

Altered emotional and BOLD responses to negative, positive and ambiguous performance feedback in OCD

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While abnormal processing of performance feedback has been associated with obsessive–compulsive disorder (OCD), neural responses to different kinds of feedback information, especially to ambiguous feedback are widely unknown. Using fMRI and a performance adaptive time-estimation task, we acquired blood oxygenation level-dependant responses and emotional ratings to positive, negative and ambiguous performance feedback in patients and healthy controls. Negative and ambiguous feedback led to increased levels of anxiety, guilt and shame in patients. Both negative and ambiguous feedback, as compared to positive feedback, induced increased activation of the insular cortex in patients. Furthermore, patients showed no differential activation to negative feedback in the putamen and to ambiguous feedback in the ventromedial prefrontal cortex (VMPFC). Finally, negative feedback induced increased activation in the midcingulate cortex in patients compared to controls. Findings indicate that both negative and ambiguous performance feedbacks are associated with abnormal negative emotions and altered brain activation, in particular increased insula activation, while activation in the putamen and VMPFC does not differentiate between feedback types in OCD patients. This suggests a parallel pattern of increased and decreased neural sensitivity to different kinds of feedback information and a general emotional hyperresponsivity to negative and ambiguous performance feedback in OCD.

Keywords: obsessive–compulsive disorder; neuroimaging; feedback processing; emotion; performance monitoring; ambiguity

INTRODUCTION

Obsessive–compulsive disorder (OCD) is a severe psychopathological disorder with an estimated lifetime prevalence of 2.3% (Ruscio *et al.*, 2010) which is characterized by the presence of recurrent obsessions and/or compulsions. Previous work suggests that OCD is associated with hyperactive performance monitoring (Pitman, 1987) and symptoms of OCD seem to be maintained by patients' dysfunctional appraisals of the outcomes of their own actions (Salkovskis *et al.*, 1999; Coles *et al.*, 2005). In particular, patients are characterized by inflated responsibility, intolerance of uncertainty and perfectionism, including excessive concerns over mistakes (Salkovskis *et al.*, 1999). The associated feelings of incompleteness or imperfection represent a major source of distress in OCD (Coles *et al.*, 2005). Thus, negative performance outcomes might be associated with enhanced negative emotions such as anxiety, guilt, shame and uncertainty, which are thought to contribute to OCD symptoms (Fergus *et al.*, 2010), although a potential link between performance outcomes and emotional responses in OCD patients has not been experimentally investigated yet. Furthermore, pathological beliefs about the tolerability of doubt and uncertainty are thought to contribute to the development and maintenance of OCD (Steketee *et al.*, 1997). Since uncertainty has been conceptualized as an emotional reaction elicited by ambiguous stimuli (Grenier *et al.*, 2005), the delivery of ambiguous performance feedback should in particular represent an aversive situation for OCD patients, in whom a postulated 'just not right' experience might be amplified when ambiguous feedback is given (Coles *et al.*, 2005). Even though emotional responsiveness to uncertain and negative feedback might be

increased in OCD, this may not be necessarily associated with increased learning from negative feedback (Nielen *et al.*, 2009) suggesting a dissociation between emotional responses to feedback and utilization of feedback signals for adaptive responses.

Efforts have been made to reveal the functional neuroanatomy underlying OCD based on different cognitive or symptom provocation paradigms (Menzies *et al.*, 2008; Rotge *et al.*, 2008). According to influential models (Graybiel and Rauch, 2000), findings provide some evidence for altered activations in fronto-striatal loops (Menzies *et al.*, 2008). Despite strong arguments for a role of altered processing of negative and ambiguous feedback in the pathophysiology of OCD, no neuroimaging studies have—to the best of our knowledge—investigated the processing of ambiguous feedback in OCD. Furthermore, no imaging studies have explored the processing of feedback valence in OCD outside the context of monetary incentives (Remijnse *et al.*, 2006; Figeo *et al.*, 2011; Jung *et al.*, 2011) with the latter studies yielding only partially consistent results. Remijnse *et al.* (Remijnse *et al.*, 2006) explored brain activation of OCD patients during a reversal task with monetary reward and loss feedback and showed attenuated activation of orbitofrontal cortex (OFC) and caudate nucleus in OCD patients to reward feedback. During loss feedback, however, no differential brain activation was observed. More recent studies reported diminished activation of the nucleus accumbens during reward anticipation and of medial frontal cortex during reward delivery in patients (Figeo *et al.*, 2011), and higher insular activation during loss anticipation relative to neutral anticipation (Jung *et al.*, 2011). None of these studies reported activation of the cingulate cortices, which are typically involved in error and conflict processing in OCD (Saxena *et al.*, 2009).

