



## Decoding moral emotions in obsessive-compulsive disorder

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### ABSTRACT

**Background:** Patients with obsessive-compulsive disorder (OCD) exhibit abnormal neural responses when they experience particular emotions or when they evaluate stimuli with emotional value. Whether these brain responses are sufficiently distinctive to discriminate between OCD patients and healthy controls is unknown. The present study is the first to investigate the discriminative power of multivariate pattern analysis of regional fMRI responses to moral and non-moral emotions.

**Method:** To accomplish this goal, we performed a searchlight-based multivariate pattern analysis to unveil brain regions that could discriminate 18 OCD patients from 18 matched healthy controls during provoked guilt, disgust, compassion, and anger. We also investigated the existence of distinctive neural patterns while combining those four emotions (herein termed *multiemotion* analysis).

**Results:** We found that different frontostriatal regions discriminated OCD patients from controls based on individual emotional experiences. Most notably, the left nucleus accumbens (NAcc) discriminated OCD patients from controls during both disgust and the multiemotion analysis. Among other regions, the angular gyrus responses to anger and the lingual and the middle temporal gyri in the multi-emotion analysis were highly discriminant between samples. Additional BOLD analyses supported the directionality of these findings.

**Conclusions:** In line with previous studies, differential activity in regions beyond the frontostriatal circuitry differentiates OCD from healthy volunteers. The finding that the response of the left NAcc to different basic and moral emotions is highly discriminative for a diagnosis of OCD confirms current pathophysiological models and points to new venues of research.

## 1. Introduction

Obsessive-Compulsive Disorder (OCD) is characterized by intrusive and unwanted thoughts, urges or images that cause anxiety and distress (obsessions), which are momentarily relieved by repetitive mental or motor acts (compulsions) (APA, 2013). OCD is a chronic, disabling, and relatively common disorder, affecting up to 3% of the general population (Fontenelle and Hasler, 2008). Although there is a consensus in the literature that OCD patients exhibit abnormalities in the cortico-striato-thalamo-cortical (CSTC) circuitry (Saxena et al., 1998; Whiteside et al., 2004), emerging evidence supports the involvement of other regions, such as the hippocampus, the amygdala and the parietal cortex (Menzies et al., 2008; Milad and Rauch, 2012; Nakao et al., 2014). Thus, not surprisingly, OCD is a pleomorphic disorder, involving heterogeneous cognitive (i.e. obsessions), affective (e.g. emotions), and

behavioral (i.e. compulsions) symptoms, each of them with a wide range of possible contents or “themes”.

Broadly speaking, OCD defining symptoms (obsessions and compulsions) can be classified into four main dimensions, i.e. contamination with washing, thoughts of harm with checking, symmetry and organization, and taboo/blasphemous thoughts with mental rituals (Abramowitz et al., 2010). However, the fact that OCD involves more emotions than just anxiety or distress was not formally recognized before the publication of the fifth edition of the Diagnostic and Statistical Manual of Mental Disorders (DSM-5), which removed OCD from the anxiety disorders chapter and highlighted that OCD patients often exhibit abnormal feelings of disgust and incompleteness (APA, 2013). By the same token, DSM-5 has also been more behaviorally focused, as the presence of repetitive behaviors and poor inhibitory control across different mental disorders [including OCD, body dysmorphic disorder,

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hoarding disorder, trichotillomania (hair-pulling disorder) and excoriation (skin-picking) disorder, among others] led to their reunion under the rubric of obsessive-compulsive and related disorders (APA, 2013). The impact of these changes in clinical practice is still unknown, though, as each of these disorders also have their own particularities. On the other hand, affective and social neuroscience may be one of the fields that will help relocate different psychiatric disorders (including OCD) into more biologically and therapeutically solid ground in future diagnostic systems (Fontenelle et al., 2015).

In addition to basic emotional abnormalities as a core part of OCD psychopathology (Lawrence et al., 2007; Moscovitch et al., 2008; Starcke et al., 2009; Whiteside and Abramowitz, 2005), there are also broader affective problems among OCD patients, including the appraisal (Calamari et al., 2008; Calkins et al., 2013), expression (Bersani et al., 2012; Pasquini et al., 2010) and recognition (Aigner et al., 2007; Bersani et al., 2012; Corcoran et al., 2008; Montagne et al., 2008) of different kinds of emotions as compared to healthy subjects. Furthermore, there is growing evidence that OCD patients exhibit heightened emotional (Becker et al., 2014; Schienle et al., 2005) and moral sensitivities (Braun et al., 2008; Harrison et al., 2012; Salkovskis et al., 1999). Thus, attempts to clarify the role of emotional processing deficits in the pathophysiology of the OCD seem warranted. Clearly, paradigms that involve the induction of different types of emotions represent an important component of such studies.

fMRI studies investigating the neuroanatomical basis of OCD have employed cognitive (e.g. reversal learning paradigm) (Remijnse et al., 2009), symptom provocation (e.g. the Maudsley obsessive-compulsive stimuli set) (Mataix-Cols et al., 2009), and emotional (e.g. face recognition) tasks. Although these studies have helped to establish a pathophysiological model of OCD, several gaps remain. For instance, cognitive tasks do not usually consider OCD symptom content, which can be extremely variable across individuals. In contrast, provocation of symptoms in OCD can be quite challenging, since a stimulus (e.g. a doorknob) that provokes symptoms in one individual (e.g. a checker) may not provoke it in another (e.g., an arranger), prompting studies to include patients from a restricted OCD subgroup (e.g. washers) tested against specific stimulus (e.g. contamination) (Gilbert et al., 2009; Olatunji et al., 2014; van den Heuvel et al., 2004).

