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Neural correlates of resolving conflict from emotional and nonemotional distracters in obsessive-compulsive disorder

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ABSTRACT

Obsessive compulsive disorder (OCD) is associated with altered processing in brain regions involved in conflict resolution. However, limited research has examined the extent to which conflict from emotional distracters characterizes OCD such that responsiveness to task-irrelevant emotional stimuli is altered compared to controls. In the present study, 16 patients with OCD and 15 healthy controls underwent functional magnetic resonance imaging (fMRI) during resolution of conflict from emotional or nonemotional distracters. Results in healthy controls demonstrated that rostral anterior cingulate cortex (rACC), middle frontal gyrus (MFG), and medial superior frontal gyrus (MSFG) showed greater activation for high conflict versus low conflict. Responses in these regions differed between the emotional and nonemotional distracter tasks, with rACC and MSFG having greater activation for conflict from nonemotional distracters and anterior MFG showing greater activation for conflict from emotional distracters. Furthermore, between-group differences revealed a region in right posterior MFG in which controls similarly exhibited greater activation during high conflict versus low conflict with emotional distracters; however, OCD patients showed the opposite pattern with greater activation during low conflict compared to high conflict. These findings suggest that activity of right posterior MFG may be relevant in better understanding inefficient responding during emotional conflict in OCD.

1. Introduction

Obsessive-compulsive disorder (OCD) is a complex and heterogeneous syndrome that is characterized by obsessions that are experienced as unwanted in that they "invade" one's consciousness and conflict with wanted internal experiences (*DSM-5*; American Psychiatric Association [APA], 2013). Compulsions are urges to engage in behaviors, such as overt or mental rituals, that reduce or remove distress associated with this conflict. Behavioral research suggests that the functional relationship between obsessions and compulsions in OCD may reflect deficits in cognitive control, the ability to regulate thoughts and behaviors in accord with internal goals (Miller and Cohen, 2001; Purcell et al., 1998). Research has shown that when exposed to conflict, the brain can rapidly adjust processing strategies to resolve that conflict (Botvinick et al., 2001). However, the detection and resolution of conflicting information is one form of cognitive control in OCD that is different from that of healthy controls (Marsh et al., 2014). For example, those with OCD symptoms have been found to make significantly more commission errors on the go/no-go task compared to those without such symptoms (Abramovitch et al., 2015). Commission errors suggests reduced response inhibition abilities in OCD when confronted with conflicting information.

Several studies suggest that OCD is also characterized by alterations in brain regions that contribute to detecting conflicts in information processing and signaling when increased top-down control is required (Carmona et al., 2007; Huyser et al., 2011; Riesel et al., 2017). Furthermore, efforts to identify the specific brain regions associated with conflict and its resolution in OCD have implicated the anterior cingulate cortex (ACC). For example, Ursu et al. (2003) conducted functional magnetic resonance imaging (fMRI) during performance on a version of the continuous-performance task with four trial types that induced graded levels of response conflict. Although a behavioral index of conflict (i.e., accuracy) was similar for those with OCD and control subjects, ACC activation was significantly increased among those with OCD during high-conflict trials. This finding is consistent with research suggesting that focus on tasks that probe high-conflict trials that require response inhibition may be a useful model of compulsive behaviors in OCD (Maltby et al., 2005). Huyser et al. (2011) also conducted fMRI during an interference task, the arrow version of the Flanker paradigm. The results revealed that compared with healthy controls, those with

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OCD showed increased activation in rostral anterior cingulate cortex (rACC) during error responses and in bilateral insular cortex during high conflict tasks.

Research has shown that OCD patients show higher activation than control participants during tasks designed to evoke emotion in the bilateral amygdala, right putamen, orbitofrontal cortex, middle temporal cortex, and left inferior occipital cortex (Thorsen et al., 2018). A related meta-analysis found that functional abnormalities in OCD showed significant dependence on the emotional or nonemotional nature of the tasks employed as circuit probes (Rasgon et al., 2017). In studies using emotional tasks, OCD patients demonstrated overactivated regions involved in salience, arousal and habitual responding (ACC, insula, caudate head and putamen) and underactivated regions implicated in cognitive and behavioral control (medial prefrontal cortex, posterior caudate). In contrast, nonemotional tasks produced overactivated regions involved in self-referential processing (precuneus, posterior cingulate cortex) and underactivated subcortical regions that support goal-directed cognition and motor control (pallidum, ventral anterior thalamus, posterior caudate). These findings highlight that emotional and nonemotional information may have distinct neural profiles that differentially relate to various cognitive processes in OCD. In fact, it is the interaction of dysregulation in the processing of information in emotional and nonemotional contexts that may partially account for the symptom heterogeneity in OCD (Goncalves et al., 2016). Accordingly, examination of conflict resolution in the context of emotional and nonemotional information is relevant to advancing current knowledge on the nature of OCD.

Although the ACC appears to be consistently associated with conflict monitoring in OCD (van Veen and Carter, 2002), the neuroanatomical networks recruited to overcome conflict may vary systematically with the nature of the conflict. For example, it has been suggested that two dissociable neural mechanisms may resolve conflict from different classes of distracters: a "cognitive control" circuit, wherein a portion of the lateral prefrontal cortex (LPFC) amplifies the processing of task-relevant stimuli in sensory cortices to overcome conflict from nonemotional distracters, and an "emotional control" circuit, wherein the rACC resolves conflict by inhibiting amygdalar reactivity to emotional distracters. To test this hypothesis, Egner et al. (2008) acquired fMRI data during a task in which emotional and nonemotional conflict conditions were varied with the use of distracters while task-relevant stimulus characteristics were kept constant. Consistent with the hypothesis, the LPFC (specifically the middle frontal gyrus [MFG]) was implicated exclusively in the resolution of nonemotional conflict, whereas the rACC was implicated exclusively in the resolution of emotional conflict.