In the current study we investigated emotional and brain responses to different categories of performance feedback in OCD relative to healthy controls. We used an adaptive time-estimation task which incorporated balanced feedback on correct and incorrect estimation performance (Miltner *et al.*, 1997), as well as a third category during

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which ambiguous performance feedback was presented. As dysfunctions in orbitofrontal, cingulate and striatal regions in OCD patients have been consistently reported (Menzies *et al.*, 2008), we expected alterations in feedback processing to be primarily reflected in altered engagement of these structures in patients. Furthermore, we hypothesized that negative as well as ambiguous feedback should be associated with amplified emotional responses and increased brain activation in areas suggested to be involved in negative affect and performance monitoring.

MATERIALS AND METHODS

Participants

Data were analysed from 24 patients with a DSM-IV diagnosis of OCD (15 females) and 24 healthy control subjects (13 females), who were closely matched for age, gender, education and general intelligence (Table 1). The current diagnostic status of OCD patients was assessed by the structured clinical interview for DSM-IV (SCID; (Wittchen *et al.*, 1996)), the mini international neuropsychiatric inventory (MINI; (Sheehan *et al.*, 1998)), the Yale–Brown obsessive compulsive

scale (Y-BOCS; (Goodman *et al.*, 1989)) and the obsessive compulsive inventory-revised (OCI-R; German version: (Gonner *et al.*, 2008)). Diagnostic interviews were conducted by an experienced clinical psychologist. All subjects were recruited from local clinical and community populations. Patients were excluded for current comorbid episodes of major depression and neurological disorders. Eleven patients had been diagnosed with one or more comorbid Axis I disorder in the past. These Axis I disorders included depressive episodes ($n = 7$), anorexia ($n = 1$) and panic disorder ($n = 3$). One Patient had an additional diagnosis of histrionic and borderline disorder. Seven patients had received pharmaceutical treatment—four subjects were medicated with SSRIs, two subjects were medicated with SNRIs and one subject was medicated with a tricyclic antidepressant. Six of these seven patients also received cognitive-behavioral therapy (CBT). Moreover, seven patients had received CBT but no pharmacological treatment. The study was approved by the Ethics Committee of the University of Jena.

Stimuli and task

The time-estimation task required participants to estimate an interval of 1 s as accurately as possible. An auditory cue of 50 ms duration marked the onset of each time-estimation trial. Participants were required to press a button with their right index finger just when they thought that 1 s had elapsed. During auditory cue presentation and for the following 4200–7600 ms (depending on a random SOA; see below), a central white fixation cross on a black background was presented. Performance feedback was administered visually after offset of fixation cross presentation and consisted of either of the letters A, B or C, which were presented for 1 s, respectively (Figure 1). Each of these letters was assigned to one of three feedback classes: it either indicated a correct response, a false response or did not convey any unambiguous information regarding estimation success. The specific assignment of letters to conditions was balanced across subjects in order to control for specific effects of visually presented feedback stimuli which were projected onto a screen inside the scanner bore.

In order to decorrelate response- and stimulus-related activation patterns, stimulus onsets were systematically jittered. Specifically, intervals between button presses and feedback presentation were offset within a range of 4200–7600 ms; intertrial intervals were offset within a range of 3200–7500 ms. Furthermore, a sliding response window algorithm was used to balance the relative presentation frequency of the three different feedback conditions. This is an important factor in the time-estimation task as it prevents subjects from building up strong expectations about the information conveyed by feedback. That is, because the local probability of a quickly learned behavioral response being sufficiently accurate is adapted trial-wise, depending on

