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Neural correlates of emotional response inhibition in obsessive-compulsive disorder: A preliminary study

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ABSTRACT

Failure to inhibit recurrent anxiety-provoking thoughts is a central symptom of obsessive-compulsive disorder (OCD). Neuroimaging studies suggest inhibitory control and disgust processing abnormalities in patients with OCD. However, the emotional modulation of response inhibition deficits in OCD and their neural correlates remain to be elucidated. For this preliminary study we administered an adapted affective response inhibition paradigm, an emotional go/no-go task, during fMRI to characterize the neural systems underlying disgust-related and fear-related inhibition in nine adults with contamination-type OCD compared to ten matched healthy controls. Participants with OCD had significantly greater anterior insula cortex activation when inhibiting responses to both disgusting (bilateral), and fearful (right-sided) images, compared to healthy controls. They also had increased activation in several frontal, temporal, and parietal regions, but there was no evidence of amygdala activation in OCD or healthy participants and no significant between-group differences in performance on the emotion go/no-go task. The anterior insula appears to play a central role in the emotional modulation of response inhibition in contamination-type OCD to both fearful and disgusting images. The insula may serve as a potential treatment target for contamination-type OCD.

1. Introduction

Failure to inhibit recurrent anxiety-provoking thoughts is a central feature of OCD (i.e. obsessions) (Chamberlain et al., 2005; 2006). Neural, cognitive, and clinical findings suggest that failures in cognitive and behavioral inhibition processes (indexed by, e.g., go/no-go and oculomotor tasks) are integral to the neuropsychopathology of OCD (Chamberlain et al., 2005). Neuroimaging evidence suggests that abnormal frontal–striatal–thalamic–cortical circuitry may underlie dysfunctional response inhibition in OCD (Rosenberg et al., 1997a; 1997b; Rosenberg and Keshavan, 1998; Chamberlain et al., 2005, 2006; Maltby et al., 2005; Roth et al., 2007; Lee et al., 2009).

Contamination (intense, persistent feeling of having been polluted or infected; Rachman, 2004) concerns are the most common obsessions associated with OCD (Rasmussen and Tsuang, 1986), presenting in up to 50% of OCD patients (Rachman and Hodgson, 1980; Rasmussen and Eisen, 1992). Compulsive cleaning is the second most common compulsion of OCD (Rachman, 2004). Studies support the role of disgust in contamination-related OCD (Mancini et al., 2001; Thorpe et al., 2003; Tsao and McKay, 2004; Olatunji and Sawchuk, 2005; Olatunji et al., 2005; 2007a; Cisler et al., 2009) and the notion that disgust is distinct from other negative affective states (e.g., anxiety, depression) (Mancini et al., 2001; Woody and Tolin, 2002; Olatunji et al., 2004; Tolin et al., 2006).

Neuroimaging studies have shown that abnormalities of the same neural regions involved in disgust processing in healthy people, the insula cortex and striatum, are also involved in OCD (Phillips et al., 2000; Stein et al., 2001; Berle and Phillips, 2006). Two structural MRI studies found that OCD patients have significantly larger anterior insular cortices bilaterally compared to healthy controls (Nishida et al., 2011; Song et al., 2011). Moreover, functional imaging studies show that OCD patients with predominantly washing symptoms have increased neural responses to washing-related stimuli (Phillips et al., 2000; Mataix-Cols et al., 2004) and to disgusting pictures (Shapira et al., 2003; Schienle et al., 2005) in brain regions implicated in disgust and autonomic response processing, including the anterior insula, ventrolateral prefrontal cortex (PFC), and putamen/globus pallidus (Phillips et al., 1997; 1998; Sprengelmeyer et al., 1998; Calder et al., 2001;

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Critchley et al., 2004; Phillips et al., 2004; Lawrence et al., 2007). Studies have also found greater right and left insula activation to disgust-inducing images in OCD patients compared to controls, but no difference in brain activation in response to threat-inducing images (Shapira et al., 2003; Schienle et al., 2006; Stein et al., 2006; Lawrence et al., 2007).

Taken together, these findings suggest inhibitory control and disgust processing abnormalities in patients with OCD. However, the emotional modulation of response inhibition deficits in OCD and their neural correlates remain to be elucidated. Therefore, we employed fMRI in this preliminary study to characterize the neural systems underlying disgust and fear-related inhibition in nine OCD patients compared to ten healthy controls. We hypothesize that compared to healthy controls OCD subjects will make more commission errors in response to emotional stimuli compared to healthy controls on our emotional go/no-go task. We also predict that OCD subjects will have greater activation of insula during emotional response inhibition compared to controls.

