



## 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

year.

## 2.2. Stimuli and task

The Moral Sentiments Association Task (MSAT) comprised 105 different audio stimuli describing action scenarios (“scripts”) designed to evoke four specific emotions (guilt, compassion, anger and disgust) and emotionally neutral social situations; The five different conditions were assessed with 21 scripts each. The current version of the MSAT was based on previous studies (Moll et al., 2007) and previously tested in 19 post-graduate students, who had a correct response rate of > 70% (see Supplementary Table 1).

All scripts were construed with the same two-short sentences grammatical structure. The first sentence described a specific social situation and the second sentence described a potential volunteers' action coupled with the resulting outcome (e.g., a guilt script: “Your mom called you and said she didn't feel well. You ignored her, and the next day she died”). We instructed participants to put themselves into the specific situation, to imagine themselves as main characters of the specific outcome, and to feel the emotion that the script aroused as vividly as possible. The script had the duration of around 7 s and the participants had 5 s to do the task (Fig. 1). Before the task started, the adequacy of the volume of the audio was individually calibrated.

To test for patients' level of arousal/sleepiness, five seconds after the presentation of a specific script, two circles, one white and one red, appeared side-by-side on randomly alternate sides. The participants were instructed to press the button attached to his right hand to indicate, with his second or third finger, whether the red circle was located on the left or right side of the screen, respectively. There were no significant differences in the arousal reported by OCD patients and controls. The 105 trials, with a 7-s duration each, were divided in 3 runs, which took 33.25 min in total. After each run, participants were asked the following questions to check whether they were able to perform the task and if they were feeling comfortable: (1) “How

difficult it was for you to feel the emotion?” (i.e. very difficultly; difficultly; neither difficultly nor easily; easily; or very easily); (2) “At which intensity did you feel the emotion?” (i.e., very strongly; strongly; weakly; very weakly; or absent); (3) “How are you feeling now?” (i.e., uncomfortable; comfortable; sleepy; anxious; or something else); (3.1) “How intensely?” (i.e. slightly; or a lot). Participants were positive about the success of emotional provocation.

All participants were trained outside the scanner with a Microsoft PowerPoint® presentation that included an example of each of the 5 conditions and the first part of the Positive and Negative Affect Scale (PANAS) (Watson et al., 1988). There were no significant differences between OCD patients and controls in the PANAS positive and negative scores before and after the scan. Higher scores in negative lifetime affects were found in OCD patients as compared to controls.

To ensure that the subjects were attentive and committed to the MSAT, we had them answer the last part of the PANAS and a Recognition Task after the scanning. The recognition task included 45 randomly chosen scripts, fifteen of which were modified. Subjects were asked to answer whether the script was the same or different from those they heard inside the scanner. To control for the emotions evoked by all the 105 scripts, they also completed a self-report MSAT, in which they had to classify the target emotion of each script with the four emotions plus the neutral category and a “not-able-to-classify” option as possible answers.

## 2.3. Functional MRI data acquisition

Functional images were collected with a 3T Achieva scanner (Philips Medical Systems, the Netherlands) using an eight-channel SENSE head coil. Head motion was restricted with foam pads and straps over the forehead and under the chin. Functional imaging was performed with T2\* blood-oxygenation-level-dependent contrast (BOLD) echoplanar imaging (TR/TE = 2000/22 ms); 37 transversal slices were acquired aligned with the anterior-posterior commissure line,