Table 1 Sample characteristics of OCD patients and control subjects

	OCD patients		Control subjects		Group differences
	Mean	SD	Mean	SD	
Age (years)	28.1	8.1	25.8	6.2	$t(43.19) = -1.08; P = 0.29$
Illness duration (years)	8.52	6.3			
Estimated intelligence ^a	109 ^b	9.4	114 ^c	13.5	$t(37.29) = -1.65; P = 0.11$
Y-BOCS	19.0	6.8			
OCI-R total	34.7	11.9	7.0 ^b	4.7	$t(29.97) = -10.6; P < 0.01$
OCI-R washing	4.1	3.0	0.5	1.1	$t(28.72) = -5.53; P < 0.01$
OCI-R checking	7.2	3.4	0.9	1.7	$t(33.46) = -8.02; P < 0.01$
OCI-R obsessing	7.5	3.0	1.3	1.5	$t(34.01) = -9.21; P < 0.01$
OCI-R hoarding	4.2	3.7	2.5	1.7	$t(32.58) = -2.06; P < 0.01$
OCI-R neutralizing	5.3	4.0	0.6	1.0	$t(25.91) = -5.54; P < 0.01$
OCI-R ordering	6.4	3.9	1.2	1.4	$t(28.66) = -6.15; P < 0.01$
HAM-D ^d	5.9 ^b	3.2			
	<i>N</i>	%	<i>N</i>	%	
Gender					
Females	15	62.5	13	54.2	
Males	9	37.5	11	45.8	
Education ^e	1:8:12:3		0:2:16:6		$\chi^2(1) = 0.34; P = 0.56$
Medication, Number	7	29.2	0	0	

^aMultiple Choice Vocabulary Test (MWT; Forms A and B).

^bData from one subject are missing.

^cData from two subjects are missing.

^dHamilton Rating Scale for Depression.

^e9 years : 10 years : 12 years : >12 years

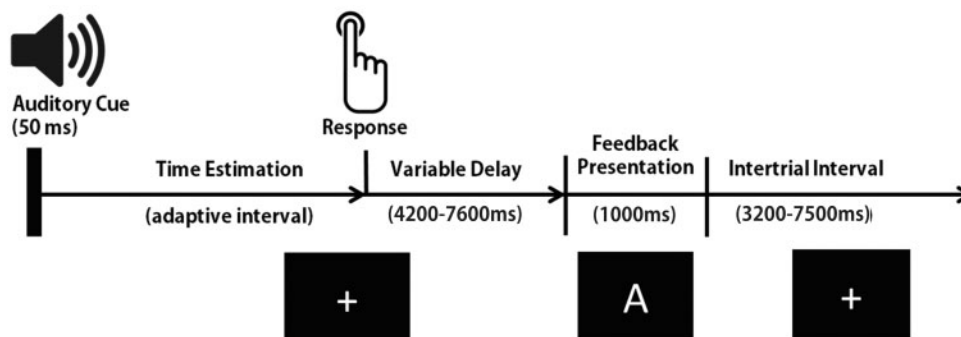


Fig. 1 Schematic representation of the sequence of trial events.

the individual's accumulated performance level, habit formation is unlikely to take place quickly. Thus, the response situation remains underdetermined throughout the experiment and feedback presentation is needed in order to clarify the response outcome.

Prior to the experiment, subjects were trained on the task and successively completed 2 runs of 66 estimation trials, respectively. Post-experimentally, subjects rated their subjective experiences during feedback evaluation on several 9-point Likert scales (1 = 'not at all', 9 = 'very much') accounting for feelings of anxiety, guilt, shame and uncertainty; in one control and one OCD patient, these rating scores are missing due to a technical error. Further, subjects were asked to reproduce the correct assignment of letters to feedback conditions. Behavioral data were analysed by means of repeated measures ANOVAs and MANOVAs using SPSS software (version 19; SPSS Inc., Chicago, IL) or by the non-parametric Mann-Whitney-U statistic when requirements of a parametric analysis were not fulfilled.

fMRI data acquisition, pre-processing and analysis

Functional magnetic resonance data were acquired at 3 T on a Siemens Magnetom Trio (Siemens, Medical Systems, Erlangen, Germany) using a standard 12-channel Siemens Head Matrix Coil. Two runs of 376 volumes, each consisting of 35 slices (slice thickness = 3 mm; interslice gap = 0.50 mm; in-plane resolution = $3 \times 3 \text{ mm}^2$) were recorded by means of a T2*-weighted gradient-echo, echoplanar sequence with a repetition time (TR) of 2300 ms, an echo time (TE) of 30 ms and a flip angle (FA) of 90°, yielding a data matrix of 64×64 voxels within a field of view (FOV) of 192 mm. Acquisition orientation was obliquely tilted $\sim 30^\circ$ relative to the anterior commissure-posterior commissure line (Deichmann *et al.*, 2003). Additionally, a T1-weighted MPRAGE structural volume was recorded for anatomical localization and a shimming field was applied prior to functional imaging.