There is evidence suggesting that neuroanatomical networks recruited to overcome conflict may vary depending on if the conflict is emotional vs. nonemotional (Egner et al., 2008). Indeed, patients with OCD experience a range of negative emotions (i.e., disgust) in response to obsessions that then motivate avoidance and compulsive behaviors (Olatunji et al., 2017). However, it remains unclear if the neuroanatomical networks recruited to overcome conflict in OCD (relative to healthy controls) vary as a function of emotional vs. nonemotional conflict, as past studies have focused largely on nonemotional conflict. Research addressing this gap in knowledge may advance current knowledge on the nature of OCD and associated emotional conflict. In the present study, we compared patients with OCD and healthy controls that underwent fMRI during resolution of conflict from either nonemotional or emotional distracters. In addition to heightened error and conflict monitoring, OCD is also characterized by the experience of various negative emotional (fear/defensive, disgust, guilt, shame) states. Indeed, there is robust evidence that those with OCD assess emotional stimuli as more unpleasant and less controllable than healthy controls (Casado et al., 2011). Given that cognitive control processes play an important role in emotional processing and these processes may be perturbed in OCD, it was predicted that greater activation in the brain regions recruited to overcome conflict (i.e., ACC) would be observed among those with OCD compared to healthy controls. It was also predicted that the pattern of activation would vary depending on if the conflict was emotional vs. nonemotional, with the largest difference in activation between those with OCD and healthy controls arising for emotional rather than nonemotional conflict.

2. Materials and methods

2.1. Participants

Twenty-four healthy individuals (12 female; 26.5 ± 5.4 years) and 22 individuals with a primary diagnosis of OCD (8 female; 27.7 ± 5.6 years) performed an emotional/nonemotional conflict task during fMRI scanning. Exclusionary criteria for all participants included a diagnosis of bipolar disorder, intellectual disability, psychosis, ADHD, developmental disorders, mental retardation, or current or past neurological diseases. Diagnoses were based upon the *Mini International Neuropsychiatric Interview* (MINI; Sheehan et al., 1998), a structured clinical interview used to assess 17 Axis I disorders. The MINI was administered by master- and doctoral-level clinicians that were trained and supervised by a clinical psychologist. The *Yale-Brown Obsessive Compulsive Scale* (YBOCS; Goodman et al., 1989a, 1989b) was also administered to those meeting diagnostic criteria for OCD to ensure that presenting symptoms were at least moderate in severity (minimum score of 16).

Among the OCD participants, 5 were excluded for missing data, 1 was excluded for a data-related error, and 1 was excluded for excessive errors and non-responses on the task. Among the controls, 5 were excluded for missing data and 2 were excluded for excessive errors and non-responses on the task. After these exclusions, the final sample for analysis of task-based data contained 15 healthy controls and 16 individuals with OCD. Many OCD patients had additional current Axis I diagnoses (63%), including 37% with an anxiety disorder diagnosis and 31% with a depressive disorder. However, OCD was determined to be the primary diagnosis with patients presented primarily with ordering, washing, and obsessing symptoms based on higher mean scores on the Obsessive-Compulsive Inventory-Revised (Foa et al., 2002) subscales. Seven of the participants with OCD were also currently on medication (mostly SSRIs). Demographic information for the final sample is provided in Table 1.

2.2. Symptom assessment

The Obsessive-Compulsive Inventory-Revised (OCI-R; Foa et al., 2002) is an 18-item measure of OCD symptoms including Washing, Checking, Obsessing, Neutralizing, Ordering, and Hoarding. The OCI-R had good internal consistency in the present study ($\alpha = 0.96$).

Table 1
Demographic information and symptom assessment by diagnostic group.

	OCD	Control
N	16	15
% female	37.5	33.3
Age	27.50 (5.33)	26.06 (4.45)
% Caucasian	94	100
Symptom assessment		
YBOCS	22.00 (5.51)	—
OCI-R*	41.93 (13.32)	6.57 (3.13)
DPSS-R*	32.33 (13.69)	16.43 (6.41)
STAI-T*	56.40 (13.84)	31.36 (5.00)

Note: OCD = obsessive compulsive disorder; YBOCS = Yale-Brown Obsessive Compulsive Scale; OCI-R = Obsessive-Compulsive Inventory-Revised; DPSS-R = Disgust Propensity and Sensitivity Scale-Revised; STAI-T = State-Trait Anxiety Inventory–Trait.

* $p < 0.001$.

Fig. 1. Congruent and incongruent trials for emotion (top) and nonemotion (bottom) conflict task.

The Disgust Propensity and Sensitivity Scale-Revised (DPSS-R; van Overveld et al., 2006) is a 16-item measure designed to assess the general tendency to respond with the emotion of disgust (Disgust Propensity) and the overestimation of the negative impact of experiencing disgust (Disgust Sensitivity). The DPSS-R total scale had good internal consistency in the present study ($\alpha = 0.93$).

The State-Trait Anxiety Inventory-Trait (STAI-T; Spielberger et al., 1983) is a 20-item measure of proneness towards experiencing anxiety and distress (trait anxiety). The STAI-T had good internal consistency in the present study ($\alpha = 0.97$).

2.3. Conflict task

An event-related fMRI task adapted from Egner et al. (2008) was used to assess brain response related to conflict resolution (see Fig. 1). During two runs of 148 trials each, participants viewed faces paired with descriptors of emotion (emotion run) or gender (nonemotion run). Rather than a continuous sequence of 148 trials, each run was broken up into 4 blocks of 37 Congruent or Incongruent trials. This was done in order to more easily ensure that a consistent number of trial sequences (Congruent-Congruent: CC, Congruent-Incongruent: CI, Incongruent-Congruent: IC, Incongruent-Incongruent: II) was presented across the entire run. Each block of 37 trials was separated by a 4s "New Block" display, and a subsequent 4s fixation period (shown under "Example emotion conflict run" in Fig. 2). A 10s fixation period was added to the end of the run to allow for the possibility of capturing the return to baseline of the hemodynamic response function of the last trial.