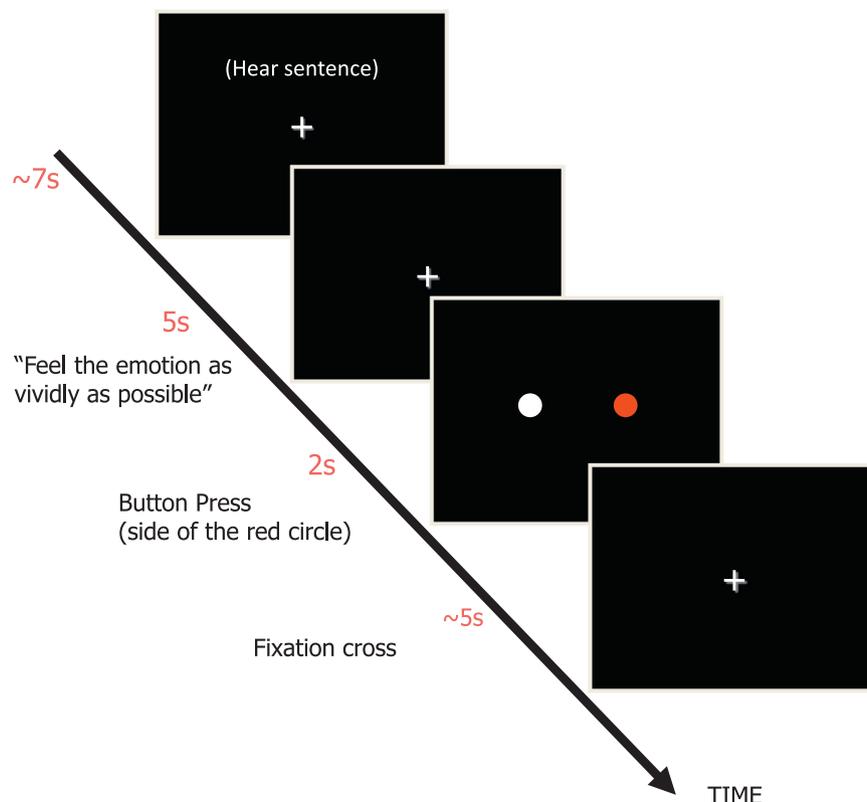


Fig. 1. fMRI Task Design.

positioning the most inferior slice such that temporal lobe was completely covered; slice thickness = 3 mm (no gap); Matrix = 80 × 80, FOV = 240 × 240 mm, flip angle = 90 degrees. High-resolution anatomical images were acquired with a 3D turbo field echo T1-weighted sequence (TR/TE = 7.1/3.4 ms, matrix 240 × 240, FOV 240 mm, slice thickness 1 mm, 170 slices). Per run 345 functional volumes were acquired (excluding the first 5 dummy volumes).

#### 2.4. Data analysis

Behavioral data analysis was carried out using SPSS (SPSS Inc., Chicago, USA, <http://www.spss.com>). The fMRI data analysis was performed with SPM 12 (<http://www.fil.ion.ucl.ac.uk/spm/software/spm12/>). Pre-processing steps included correction for head movement and slice-timing, affine spatial normalization to the EPI template and spatial smoothing (FWHM = 6 mm).

A general linear model (GLM) was applied by performing multiple linear regression of the BOLD response time-course on each voxel, modelling the four emotions (Guilt, Compassion, Anger, and Disgust) plus the neutral conditions with onset directly after the audio script presentation and 5 s duration, and auditory responses with a single regressor for all conditions plus the six movement parameters as nuisance regressors. We excluded any subject due to excessive movement with head dislocation of > 6 mm (or degrees) in any of the 6 coordinates (x, y, z, pitch, roll, yaw) in a great number of volumes during the exam. Additionally, motion corrected volumes were visually inspected, aided by Artifact Detection Tools (ART) (Mazaika et al., 2005) and volumes with excessive movements repaired with our in-house software (“Denoiser”).

We applied a multivoxel pattern analysis (MVPA) with the standard spherical searchlight approach (Bode and Haynes, 2009; Kriegeskorte and Bandettini, 2007; Kriegeskorte et al., 2006) using linear support vector machine (SVM) on the group level (OCD vs. controls). A 9 mm radius sphere was employed as the search volume. Four separate searchlight analyses were done using the first-level contrasts (Guilt, Compassion, Anger and Disgust vs. Neutral) as input images. Additionally, we also ran a multiemotion analysis concatenating the four emotional contrasts together as 4D input image, resulting in  $4 \times 123 = 492$  features representing a hypersphere in the searchlight.

This multi-variate searchlight analyses have been shown to benefit from local spatial information content thus providing greater power than mass-univariate analysis (Kriegeskorte et al., 2006). Additionally, it does not require any a priori selection of brain regions and is able to identify brain regions while minimizing the curse of dimensionality in comparison to using all voxels of the entire brain at once (Etzel et al., 2013). Every searchlight run was composed of 36 classifications (folds) using a leave-one-subject-out cross-validation scheme. For each fold and each location in the brain mask, we extracted the voxels contained in the searchlight sphere, trained the SVM on 35 subjects and classified the subject left-out for test. The percentage of correct classifications over the 36 folds was then mapped into the centre of the sphere to create the accuracy maps.