Our approach focuses on understanding how neural circuits associated with response inhibition may become dysregulated in the context of emotion in OCD. Prior research examining inhibitory control in OCD has localized group differences to orbitofrontal–striatal circuitry; however, the use of non-emotional, neutral stimuli in those studies neglects to address the importance of emotion processing, potentially obscuring the identification of broader neural dysfunction in the disorder. This is particularly important for understanding neural mechanisms of inhibitory control in OCD, which is characterized by difficulty regulating behaviors in response to specific symptom-related stimuli that elicit fear and disgust. As such, a thorough understanding of the neural mechanisms underlying impaired response inhibition in OCD must take into account the types of emotional situations that elicit this impairment. Our use of a novel emotional go/no-go task represents an important step toward characterizing behavioral and neural functioning using an ecologically-valid measure that taps directly into symptoms of OCD.

2. Methods

2.1. Participants

Twenty participants between the ages of 18 and 65 (inclusive) were recruited for this study. The study was carried out in accordance with the Declaration of Helsinki, and written informed consent was obtained from all participants.

2.2. Screening measures and questionnaires

At screening, participants were administered the Wechsler Abbreviated Scale of Intelligence (WASI) (Wechsler, 1999); exclusion criteria (IQ $\leq$ 70) and the Structured Clinical Interview for DSM-IV Axis I Disorders (SCID-I) (First et al., 1997). Participants in the OCD group were required to meet diagnostic criteria for contamination-type OCD with minimal comorbid diagnoses, while a diagnosis of any clinical disorder on the SCID-I precluded participation as a healthy control. All eligible participants were given a visual acuity test and a toxicology test, and all female applicants were tested for pregnancy. Participants who failed any of these tests were excluded. (Note: one healthy control subject had insufficient specimen for an extended toxicology panel.)

Participants were also administered the following clinical measures: Yale–Brown Obsessive Compulsive Scale (Y-BOCS) (Goodman et al., 1989), Disgust Scale – Revised (DSR) (Olatunji et al., 2007b), Hamilton Measure of Depression (HAM-D) (Hamilton, 1960), and the State-Trait Anxiety Inventory (STAI) (Spielberger et al., 1971).

2.3. Imaging task

2.3.1. Emotion go/no-go task

The emotion go/no-go task was adapted from an established face go/no-go task (Schulz et al., 2009, 2013). The task consisted of six 5-min blocks that each began and ended with a 30-s central fixation-cross. Each block contained 72 (75%) go cues and 24 (25%) no-go cues, yielding a total of 432 go cues and 144 no-go cues. Images from the International Affective Picture System (IAPS) (Lang et al., 2008) that conveyed fear (depicting snakes, guns, and attacks), disgust (depicting roaches, garbage, feces, and vomit; and three non-IAPS images), and neutral (depicting modes of transportation) content served as cues for no-go trials. Fear and disgust images were selected based on ratings published in Mikels et al. (2005). The images were matched on ratings of arousal and dominance, but differed in ratings of valence ($F_{2,\ 66} = 108.44$, $p < 0.001$; Lang et al., 1997). Fear and disgust images were rated as more unpleasant than neutral images (both $p < 0.01$), but did not differ from each other ($p > 0.05$).

The fear, disgust, and neutral images were alternated as no-go trial cues across the six blocks in an ABBCCA design that was fixed for all subjects, in order to test the emotional modulation of response inhibition. IAPS images that depicted household images served as go trial cues across all six blocks. Trial cues were presented in the center of the screen for 1000 ms with an inter-stimulus interval that was pseudo-randomized from 1250 to 1750 ms (mean per block = 1500 ms) and denoted by a fixation-cross. Participants were instructed to respond as rapidly as possible to go cues using a fiber optic button system and withheld responses for no-go cues. Responses provided measures of reaction time and accuracy.

2.3.2. Image acquisition

All participants were scanned on a 3.0 T Siemens Allegra (Siemens, Erlangen, Germany) head-dedicated MRI scanner. Functional T2*-weighted images depicting the blood oxygenation level-dependent (BOLD) signal were obtained in six runs of 120 volumes each using gradient-echo echo-planar images (TR = 2500 ms, TE = 27 ms, flip angle = 82°, FOV = 240 mm, matrix = 64 × 64, slice thickness = 4 mm contiguous, in-plane resolution = 3.75 mm^2). A high-resolution T2-weighted anatomical image was acquired at the same 40 slice locations with a turbo spin-echo (TSE) pulse sequence (slice thickness = 4 mm contiguous, in-plane resolution = 0.41 mm^2). Images were acquired in the axial plane with slices positioned parallel to the anterior commissure–posterior commissure line.

2.3.3. Behavioral data analysis

The percentage of correct inhibitions on no-go trials served as the measure of response inhibition and was tested with a repeated-measures analysis of variance (ANOVA) that included emotion (disgust vs. fear vs neutral) as the within-subjects factor and group (OCD vs. controls) as the between-subjects factor. Group differences in reaction time (RT) and the percentage of correct responses on go trials were tested with independent sample *t*-tests. The two-tailed *p*-value for significance was 0.05. Partial eta squared (η_p^2) and Cohen's d values were calculated to estimate the size of the emotion and group effects on behavioral performance. Performance data were not available from one adult with OCD due to technical difficulties.

2.3.4. fMRI data analysis

Event-related analyses were performed with SPM8 software (http://www.fil.ion.ucl.ac.uk/spm/). The six functional series for