Differently from “basic” emotions, which are shared by most mammals, moral emotions are unique human features that reflect the interests or welfare of the society as a whole or of persons other than the judge or agent (Haidt, 2003). Moral emotions foster prosocial behaviors associated with cooperation, helping, reparative actions as well as social reciprocity (including happiness, guilt, compassion and gratitude); yet, moral emotions also favor avoidance and aggression, such as when witnesses a violation of norms and rights, which induces specific emotional states, typically moral disgust (contempt) and moral anger (indignation) (Haidt, 2003; Zahn et al., 2012). Moral emotions are in general more complex than basic emotions, and are thought to emerge as neural representations that rely on the activation of a distributed brain network coding for the perception of social cues (temporoparietal junction), social conceptual knowledge (anterior temporal cortex), abstract event sequence knowledge (prefrontal cortex), and basic emotional states (rostromedial basal forebrain) (Moll et al., 2008).

Investigation of the neural basis of moral emotions is an emerging field that is clarifying the symptomatic expression and pathophysiology basis of many psychiatric disorders. It may be especially relevant in OCD (Fontenelle et al., 2015) and related disorders. For instance, research has found disgust to be particularly relevant in contamination fears/washing compulsions (Olatunji et al., 2017), while guilt/compassion seems to be implicated in taboo thoughts/checking compulsions (Melli et al., 2017); and anger associated with symmetry/ordering symptoms (Whiteside and Abramowitz, 2005). Thus, deficits in the way different frontotemporal and subcortical regions process moral emotions can contribute to the pleomorphic symptomatic expression exhibited by individual patients. As suggested by early theorists (Freud,

1965) and expanded in more recent models (Gonçalves et al., 2015), anxiety in OCD may also be the expression of an imbalance between defensive and appetitive mechanisms which results in a range of moral emotions such as disgust, guilt/compassion, and anger, among others. In addition, there may also be brain regions whose dysfunction may not be emotion-specific, but rather implicated in a generalized deficit in processing moral emotions. Thus, in this study, we investigated whether brain regions engaged by the experience of guilt, compassion, anger and disgust are able to differentiate patients with OCD from controls. For that aim, we took advantage of the searchlight analysis (Kriegeskorte et al., 2006), a powerful machine learning approach that has been successfully applied in modelling local and distributed responses in fMRI datasets.

## 2. Methods and materials

### 2.1. Subjects

A sample of 38 DSM-IV OCD and 34 healthy controls were initially assessed for participation in our study. Patients have been selected among individuals being treated in the OCD clinic of the Institute of Psychiatry of the Federal University of Rio de Janeiro (IPUB/UFRJ), while healthy controls were mostly people from the D’Or Institute for Research and Education (IDOR) and IPUB/UFRJ administrative staff. After careful matching for socio-demographic and behavioral performance, 18 OCD and 18 healthy controls were included in the final sample, which was perfectly matched for age, sex (7 female and 11 male), handedness and education. Exclusions among the OCD sample ( $n = 20$ ) were ascribed to image acquisition problems, especially movement ( $n = 8$ ), diagnostic ambiguities ( $n = 2$ ), fMRI task underperformance ( $n = 3$ ), self-report assessment inconsistencies ( $n = 4$ ) and inability to be matched to healthy controls based on age, sex or education ( $n = 3$ ). Conversely, a total of fifteen healthy controls have been excluded due to problems in image acquisition ( $n = 7$ ), subclinical psychiatric diagnosis ( $n = 1$ ), inconsistent self-report responses ( $n = 4$ ), and suboptimal matching ( $n = 3$ ). The Ethics Committee of the Federal University of Rio de Janeiro approved this research protocol. A written informed consent was obtained from all participants. Volunteers were not paid, but received the MRI structural data as an incentive.

A board certified psychiatrist (IF) interviewed all participants with the Structured Clinical Interview for Disorders of Axis I Diagnosis (SCID) (First et al., 1997); the Structured Interview for DSM-IV Personality (SIDP) (Pfohl et al., 1997); the Global Assessment of Functioning Scale (GAF) (Hall, 1995); the Yale-Brown Obsessive-Compulsive Symptom Scale (YBOCS) (Goodman et al., 1989); the Dimensional Obsessive-Compulsive Scale (DOCS) (Abramowitz et al., 2010); and the Detection test of involvement with alcohol, tobacco and substances (ASSIST) (Humenuk et al., 2008). The participants also answered the following self-report instruments: the Questionnaire from the Brazilian Association of Population Studies (ABEP) (<http://www.abep.org/>); the Handedness Questionnaire (Oldfield, 1971); and the Beck Depression Inventory (BDI) (Beck et al., 1961).

The inclusion criteria comprised (i) age between 18 and 65 years, (ii) at least high school education, (iii) a minimum score of 16 on the YBOCS for OCD patients, and (iv) a minimum score of 60 on the GAF for controls. The exclusion criteria included Borderline and Antisocial Personality Disorders, Alcohol or any Substance Abuse, increased suicidality (judged to be present on clinical grounds), Claustrophobia or any contraindication to the MRI. Almost all OCD patients were medicated with serotonin reuptake inhibitors, with the only exception being one subject being treated with a serotonin norepinephrine reuptake inhibitor. Seven patients were also medicated with antipsychotics, six with benzodiazepines, one with a tricyclic antidepressant, one with topiramate and another one with memantine. One healthy control was medicated with a serotonin reuptake inhibitor due to Major Depression in the past; however this subject was asymptomatic for more than one

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