In order to validate statistically our results and to correct for multiple comparisons, we performed permutation testing, following previous recommendations (Stelzer et al., 2013). Exactly the same leave-one-subject-out classification was executed 5000 times, only shuffling the Patient/Control label from the subjects. We used a voxel-wise (cluster-defining) threshold of  $p < 0.005$  and  $p < 0.05$  to correct for multiple comparison at cluster level, resulting for our data in minimum cluster sizes of 19 voxels in the single condition and 16 voxels for the multi-condition analysis.

An alternative analysis using first level modelling of individual responses to scripts was also performed. In this analysis, all responses not corresponding to the expected “correct” ones based on the normative sample were not modeled (i.e., they were aggregated with null events in the design matrix). The searchlight procedure was identical as

described above, but was performed on the first level SPM data using individual responses.

### 3. Results

#### 3.1. Behavioural data

Our sample was matched for age (in years), education (in years) and socioeconomic status (ABEP scores). Research subjects were also perfectly matched for gender, with seven female and 11 male in each group, given the differences in emotional-processing style by males and females (Wager et al., 2003); four OCD patients and four healthy controls were excluded due to this matching process. No controls had clinically significant depression; on the other hand, six OCD patients had current, seven had past and two had both current and past Major Depression Episodes. All OCD patients were symptomatic, with Y-BOCS obsessions mean score of 13.56 (SD 3.26), Y-BOCS compulsions mean score of 13.94 (SD 2.84), and Y-BOCS total mean score of 27.5 (SD 5.95).

#### 3.2. Task data

All subjects included in the final analysis scored 66% or higher in the Red Circle embedded attentional task (three OCD patients were excluded due to poor performance). Also, performance on the recognition task was above 75% in both groups, further indicating that participants were highly engaged in the task and could recall the scripts. Finally, all participants included in the final sample correctly classified scripts according to the independent normative sample, with over 50% accuracy within each emotion condition of the MSAT (four OCD patients and five controls were excluded based on this criterion). The two groups had a matching performance on the MSAT, which was critical for the interpretation of the categorical classification of the fMRI data (see Supplementary Table 2).

#### 3.3. fMRI results

##### 3.3.1. Guilt

The regions that discriminated OCD patients from controls during guilt provocation were the left postcentral and angular gyri, both with an accuracy of 86.1%. For further interpretation of the classification results, we went back to the GLM and built ROIs with the MNI coordinates that resulted from the clusters in searchlight to extract the beta values. These values have the purpose of displaying signal direction; they were not used to compute statistical tests. The extracted beta values from the GLM analysis showed that this classification results were driven by an overall higher activity in the postcentral gyrus of the OCD group and higher activity in the angular gyrus of controls, compared to each other (Table 2).

##### 3.3.2. Compassion

The only discriminative region during compassion provocation was the dorsal anterior cingulate, with an accuracy of 94.4%. The mean beta value in this region was higher in OCD patients compared to controls (Table 2).

##### 3.3.3. Anger

The results from anger provocation showed that multivoxel pattern activity in the caudate nucleus and in the angular, paracingulate and precentral gyri discriminated the OCD and control groups with accuracies of 88.9%, 88.9%, 86.1% and 86.1%, respectively. Mean beta values in the caudate nucleus and paracingulate and precentral gyri were higher in OCD, whereas controls had higher values in the angular gyrus (Table 2).

### 3.3.4. Disgust

During disgust provocation, the left nucleus accumbens and the medial frontal cortex/paracingulate gyrus were discriminative between OCD patients and healthy controls, both with an accuracy of 88.9%. Beta values in the left nucleus accumbens were higher in controls, but higher in the medial frontal/paracingulate cortex in OCD patients (Table 2).

### 3.3.5. Multiemotion analysis

The combined emotion MVPA analysis revealed that the left NAcc, the lingual and the middle temporal gyri discriminated OCD from controls with accuracies of 88.9%, 88.9% and 83.3%, respectively. The beta values in the left NAcc and in the middle temporal gyri were higher in controls than in OCD patients. Beta values in the lingual gyrus were higher in OCD patients compared to controls (Table 3).