It should be noted that each trial was coded for its sequence based on both the current trial type (Congruent or Incongruent) and the type of the immediately preceding trial (Congruent or Incongruent). This is best illustrated by the "Example emotion conflict block trial sequence" section in Fig. 2. The second trial in the block is coded as a "CI" trial sequence because it is an Incongruent trial and the first trial in the block is a Congruent Trial. Similarly, the third trial in the block is coded as an "II" trial sequence because it is an Incongruent trial following a preceding Incongruent trial. Within each block, there are 36 (rather than the full 37) trials that can be coded based on sequence since there is nothing preceding the first trial in the block. This results in 9 trials per sequence (CC, CI, IC, II) within a block, and 36 trials per sequence across the 4 blocks.

The faces of 10 individuals from the Karolinska Directed Emotion Face stimulus set were used (5 males, 5 females). In the emotion run, presented faces could have one of two expressions: "Happy" or "Disgust". Disgust was employed as an emotional cue given the literature suggesting that disgust may be more relevant to OCD than fear/anxiety (Olatunji et al., 2017). Participants were instructed to indicate the expression of the presented face while ignoring the overlaid descriptor ("Happy" or "Disgust"; see Fig. 1). Similarly, in the nonemotion run, participants were instructed to indicate the gender ("Male" or "Female") of the presented face while ignoring the overlaid descriptor. Participants were instructed to respond via button press with the emotion or gender of the face, depending on the run. In the emotion run, participants were told to respond with their index finger if the face expressed disgust and with their middle finger if the face was happy. In the gender run, participants were instructed to respond with their index finger if the face was male and their middle finder if the face was female. Participants were given instructions about what responses to use for the task prior to each run. No cue was given during the trials. Participants were told to respond as fast as possible while avoiding errors.

The emotion and non-emotion runs were counterbalanced across subjects. The emotion and non-emotional trials were presented in separate runs because we followed the design of Egner et al. (2008) in which trials were presented in 4 orders to create separate emotional and non-emotional conflict conditions (Congruent-Congruent, Congruent-Incongruent, Incongruent-Congruent, Incongruent-Incongruent). In each trial, the word overlaid on a face could be either congruent or incongruent with the face. For example, in the emotion run the word "happy" would be congruent with a happy face but incongruent with a disgusted face. Meanwhile, in the nonemotion run the word "male" would be incongruent with a female face. The task is intended to induce conflict that must be resolved in order to correctly respond when presented with an incongruent trial. Each trial was presented for 2 seconds with an intertrial interval (ITI) that ranged from 3 to 7 seconds with a mean of 3.97 seconds. From a psychological perspective it is advantageous to have smaller ITIs, however from a statistical standpoint a smaller range in ITI diminishes the ability to estimate trial-by-trial neural responses in fMRI data (Serences, 2004). As previously noted, four main conditions were used each with 36 trials pseudorandomized within each run (Egner et al., 2008): congruent following congruent trial (CC), congruent following incongruent trial (IC), incongruent following congruent trial (CI), and incongruent following incongruent trial (II). However, the primary contrast of interest was brain response during presentation of high conflict (II) and low conflict (CI).

2.4. Imaging data acquisition

Images were acquired using a 3T Phillips Intera Achieva MRI scanner (Phillips Medical Systems, Andover, MA). The experimental task was projected from behind on a mirror mounted on the head coil. Each of the two functional runs (field echo echo-planar imaging [FEEPI]) lasted 15.7 minutes and consisted of 464 dynamics collected over 38 slices, 3.2 mm thick with 0.35 mm gap, FOV = 240 × 240 mm, flip angle = 90, TR 2 s, and TE 28 ms. A high resolution T1-weighted turbo field echo (TFE) anatomical scan consisted of 1 dynamic collected over 170 slices, 1 mm thick, FOV = 256 × 256 mm, flip angle = 8, TR 8.9 ms, and TE 4.6 ms.

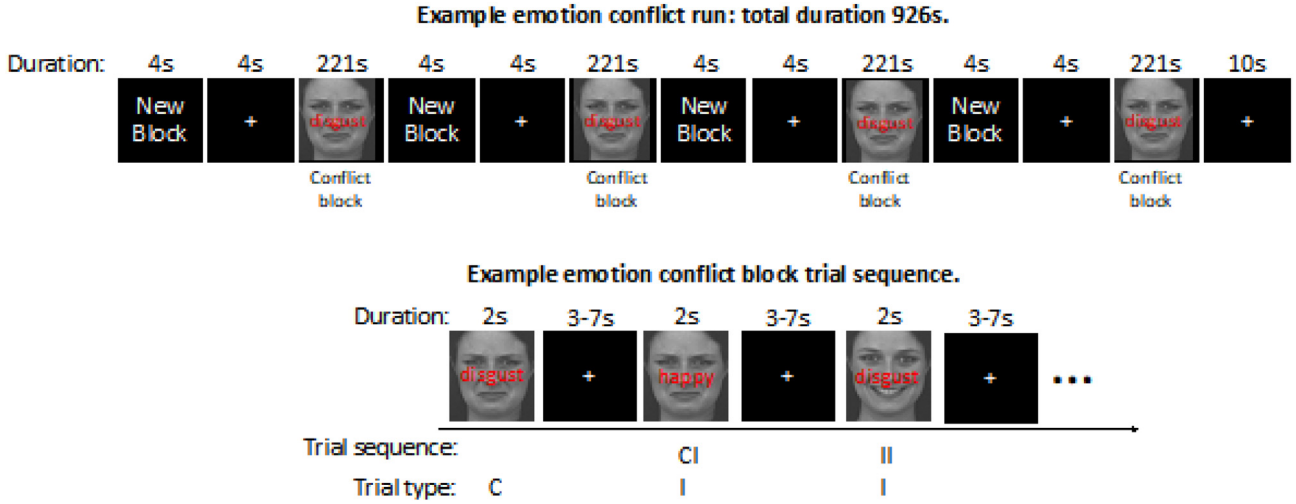

Fig. 2. Example of an emotion conflict run and block trial sequence.