Pre-processing and analysis of the functional data were performed using Brain Voyager QX software (BVQX 1.10 and 2.3; Brain Innovation B. V., Maastricht, The Netherlands). The first four volumes of each run were discarded as dummies in order to ensure steady state tissue magnetization. Realignment to the first volume of each run was performed via least squares estimation of six rigid body parameters in order to reduce effects of head movements on volume time course analysis. Further data pre-processing comprised a correction for slice time errors and spatial (8 mm full-width at half-maximum [FWHM] isotropic Gaussian kernel) as well as temporal (high pass filter: 8 cycles per run; low pass filter: 2.8 s FWHM; Linear Trend Removal) smoothing. Anatomical and functional images were co-registered and normalized to the Talairach space (Talairach and Tournoux, 1988).

The statistical analysis of fMRI data was based on the general linear model (GLM) with adjustment for autocorrelation following a global AR(1) model. The stimulation protocols comprised predictors for auditory cue presentations, positive, negative and ambiguous feedback, as well as missed trials. Based on these protocols, reference functions were derived. The expected blood oxygenation level dependent (BOLD) signal change for each predictor was modeled by convolving these reference functions with a 2-gamma hemodynamic response function to account for the delayed onset and typical shape of the BOLD signal time course. Beta-weights for the random-effects group GLM were based on *z*-standardized time course data and determined by a least squares estimation. The main focus of analysis was on a priori defined feedback-relevant Regions of Interest (ROIs) which included the insula, the midcingulate cortex (MCC), ventral and dorsal striatum and OFC and ventromedial prefrontal cortex (VMPFC) (Nieuwenhuis *et al.*, 2005). Based on these regions' Talairach coordinates as provided by Talairach Client software (Lancaster *et al.*, 2000) search regions were defined. A cluster-size

threshold estimation procedure was used (Goebel *et al.*, 2006) to correct for multiple comparisons within these search regions. Significant clusters of contiguously activated voxels within these search regions were determined by a Monte Carlo simulation based on 1000 iterations. After setting the voxel-level false positive rate to $P < 0.005$ (uncorrected), and specifying the FWHM of the spatial filter, the simulation resulted in a minimum cluster size of contiguously activated voxels corresponding to a false positive rate of 5%.

RESULTS

Behavioral

On average, participants received 31.4% positive (SEM: $\pm 0.6\%$), 33.7% negative (SEM: $\pm 0.5\%$) and 32.2% ambiguous (SEM: $\pm 0.4\%$) feedback. There were no significant between-group differences as to the number of presented feedbacks in any condition (Roy's Largest Root = 0.13; $F[3,44] = 1.901$; $P = 0.143$) nor did any significant within-subjects differences emerge for presentation frequencies of positive ($F[1,46] = 2.172$; $P = 0.147$), negative ($F[1,46] = 1.596$; $P = 0.213$), or ambiguous feedback ($F[1,46] = 0.889$; $P = 0.351$).

Across all subjects, the mean range of the time interval within which a response was regarded as correct was 338 ms (SEM: 17.8); even though there was a tendency for longer intervals in OCD patients (OCD: $M = 367$ ms, SEM = 30.7; Controls: $M = 309$ ms, SEM = 16.7), the group difference was not significant ($t_{46} = 1.650$, $P = 0.106$). More importantly, the average number of violated response deadlines (35.2 across all subjects) did not differ significantly between the groups ($t_{46} = 1.570$, $P = 0.125$). All of these findings strongly imply that the sliding time window algorithm effectively balanced the presentation frequency of the different feedback conditions by adjusting the window's width.