The confirmatory whole-brain searchlight analysis excluding all incorrect hits from the MSAT self-report from the GLM first level analysis of each subject led essentially to the same results, and is therefore not reported herein. Mean BOLD responses for each region found to be discriminative during emotional provocations are provided in Supplementary Table 3. The reader can visualize different discriminative regions in Supplementary Figs. 1 and 2).

## 4. Discussion

In this study, we were able to demonstrate that multivariate decoding of activity in cortical and subcortical regions during the experience of specific moral and non-moral emotions (guilt, compassion, disgust and anger) can accurately discriminate OCD patients from healthy controls. Importantly, activity in some brain regions was particularly accurate in discriminating between groups for a given emotion, whereas other regions contributed to discrimination when analyzed in conjunction. Accuracy of individual regions ranged from 86 to 94%. In addition, we also found brain regions whose dysfunction may not be emotion-specific, but rather implicated in a generalized moral emotions' processing deficit that was also able to differentiate OCD from healthy controls. It should be emphasized that these results derived from cross-validation analyses using permutation methods to empirically estimate statistical effects.

These findings contribute to the emerging body of evidence suggesting a promising role of pattern recognition methods for identifying imaging biomarkers in psychiatric disorders (Sato et al., 2011, 2015); including OCD (For a review, see (Frydman et al., 2016)). It should also be emphasized that the classification results are fundamentally different from conventional fMRI univariate analysis: whereas the multivariate classification tells the accuracy of a given region in distinguishing brain responses, typical fMRI analyses simply shows that the activity of a given region is higher or lower, but does not inform how specific that effect is at the single subject level. Our findings thus demonstrate the potential of this approach in identifying the discriminative power of moral emotion-related activation patterns in OCD.

In contrast to most recent studies, we have employed a task that reliably elicited both non-moral and moral emotions, both believed to be relevant for OCD psychopathology. Importantly, this multi-emotional task design allowed the selection of a symptomatically heterogeneous group who were thought to be representative of OCD patients seen in general outpatients' clinics. Our approach also differed substantially from studies employing the passive exposure to pictures that may be actually neutral to healthy controls (such as a doorknob or a toilet seat) and highly aversive for certain OCD patients. Our task and its conditions, in contrast, were carefully designed and tested in order to reliably elicit similar categorizations between OCD and healthy volunteers. The lack of significant behavioral differences in task performance allows us to safely attribute differential fMRI patterns to underlying differences in how their brains respond to equivalent stimuli (at least at the categorical level).

To the best of our knowledge, the only study that employed a similar multivoxel pattern classification strategy (i.e. searchlight) in OCD patients achieved very high accuracies in discriminating functional responses in the orbitofrontal cortex and caudate nucleus during fear-inducing vs. neutral pictures (Weygandt et al., 2012). However, the findings of this previous study are difficult to compare with ours. While the former authors have used a task that included fear, disgust and neutral pictures and pre-defined regions of interest, our task employed a series of auditory stimuli describing rich hypothetical scenarios that reproduce first-person situations and demonstrably elicit non-moral and moral emotions. Further, a second-level whole-brain multivoxel pattern analysis was employed at the second-level to test the discriminant responses at the whole brain level.

Overall, the former searchlight study and ours concur that the pattern of brain activation in OCD patients can be discriminated from that of healthy controls during experimental emotional elicitation. However, our study further extends these findings by showing that moral sentiments also differ between OCD and controls. Cognitive models suggest that the ability of patients with OCD to tolerate aversive emotions, such as guilt and disgust, may contribute to the maintenance of OCD symptoms (Calkins et al., 2013). Although exposure and response prevention (ERP), the most effective non-pharmacological treatment for OCD, has generally focused on the confrontation of obsessive fear and anxiety (Marks, 1997), our results suggest that the elicitation of higher-order aversive emotions could also benefit at least some patients with OCD during ERP.