2.5. Statistical analysis of task-based fMRI data

Imaging data were analyzed using SPM12 (Wellcome Department of Cognitive Neuroscience, London UK). During preprocessing, functional images were slice-time corrected, realigned to the mean image, co-registered with the anatomical image, normalized to the SPM EPI template, and smoothed using a 5 mm full width half maximum Gaussian smoothing kernel. A subject-level general linear model (GLM) was estimated using four regressors in each task separately: congruent-congruent trials (CC; no conflict), congruent-incongruent trials (CI; low conflict), incongruent-congruent trials (IC), and incongruent-incongruent trials (II; high conflict). These regressors were chosen in order to test the contrast of "high conflict" versus "low conflict" (Egner et al., 2008). Additional regressors included the six motion parameters from rigid-body realignment. Error trials were not included in the model; however, few were observed (see Table 2). A group-level GLM was estimated to test for group differences within the "high conflict" versus "low conflict" contrast. Both subject-level and group-level contrasts are bidirectional.

Table 2
Mean task response time (RT) and accuracy by run and group.

Emotion	OCD Mean ± SD	Control Mean ± SD
High conflict (II) RT	928.01 ± 190.49	887.07 ± 160.26
Low conflict (CI) RT	931.88 ± 182.55	904.84 ± 165.52
No conflict (CC) RT	869.19 ± 218.75	812.48 ± 168.08
IC RT	871.41 ± 180.38	838.47 ± 152.66
Mean RT	900.12 ± 191.37	860.71 ± 161.92
High conflict (II) accuracy	0.97 ± 0.03	0.96 ± 0.04
Low conflict (CI) accuracy	0.95 ± 0.07	0.96 ± 0.04
No conflict (CC) accuracy	0.98 ± 0.04	0.99 ± 0.02
IC accuracy	0.97 ± 0.06	0.97 ± 0.04
Mean accuracy	0.97 ± 0.05	0.97 ± 0.04
Nonemotion		
High conflict (II) RT	828.86 ± 172.26	748.80 ± 155.67
Low conflict (CI) RT	809.03 ± 145.57	733.93 ± 140.03
No conflict (CC) RT	751.79 ± 136.43	692.02 ± 127.31
IC RT	798.12 ± 164.08	709.69 ± 126.99
Mean RT	796.95 ± 154.16	721.11 ± 136.24
High conflict (II) accuracy	0.98 ± 0.03	0.98 ± 0.03
Low conflict (CI) accuracy	0.96 ± 0.04	0.99 ± 0.02
No conflict (CC) accuracy	0.99 ± 0.03	0.99 ± 0.01
IC accuracy	0.99 ± 0.02	1.00 ± 0.00
Mean accuracy	0.98 ± 0.03	0.99 ± 0.02

Note: no significant group differences when controlling for multiple comparisons. SD = standard deviation.

Whole-brain group-level statistical maps were created using a voxel-wise threshold $p < 0.001$, corrected for multiple comparisons to $p < 0.05$, using a cluster threshold of 90 voxels as determined by Monte Carlo simulation implemented with 3dClustSim in AFNI using spatial autocorrelation (acf) values calculated using 3dFWHMx (Cox, 1996). Furthermore, analyses were conducted in four search regions of interest (ROIs) also used in Egner et al. (2008): bilateral ACC, amygdala, MFG, and medial superior frontal gyrus (MSFG). ROIs were defined using the anatomical automatic labeling atlas (Tzourio-Mazoyer et al., 2002) and created using the Wake Forest University Pickatlas toolbox (Maldjian et al., 2003). Using the same cluster threshold determination as above, a voxel-wise threshold of $p < 0.005$, corrected for multiple comparisons to $p < 0.05$, was applied for each search ROI analysis (ACC: 28 voxels, amygdala: 8 voxels, MFG: 27 voxels, and MSFG: 44 voxels). Voxel-wise thresholds for whole-brain ($p < 0.001$) and ROI ($p < 0.005$) analyses were chosen to be similar to those used in Egner et al. (2008). For additional analyses, GLM beta parameters were extracted from ROIs using MarsBaR (Brett et al., 2002).

2.6. Procedure

Participants first provided informed consent prior to participation. The MINI was then administered by master- and doctoral-level clinicians. The structured diagnostic interview was then followed by administration of the YBOCS in order to determine OCD symptom severity. Participants then completed the symptom assessments which were then followed by the fMRI conflict task. They were then provided with a monetary reimbursement and debriefed. The study protocol was approved by the University Institutional Review Board and conformed to principles of the World Medical Association's Declaration of Helsinki.

3. Results

3.1. Symptom assessment and behavioral outcomes

Table 1 shows that patients with a primary diagnosis of OCD and healthy controls were well matched on age, gender, and ethnicity as no significant group differences were observed for these demographic variables (all $p > 0.35$). However, Table 1 also shows that patients with OCD reported significantly more OCD symptoms, disgust proneness, and trait anxiety than healthy controls (all $p < 0.001$). Additionally, there were significant correlations among symptom measures collected for all subjects (OCI-R, DPSS-R, STAI-T; all $r > 0.75$, $p < 0.001$).