Self-reports

All subjects were able to reproduce the assignment of letters to feedback conditions correctly. Analyses of self-report scores by means of a repeated measures ANOVA revealed a main effect of group for uncertainty ($F[1,43] = 9.40$; $P < 0.05$), independent of feedback category in OCD patients (Figure 2). According to the Mann-Whitney-U test, anxiety (negative: $Z = -3.44$; $P < 0.05$; ambiguous: $Z = -2.94$; $P < 0.05$), guilt (negative: $Z = -3.00$; $P < 0.05$; ambiguous: $Z = -2.16$; $P < 0.05$) and shame (negative: $Z = -3.09$; $P < 0.05$; ambiguous: $Z = -2.70$; $P < 0.05$) ratings differed between groups for negative and ambiguous feedback, but not for positive feedback (Figure 2).

Neuroimaging between-group differences

Negative vs positive

Analysis of brain activation revealed several significant clusters in OCD patients relative to controls for the contrast negative > positive feedback (Table 2). There were significant activations in the right posterior putamen and bilaterally in insular cortex as well as MCC. The effect in the putamen was due to the fact that positive and negative feedback did not induce different activations in patients ($P > 0.05$, corr.), while controls showed relatively stronger activation to positive as compared to negative feedback ($P < 0.05$, corr.) (Figure 3). Furthermore, the clusters within the right and left insula reflected amplified activation to negative feedback in OCD patients (Figure 3). In addition, a cluster within the MCC also resulted from patients' elevated activation in response to negative feedback as compared to positive feedback, while controls showed the opposite trend (Figure 3). There was no increased activation in controls compared to patients for this contrast.