Different studies employing disgust-induced stimuli (mostly pictures but also odors) have consistently found increased activation in the insula, but also in other frontal, temporal, parietal and subcortical regions (Berlin et al., 2015, 2017; Schienle et al., 2005; Shapira et al., 2003; Stein et al., 2006). Fewer studies on brain activation of OCD during guilt have been performed thus far, though (Basile et al., 2014; Hennig-Fast et al., 2015). They have reported heterogeneous results likely to reflect methodological sampling and/or differences, including reduced activation in the anterior cingulate cortex and frontal gyrus (Basile et al., 2014) and increased activity in frontal, limbic and temporal areas (Hennig-Fast et al., 2015). Unfortunately, though, we believe these findings are difficult to compare for a handful of reasons. Most importantly, our searchlight analysis report regions that were able to discriminate OCD and healthy controls but did not necessarily include other brain regions that, despite differing between groups to a significant extent, were unable to discriminate both diagnostic groups.

In fact, regions that discriminated OCD patients from controls in the present study overlapped only partially with the networks that were implicated in moral emotions in a previous study using a first version of the MSAT in normal controls (Moll et al., 2007). More specifically, while the present study found the activation of the dorsal anterior cingulate during compassion to discriminate OCD from controls with a 94.4% degree of accuracy in the present study, the previous MSAT study in controls reported that, compared to emotionally neutral agency, "prosocial emotions" (i.e. guilt and compassion) also activated the superior temporal sulcus and the mesolimbic pathways (Moll et al., 2007). In contrast, "other-critical emotions" (including disgust) in controls activated amygdala, parahippocampal and fusiform areas (Moll et al., 2007), which, unlike the accumbens and the medial frontal cortex, did not discriminate OCD patients from controls in the present study. Our findings suggest that structures pertaining to the default mode network, thought to be relevant to experiences related to the individual self, may somehow be implicated in the moral emotions (particularly compassion, anger, and disgust), in OCD patients.

The remarkable discriminative power of the left accumbens activation during disgust provocation and in the multiemotion condition is consistent with existing pathophysiological models of OCD. The NAcc lies at the crossroads of motivation, reward and action (Haber and Knutson, 2010) and has been both increased in volume (Carlisi et al., 2017) and an effective target for deep brain stimulation in refractory

**Table 1**  
– Sociodemographic characteristics of the sample.

	OCD (n = 18)	Controls (n = 18)	Statistics
Gender			
Female	7	7	
Male	11	11	
Marital Status			$\chi^2 = 1.03; p = 0.6$
Single	13	13	
Married	3	4	
Divorced		1	
Age	34.8 (SD 11.5)	32.4 (SD 9.2)	$t = 0.7; p = 0.48$
Education	15.17 (SD 1.7)	15.4 (SD 2.5)	$t = -0.3; p = 0.76$
GAF	46.4 (SD 8.4)	91.7 (SD 9.2)	$t = -15.4; p < 0.001$
BDI	17.65 (SD 8.27)	4.44 (SD 3.3)	$t = 6.3; p < 0.001$
ABEP scores	26.44 (SD 10.26)	24.18 (SD 5.8)	$t = 0.8; p = 0.43$
DOCS			
Contamination	4.89 (SD 5.29)	0.94 (SD 0.96)	$t = 3.11; p = 0.006$
Harm	7.94 (SD 6.42)	1.53 (SD 1.94)	$t = 4.04; p = 0.001$
Taboo	9.89 (SD 6.97)	1.41 (SD 2.18)	$t = 4.90; p < 0.001$
Symmetry	5.28 (SD 4.77)	0.76 (SD 1.20)	$t = 3.88; p = 0.001$
Total	28.00 (SD 16.21)	4.65 (SD 4.83)	$t = 5.84; p < 0.001$
Y-BOCS			
Obsessions	13.56 (SD 3.26)	NA	NA
Compulsions	13.94 (SD 2.84)	NA	NA
Total	27.50 (SD 5.95)	NA	NA

OCD = Obsessive-Compulsive Disorder; GAF = Global Assessment of Functioning; BDI = Beck Depression Inventory; ABEP = Brazilian Research Companies Association; DOCS = Dimensional Obsessive-Compulsive Scale; Y-BOCS = Yale-Brown Obsessive-Compulsive Scale; SD = Standard deviation.

OCD (Kisely et al., 2014). Its activity has been reduced in OCD patients during reward anticipation, particularly in individuals with contamination fears (Figue et al., 2011). Accordingly, we have also found that OCD washers report more positive affect in anticipation of their compulsions than other OCD groups (Ferreira et al., 2017). The findings regarding the discriminative ability of the lingual, middle temporal and angular gyri also dovetail with a model that extends beyond the traditional OCD corticostriatal circuit (Eng et al., 2015; Hu et al., 2016; Jung et al., 2013; Nakao et al., 2014; Piras et al., 2015; Tian et al., 2016; Wood and Ahmari, 2015).