Similar to the results in the study by Egner et al. (2008), we found significant differences in mean response time (RT) as well as mean

accuracy between the two tasks using separate 2 (task: emotion vs. nonemotion) × 2 (group: healthy control vs. OCD) analyses of variance (ANOVA; main effect of task on RT: $F(1, 58) = 8.92$, $p = 0.004$, main effect of task on accuracy: $F(1, 58) = 4.31$, $p = 0.04$) with greater mean RT and lower mean accuracy in the emotion run. However, overall mean accuracy for each group was high during both tasks (see Table 1). Additionally, mean RT and accuracy were similar for both groups (mean RT: $F(1, 58) = 2.01$, $p = 0.16$, mean accuracy: $F(1, 58) = 1.81$, $p = 0.18$), and the results did not indicate any task × group interaction effects (mean RT: $F(1, 58) = 0.20$, $p = 0.66$, mean accuracy: $F(1, 58) = 0.17$, $p = 0.68$).

In order to understand behavioral differences in conflict resolution related to OCD, group differences for overall mean RT and accuracy within each task were tested with t-tests (Table 2); however, no significant differences were observed (all $p > 0.07$). Furthermore, Pearson correlations were computed within the OCD group between YBOCS scores and overall mean accuracy as well as mean RT for each task, again resulting in no significant findings (all $p > 0.47$). The same t-tests and correlations were conducted using the mean RT and accuracy from high conflict (II) and low conflict trials (CI), revealing no significant between-group differences (all $p > 0.05$) nor correlations with YBOCS scores in the OCD group (all $p > 0.4$). There were also no significant correlations between the other symptom measures (OCI-R, DPSS-R, STAI-T) and overall mean RT or accuracy (all FDR-corrected $p > 0.27$) nor mean RT or accuracy from high conflict or low conflict trials (all FDR-corrected $p > 0.33$). These results demonstrate that although the groups differed in terms of symptomatology, these differences did not appreciably affect task performance. However, it is important to note that the small sample sizes might have contributed to the nonsignificant results.

3.2. fMRI response to conflict resolution

First, we sought to replicate the results found by Egner et al. (2008) by testing the high conflict (II) versus low conflict (CI) contrast within the healthy control group. Due to the aforementioned differences in mean RT between the two tasks—which may be an indication of a relative difference in difficulty—between-task mean RT differences were included in all group-level GLMs as a covariate. The high conflict versus low conflict contrast was first tested in the emotion task for each of the four search ROIs (ACC, amygdala, MFG, and MSFG), which resulted in two significant clusters in anterior MFG (Table 3). The same contrast tested in the nonemotion run revealed two significant clusters in rostral ACC (rACC), one cluster in anterior MFG, and one cluster in dorsal MSFG (Table 3). These results demonstrated that rACC, anterior MFG, and dorsal MSFG showed greater activation for high conflict compared to low conflict in the healthy control group. Interestingly, whereas Egner et al. (2008) observed greater activation in rACC during the emotion compared to nonemotion task, our results showed greater activation during the nonemotion compared to emotion task in rACC and dorsal MSFG ($t(14) = 2.51$, $p = 0.03$ and $t(14) = 2.20$, $p = 0.05$, respectively; Fig. 3). Furthermore, Egner et al. found greater activation in posterior MFG during the nonemotion compared to emotion task, however we observed greater activation during the emotion versus nonemotion task in anterior MFG ($t(14) = 2.64$, $p = 0.02$; Fig. 3). We further conducted a 2 (task: emotion vs. nonemotion) × 2 (ROI: rACC vs. MFG) ANOVA, which confirmed a significant interaction with greater activation in rACC during nonemotion versus emotion task and greater activation in MFG during emotion versus nonemotion task ($F(1, 56) = 10.56$, $p = 0.002$).

Since the ROIs tested in the present study required cluster thresholding larger than that used in Egner et al. (2008), it is possible that the current analyses could miss the smaller regions that were found by Egner et al. Therefore, we decided to test the specific peak regions found by Egner et al. for group and task differences. As was done in Egner et al., we created ROIs around the regions of peak activation that were found by Egner et al. using MarsBaR (rACC: 6 mm radius centered at [-12, 44, -2], MFG: 4 mm radius centered at [38, 16, 54]). We then tested for significant differences of activation within each ROI with a paired t-test between tasks for the healthy control group and with a 2 (task: emotion vs. nonemotion) × 2 (group: healthy control vs. OCD) ANOVA. Neither between-task differences within the healthy control group (rACC: $t(14) = -1.33$, $p = 0.21$, MFG: $t(14) = -0.13$ $p = 0.90$) nor main effects for task (rACC: $F(1, 58) = 0.73$, $p = 0.40$, MFG: $F(1, 58) = 0.58$, $p = 0.45$) or group (rACC: $F(1, 58) = 2.40$, $p = 0.13$, MFG: $F(1, 58) = 0.43$, $p = 0.52$) were found for either ROI. Furthermore, there were no task × group interactions (rACC: $F(1, 58) = 0.90$, $p = 0.35$, MFG: $F(1, 58) = 0.25$, $p = 0.62$).