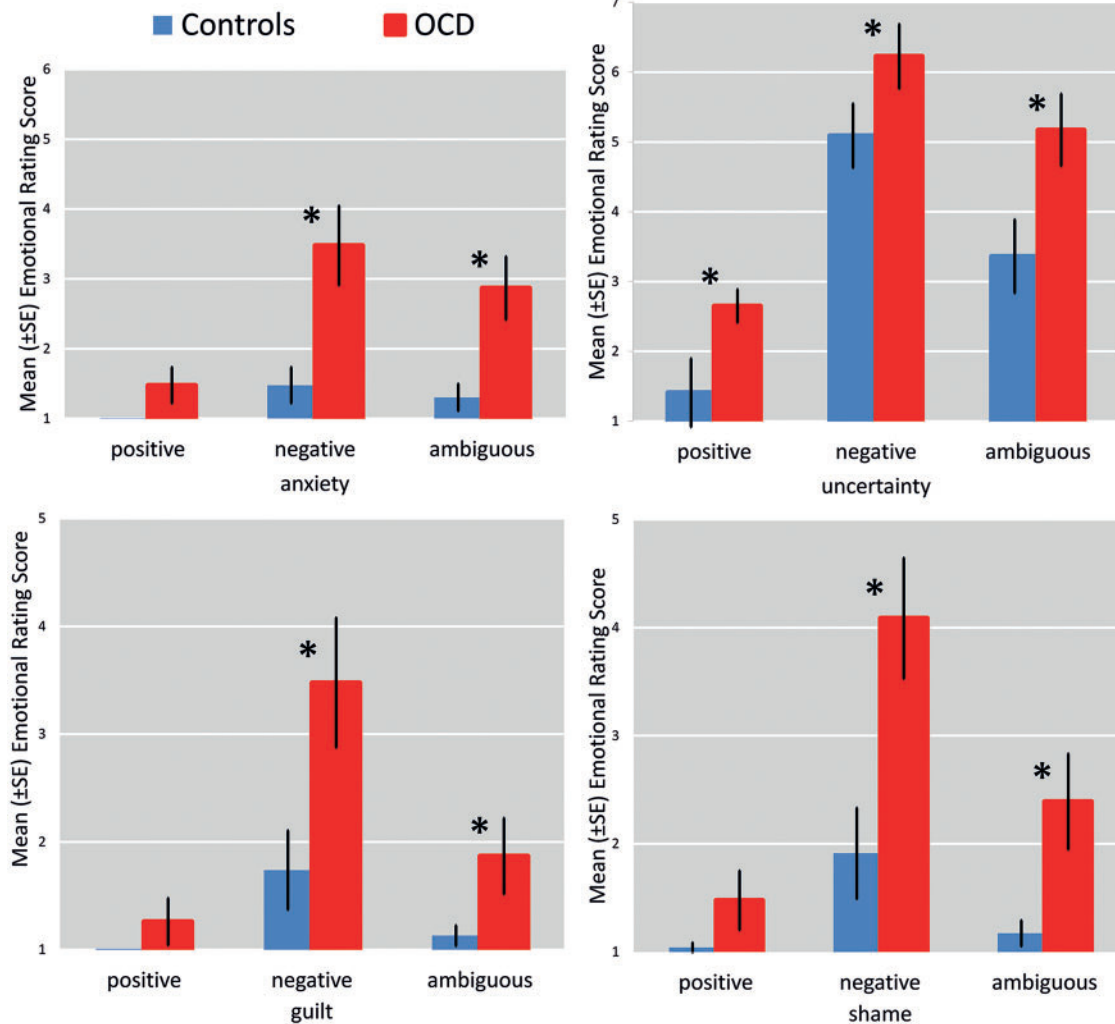


Fig. 2 Post-experimental ratings of anxiety, uncertainty, shame and guilt in OCD patients and controls for positive, negative and ambiguous feedback.

Ambiguous vs positive

For the contrast ambiguous > positive feedback, the insular cortex showed significantly stronger bilateral activation in OCD patients relative to controls. Between-group activation differences in the left insular cortex were due to increased activation to ambiguous feedback, an effect which was similar to findings for negative vs positive feedback (Figure 4; Table 2).

Controls showed for this contrast increased activation in VMPFC as compared to patients. This was due to increased activation to ambiguous as compared to positive feedback in controls ($P < 0.05$, corr.) and lack of a significantly differential response in patients ($P > 0.05$, corr.).

Ambiguous vs negative

The contrast ambiguous feedback > negative feedback yielded no areas with significantly increased activation in patients as compared to controls. However, controls showed increased responses within VMPFC and in the right putamen. Both clusters reflected reduced differential activation to ambiguous vs negative feedback in patients, while controls showed generally amplified activation to ambiguous vs negative feedback (Figure 4; Table 2).

We found no differences between medicated and unmedicated patients for any of the peak effects described above, except for the putamen cluster identified by the contrast ambiguous > negative feedback. At this location, unmedicated patients showed increased

activation compared to medicated patients ($P < 0.05$, corr.). Further, we used criterion cut-off scores presented by Gonner *et al.* (2009) for the six OCI-R subscales (see also Table 1) in order to divide OCD patients in subgroups according to their main symptom domains and tested the main contrasts as described above for differences between these subgroups within our ROIs. No differences between these subgroups could be obtained from the resulting volume maps fully corrected for the number of tests performed.

DISCUSSION

We investigated emotional responses and brain activation to positive and negative valid as well as ambiguous performance feedback in OCD patients and healthy control subjects. Negative and ambiguous feedback led to increased ratings of anxiety, guilt and shame in patients as compared to controls. Both negative and ambiguous feedback relative to positive feedback induced increased activation in the insular cortex in OCD. Furthermore, negative vs positive feedback was associated with increased brain activation in MCC. In contrast to healthy control subjects, patients showed no differential activation to negative vs positive feedback in the putamen and to ambiguous vs valid feedback in the VMPFC.

The emotional rating data suggest that OCD patients exhibit increased aversive emotional responses to negative as well as to ambiguous feedback. Moreover, this rating pattern was not only found for

Table 2 Significant between-groups differences in activation for the three contrasts of interest

Region	Lateralization	Talairach coordinates			T scores	Cluster size (mm ³)	Talairach coordinates			T scores	Cluster size (mm ³)
		x	y	z			x	y	z		
OCD > Controls											
Negative feedback > positive feedback											
Insula	R	32	-11	16	3.57	2538					
	L	-39	-10	22	3.41	243					
Putamen/caudatum	R	32	-4	5	5.16	1431					
Midcingulate cortex	R	13	9	32	3.37	378					
Ambiguous feedback > Positive feedback											
Insula	R	39	-1	7	2.84	135					
	L	-41	-7	20	3.01	216					
Controls > OCD											
Ambiguous feedback > Negative feedback											
Ventromedial prefrontal cortex	L/R	0	65	-2	3.27	405					
Ventromedial prefrontal cortex	L	-3	62	-2	3.28	2457					
Putamen/caudatum	R	24	-10	-3	4.28	189					

