgust, and vice versa. Conversely, just as benzodiazepines impair recognition of anger but not disgust [79], so certain agents may selectively impair disgust. In fear disorders such as panic disorder and post-traumatic stress disorder, there may be differential hypersensitivity to various panicogens, although in OCD there may instead be hypersensitivity to disgust elicitors.

Similarly, it might ultimately be possible to develop differential psychopharmacologic and psychotherapeutic treatments (exposure to disgust rather than simply to fear [80]), which specifically normalize dysfunction thought to be characteristic of OCD.

Conclusion

In conclusion, the incorporation of disgust into a psychobiologic model of OCD would appear to have prima facie validity, is supported by some preliminary research, and suggests a number of avenues for further work. The authors hope that this review will encourage additional research in this area.

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