Next, we were interested in comparing group differences related to high and low conflict in each task. Testing between-group differences within our four ROIs, we found one significant cluster at the multiple comparison threshold in right posterior MFG for the emotion task (Fig. 4 and Table 4). Extracting beta parameters from the ROI demonstrated that although healthy controls had greater activation during high conflict compared to low conflict, OCD participants showed the opposite pattern with greater activation during low conflict trials compared to high conflict. Testing group differences at the whole-brain level revealed a significant cluster in supplementary motor area (SMA) for the nonemotion task (Fig. 4 and Table 4). Similarly, the healthy control group showed greater activation during the high conflict trials compared to low conflict, however the OCD group showed slightly more activation in the low conflict compared to high conflict condition. Furthermore, separate 2 (task: emotion vs. nonemotion) × 2 (group: healthy control vs. OCD) ANOVAs revealed a significant interaction for both regions (right MFG: $F(1, 58) = 4.68$, $p = 0.03$, SMA: $F(1, 58) = 11.69$, $p = 0.001$). These results suggest that posterior MFG and SMA may be candidate regions for understanding conflict resolution deficits in patients with OCD and further demonstrate the differences between resolving conflict with emotional and nonemotional distracters.

4. Discussion

The present study revealed no significant group differences in

Table 3
Peak regions from ROI analyses of healthy control group.

Healthy control: high conflict > low conflict Peak *t* score intensity	Peak MNI coordinates (X, Y, Z)	Size (voxels)	Peak region	Task
4.57	-42 50 6	58	Left MFG	Emotion*
3.84	42 40 4	28	Right MFG	Emotion
7.14	−4 36 4	105	Left rACC	Nonemotion*
4.01	0 24 18	32	ACC	Nonemotion
5.10	8 30 60	60	Right MSFG	Nonemotion*
5.56	−34 46 16	63	Left MFG	Nonemotion

Note: Cluster threshold $p < 0.005$, $k = 28$ (ACC), 8 (AMG), 44 (MSFG), 27 (MFG).
* $p < 0.05$ testing significant differences of mean activation between emotion and nonemotion tasks (see Section 3.2).

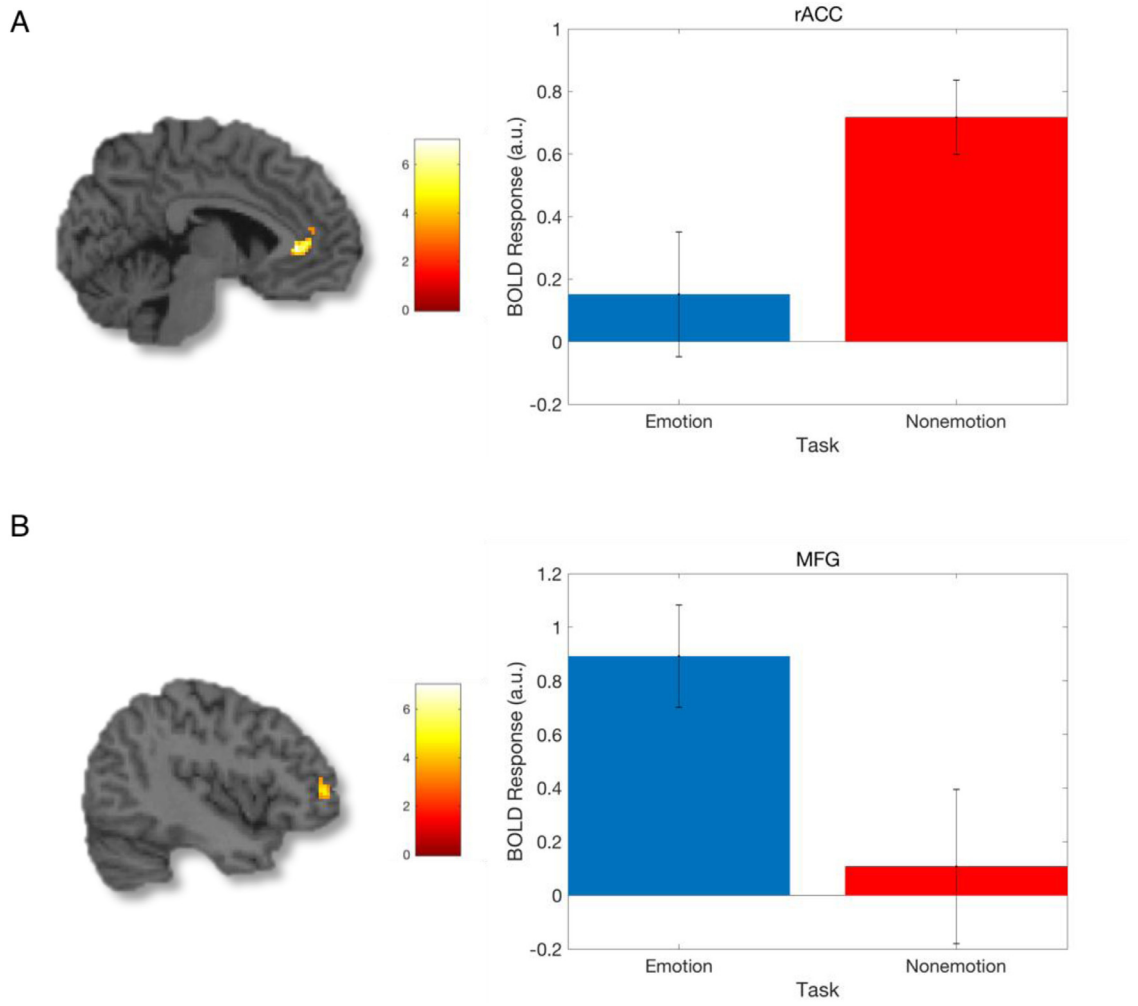

Fig. 3. (A) Greater activation during nonemotion task than emotion task in left rACC (−4, 36, 4) for high conflict compared to low conflict in healthy controls. (B) Left anterior MFG (−42, 50, 6) showed the opposite pattern with greater activation during emotion task than nonemotion task for high conflict versus low conflict in healthy controls. Multiple comparisons corrected to $p < 0.05$ using cluster threshold of 28 (ACC) and 27 (MFG) voxels with a voxel-wise p value of 0.005.