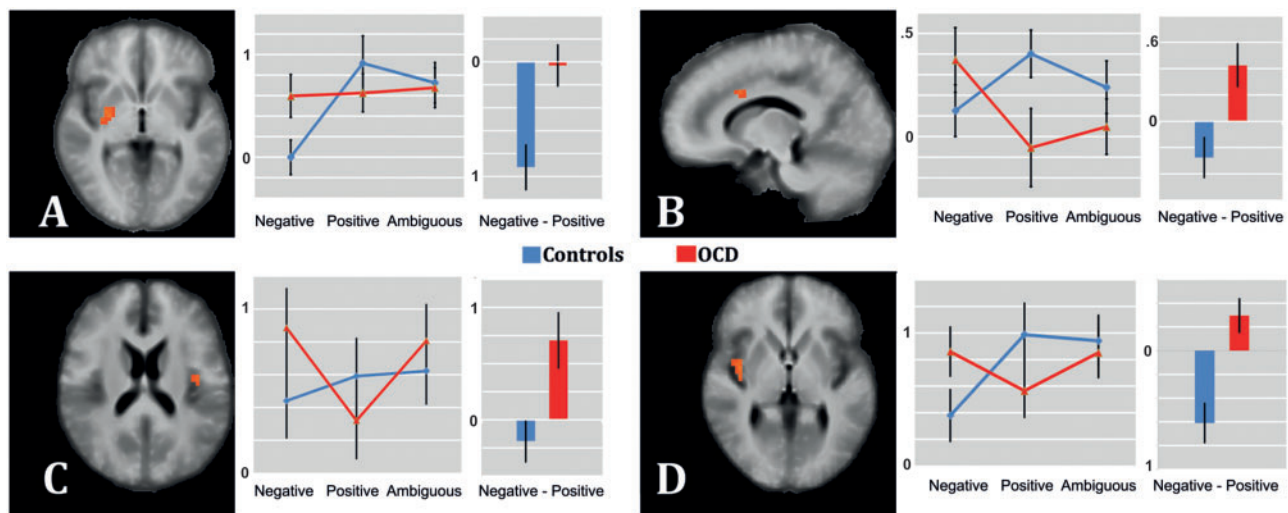


Fig. 3 Between-groups differences in activation to negative relative to positive feedback. Significant activation differences between OCD and controls in putamen (A; z = 1), MCC (B; x = 10), left (C; z = 4) and right insula (D; z = 17) are shown. Images are in radiological convention. OCD (red) and control group (blue) parameter estimates are shown group-wise for each condition (left) and contrast with ordinates' scales indicating parameter estimates.

anxiety but also for shame and guilt ratings, emotions whose role in the etiology of OCD has repeatedly been emphasized. Specifically, feelings of guilt (Mancini and Gangemi, 2004) and shame (Fergus *et al.*, 2010) have been strongly linked to a pathological inflation of responsibility obsessions. In OCD, dysfunctional beliefs about uncertainty have been hypothesized as one of several contributing factors in the pathogenesis of anxiety and indecisiveness (Salkovskis *et al.*, 1999; Coles *et al.*, 2005). Cognitions in OCD are at least in part characterized by patients' heightened insecurity and excruciating doubt about the implications of self-appraised and usually egodystonic thought-contents. In consequence, those individuals are likely to develop cognitive styles within which ambiguity, ambivalence and unpredictability appear threatening and unbearable and call for immediate resolution by application of lucid rules.

Paralleling the patterns of emotional ratings, we detected increased insular cortex activation during negative and ambiguous feedback as compared to positive feedback in OCD patients. In recent years, the role of the insular cortex in homeostatic integration, interoception and

emotional perception has been explored (Craig, 2009; Paulus and Stein, 2010). Activation of the insular cortex has been broadly reported in the context of negative and aversive emotional experiences and has been hypothesized to play a key role in linking belief systems to perceptions of internal states (Paulus and Stein, 2010). Consequently, functional alterations of the insula are assumed to contribute to manifestations of anxiety disorders, where valence and meaning of spontaneously fluctuating bodily signals are often misinterpreted to indicate threatening and anxiety-provoking deviations from a homeostatic equilibrium.