There are some important caveats in our study. Firstly, our OCD sample was relatively small, symptomatically heterogeneous, and under multiple pharmacological treatments, mostly serotonin reuptake inhibitors. Yet, they were carefully matched and still substantially symptomatic (mean YBOCS score > 27). Further, our findings remained significant despite the blunting effects of both serotonin reuptake inhibitors (Price et al., 2009) and depression (Zahn et al., 2015) on the experience and/or expression of emotions. In addition, the inclusion of OCD patients scoring differently on multiple symptom dimensions (see Table 1) was a deliberate research strategy, as subjects were assessed with the MSAT, designed to tap emotions thought to be relevant to the diverse phenomenology of OCD. Secondly, given our emphasis on the searchlight approach and its intrinsic categorical nature, we have not attempted to explore correlations with severity of OCD symptoms, which would require a larger sample size with a broader range of score variability.

One final potential limitation of our study is the difficulty in assessing whether participants were able to subjectively experience the intended emotions. This is a potential weakness of most emotion-provocation studies using fMRI. In addition to a large body of studies showing that there is a good correspondence across several fMRI studies and the present one on the brain regions typically engaged by images and script narratives, a few additional points deserve consideration: (1) our participants were asked to put themselves in the specific situation by adopting a first-person perspective, which facilitates engagement in the proper emotional experience; in contrast, several previous studies simply presented images passively, in which a third-person perspective was used; and (2) participants were specifically asked, between the

**Table 2**  
Searchlight discriminative regions during emotion provocation.

	Direction of BOLD effects (beta)	%	MNI coordinates
Guilt			
Postcentral gyrus	OCD > Ctl	86.11%	-39 -34 46
Angular gyrus	OCD < Ctl	86.11%	-57 -55 19
Compassion			
Dorsal anterior cingulate	OCD > Ctl	94.44%	9 35 19
Anger			
Caudate nucleus	OCD > Ctl	88.89%	18 17 19
Angular gyrus	OCD < Ctl	88.89%	-45 -61 22
Paracingulate gyrus	OCD > Ctl	86.11%	0 47 19
Precentral gyrus	OCD > Ctl	86.11%	-36 -16 46
Disgust			
Accumbens	OCD < Ctl	88.89%	-9 14-8
Medial frontal/ paracingulate cortex	OCD > Ctl	88.89%	18 47 7

OCD = Obsessive-Compulsive Disorder; Ctl = Controls; BOLD = Blood-oxygen-level dependent; MNI coordinate = Montreal Neurological Institute coordinate.

**Table 3**  
Searchlight discriminative regions in the multiemotion analysis.

Multiemotion condition	Direction of BOLD effects (beta)	%	MNI coordinates
Accumbens	Ctl > OCD	88.89%	-9 14-8
Lingual gyrus	OCD > Ctl	88.89%	-12 -76 4
Middle temporal gyrus	Ctl > OCD	83.34%	-57 -61 10

OCD = Obsessive-Compulsive Disorder; Ctl = Controls; BOLD = Blood-oxygen-level dependent; MNI coordinate = Montreal Neurological Institute coordinate.

runs, whether they were able to feel the specific emotions and whether they were able to perform the task as intended. Overall, participants reported that they successfully engaged in the emotional provocation task.

Taken together, our results indicate that (i) the experience of both basic and moral emotions can be effectively decoded from multivoxel activity patterns in the brain, which can differentiate patients with OCD from healthy controls; (ii) shared or common brain regions, including the nucleus accumbens, lingual gyrus and middle temporal gyrus, are able to discriminate OCD patients from healthy controls across distinct emotions; and (iv) these neural correlates overlap only partially with the frontostriatal circuitry (CSTC), which has traditionally been implicated in OCD pathophysiology. These findings are consistent with the conceptualization of OCD as a brain disorder that involves several different neural circuits. They suggest that current pathophysiological models should incorporate this new evidence, which may also point to new therapeutic targets and purposes. Further studies aiming to establish causality are nevertheless required.

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