behavioral performance suggesting that OCD is not associated with general slowing of motor responses or alteration in task motivation. However, the present findings did show that emotional distracters and nonemotional distracters significantly differed in the pattern of brain activation observed among healthy individuals. More specifically, nonemotional distracters were characterized by heightened brain activation in left rACC and right dorsal MSFG during high conflict trials compared with low conflict trials. In contrast, left anterior MFG showed greater activation for emotional distracters during high versus low conflict trials. This finding is partially consistent with previous research suggesting that there may be different neural mechanisms for the resolution of interference from nonemotional versus emotional conflicting distracter stimuli. However, Egner et al. (2008) found that the right posterior MFG was involved in conflict resolution in a nonemotional task, but not in an emotional task. In contrast, rACC was involved in resolving conflict in the emotional task, but not in the nonemotional task. Interestingly, the current results within the healthy control group showed the opposite pattern. Although MFG and rACC appear to serve different functions during conflict resolution from emotional and nonemotional distracters, further research is needed to understand the precise difference.

The discrepancy between the present study and that of Egner et al. (2008) may be resolved by consideration of differences in how the task was implemented. For example, the two studies differed in the duration of each trial and the corresponding ITI. The potential overlap in brain regions that function to resolve emotional and nonemotional conflict may also inform interpretation of the present findings. For example, Chiew and Braver (2011) employed an adaptation of the AX Continuous Performance Task (AX-CPT), a stimulus-response incompatibility paradigm, to examine the neural basis of emotional and nonemotional conflict. Emotional conflict was manipulated on a trial-by-trial basis, by requiring that subjects responded to emotional images with a facial expression that was either affectively compatible (low conflict) or incompatible (high conflict). The findings showed that components of the cognitive control network, including dorsal ACC *and* LPFC, showed conflict-related activation increases in both emotional and nonemotional conditions, but with higher activity during responses to the emotional probe stimuli. Furthermore, similar to the present study, Chiew and Braver (2011) did not find emotional conflict effects in rACC, a region typically associated with affective processing. This suggests that there may be a domain-general neural system that is active for both emotional and nonemotional conflict processing. Consistent with this view, Ochsner et al. (2009) found that bilateral dorsal ACC, posterior medial frontal cortex, and dorsolateral PFC were active during emotional and nonemotional conflict on the Eriksen flanker task.

A major aim of the present study was to examine the brain regions that reflect the influence of OCD on the resolution of conflict from either emotional or nonemotional distracters. Here, significant differences were found between healthy controls and patients with OCD in right posterior MFG during conflict resolution from emotional

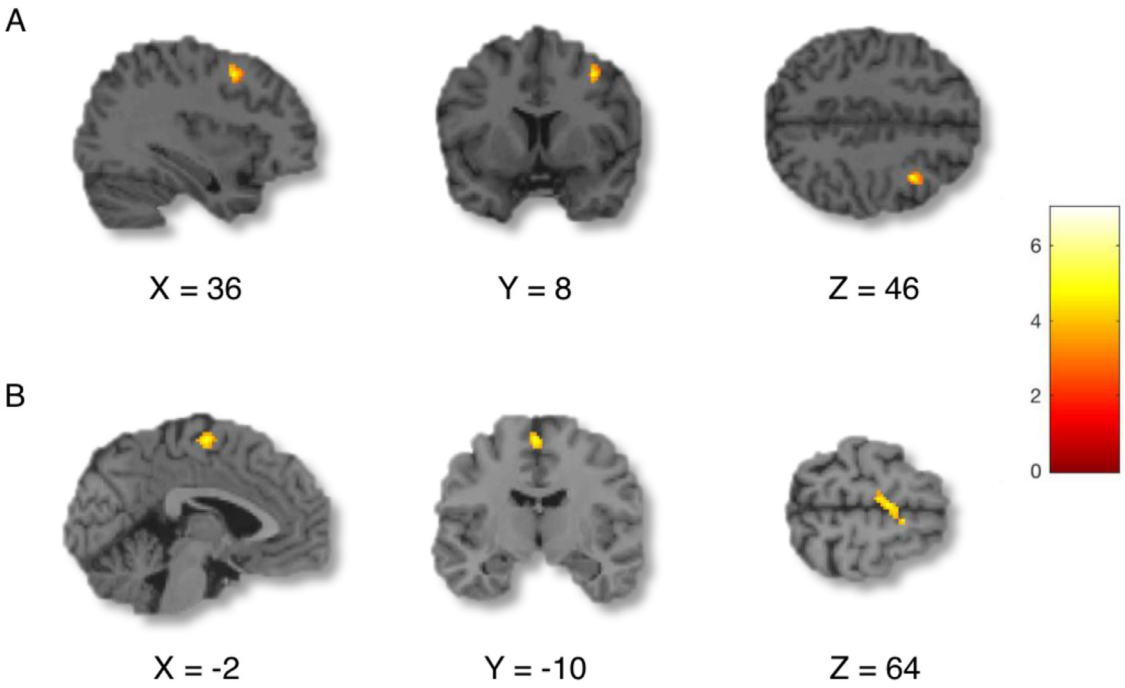

Fig. 4. (A) Right posterior MFG showed greater activation in healthy controls compared to OCD subjects for high conflict versus low conflict during emotion task. (B) Healthy controls also showed greater activation in the left SMA at the whole-brain level for high conflict versus low conflict during nonemotion task. Multiple comparisons corrected to $p < 0.05$ using cluster threshold of 27 (MFG) and 90 (whole-brain) voxels with a voxel-wise p value of 0.005 and 0.001, respectively.

distracters and left SMA during conflict from nonemotional distracters. Furthermore, whereas healthy controls showed greater activation in response to high conflict versus low conflict in these regions, patients with OCD showed greater activation in response to low compared to high conflict. This pattern of findings is particularly striking since previous research has typically found that OCD participants have excessive activation compared to controls. For example, Marsh et al. (2014) examined brain activation among adults with OCD and healthy controls during performance of a Simon Spatial Incompatibility task. The task requires the subject to ignore a task-irrelevant feature of a stimulus (the side of the screen on which an arrow appears) when it conflicts with a more task-relevant one (the direction the arrow points). Similar to the present study, behavioral performance did not differ between groups, however OCD subjects did show greater activation compared to controls in right putamen, insula, and inferior frontal gyrus when viewing conflict-laden stimuli. However, it is important to note that the findings by Marsh et al. were not driven by conflict on a current trial but by response to the alternation of stimulus congruence (incongruent or congruent) across trials. Accordingly, navigating stimulus congruence rather than emotional conflict may more robustly characterize those with OCD compared to healthy controls by excessive activation in the fronto-striatal circuit.

The finding that those with OCD showed less activation than controls in right posterior MFG in response to high conflict versus low conflict from emotional distracters is consistent with previous research indicating deficits in this region. Indeed, a meta-analysis of voxel-based morphology studies related to OCD demonstrated that patients with OCD have lower gray matter density in MFG compared to healthy individuals (Rotge et al., 2010). The present findings suggest that the self-regulatory mechanism that is represented in MFG may not be efficiently deployed during periods of high emotional conflict among patients with OCD. The MFG has been implicated in both conflict/error monitoring (Fan et al., 2003) and emotional processing (Teasdale et al., 1999). However, an alternative interpretation that should be examined in future research is that greater activation in the MFG of OCD patients relative to controls during low conflict relative to high conflict resolution reflects a compensatory response during low cognitive demand that is no longer active during higher cognitive demand. Although not observed in the present study, other research suggests that deactivation in this context among patients with OCD may not be unique to MFG. In a previous study, Yücel et al. (2007) examined the neural basis of cognitive control among patients with OCD and healthy controls that performed the Multi-Source Interference Task. Compared with controls, OCD patients had greater hypoactivation of rACC during high vs. low conflict trials. Although these findings highlight inefficient deployment of specific brain regions during high conflict in OCD, an alternative hypothesis is that hypoactivation in frontal regions of the brain during cognitive control tasks may reflect an inability to appropriately distinguish when, or how much this node of the cognitive control network is adaptively engaged. However, it should be noted that this lack of engagement did not result in deficient task performance among those with OCD.

Those with OCD also showed greater activation in the SMA in response to low compared to high conflict from nonemotional distracters

Table 4
Peak regions from analyses comparing healthy control and OCD groups.

Healthy control > OCD: high conflict > low conflict Peak t score intensity	Peak MNI coordinates (X, Y, Z)	Size (voxels)	Peak Region	Task
4.73	36 8 46	57	Right MFG	Emotion*
4.90	−2 -10 64	125	Left SMA	Nonemotion*

Note: Cluster threshold $p < 0.005$, $k = 27$ (MFG; ROI approach), $p < 0.001$, $k = 90$ (SMA; whole-brain approach).
* $p < 0.05$ task × group interaction (see Section 3.2).

in the present study, a finding that is in line with research implicating the SMA in the pathophysiology of OCD. Indeed, the reduced ability of those with OCD to inhibit obsessions and repetitive compulsions has been associated with excessive activity in orbitofronto-striatal regions, but also in medial and lateral frontal areas like the SMA (i.e., Grutzmann et al., 2016). Given that SMA functions to facilitate the rapid resolution of conflicting action plans, the heightened activation in SMA in response to low conflict from nonemotional distracters may reflect inefficient neural processing that supports resolution of conflicting action plans in OCD. This finding is consistent with previous research suggesting that inefficient neural processing within the SMA may represent a neurocognitive endophenotype of OCD that may be an important treatment target (de Wit et al., 2012). Indeed, research has shown that low-frequency repetitive transcranial magnetic stimulation applied bilaterally to the SMA significantly improves clinical symptoms of OCD (Hawken et al., 2016). It is important to note however that the present findings are partially inconsistent with those of Yücel et al. (2007) who found that OCD patients had greater activation of the SMA during high vs. low conflict trials compared to controls. However, the pattern of activation associated with the SMA during periods of high vs. low conflict may vary as a function of the distractor (emotional vs. nonemotional).

Although the present study observed differences in brain activation between those with OCD and controls regarding the resolution of conflict from nonemotional and emotional distracters, robust group differences in the expected brain regions such as the ACC were not observed. Indeed, it is unclear why between-group differences would be limited to only the right posterior MFG. In light of the existing literature, this absence of a group difference in the expected brain regions may reflect limitations of the present study. These limitations include: (1) the use of a small sample; (2) an OCD group that was not medication-free; and (3) an OCD group with comorbidity. While the diagnosis of OCD was required to be primary for those with comorbid conditions and presenting OCD symptoms were required to be at least moderate in severity, it is unclear if the present findings are an artifact of the comorbid conditions. Accordingly, the present findings need to be replicated in a larger sample of patients whose OCD diagnosis is better characterized. Despite these limitations, the present study does suggest that future research may benefit from examining activity of right posterior MFG and left SMA as potential indices of inefficient responding in OCD when presented with conflict from emotional and nonemotional distracters. However, it is unclear if the task employed in the present study is the most useful for pursuing this program of research in OCD. The task may be especially limited when employing stimulus cues that may be related but not specific to OCD. Furthermore, the group differences that were observed were isolated to specific regions and the effects were not especially robust. Research along these lines employing multiple tasks will be needed to further clarify the neural basis of cognitive control in OCD.

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