Furthermore, we also observed that controls showed increased activation to positive vs negative feedback in the putamen, while OCD patients showed similar activations to the different kinds of feedback. Remarkably, a coordinate-based meta-analysis of fMRI activation differences between OCD patients and controls has localized the most prominent cluster of between-group differences in BOLD-R within the putamen (Menzies *et al.*, 2008), which seems to be in accordance with classical neural models of OCD. Next to its role in the selection,

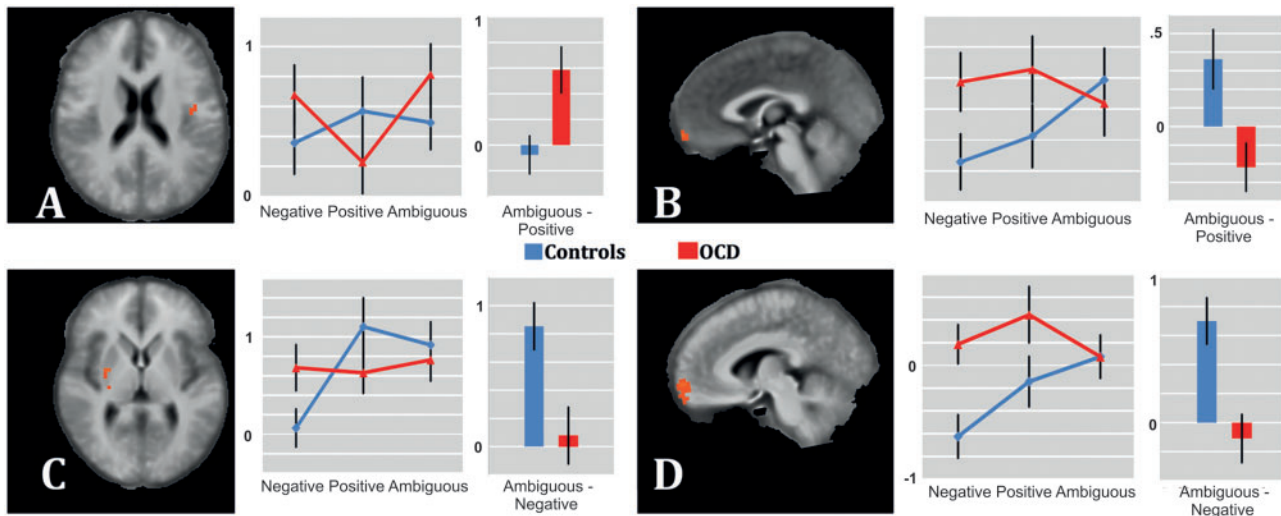


Fig. 4 Between-groups differences in activation to ambiguous relative to negative feedback and ambiguous relative to positive feedback. Significant activation differences between OCD and controls in left insula (A; $z = 20$), vmPFC (B; $\chi = -1$; and D; $\chi = -6$) and putamen (C; $z = 5$) are shown. Images are in radiological convention. OCD (red) and control group (blue) parameter estimates are shown group-wise for each condition (left) and contrast with ordinates' scales indicating parameter estimates.

execution and evaluation of motor programs, the putamen features prominently in cognitive and motivational theories. It has been implied in the anticipation and evaluation of reward-related feedback, particularly in elicitation of a neural response to reward prediction errors (Haruno and Kawato, 2006). The putamen has been suggested to be important for integration of stimulus–action–reward associations (Haruno and Kawato, 2006) and might mediate action selection by computing and evaluating their values in terms of sensory contexts and rewards. Therefore, the lack of a differential response of the putamen in OCD patients to different kinds of feedback could indicate insensitivity to action outcomes in the context of future action selection. Accounts that activation of the putamen has been shown to track differences in the flexibility of motor learning (Schonberg *et al.*, 2007) and appears to be involved in categorization learning (Daniel and Pollmann, 2010) lend further credence to this interpretation.

In the VMPFC we observed that healthy controls showed a clear differentiation between feedback types with highest activation to ambiguous and lowest activation to negative feedback. This differentiation was absent in OCD patients. Patients showed no difference between negative and ambiguous feedback. Next to its role in the default network (Buckner *et al.*, 2008), the VMPFC has been implicated in a broad range of valuation paradigms (Grabenhorst and Rolls, 2011), most notably in the processing of subjective stimulus values (Hare *et al.*, 2011), especially under ambiguity (Levy *et al.*, 2010) or uncertainty about current expectations (Rushworth and Behrens, 2008). While the exact parcellation of the VMPFC and the respective functional roles are still being discussed (Kringelbach, 2005), studies generally report changes in specific aspects of emotional and behavioral regulation. Seminal neuropsychological findings in humans suggest that lesions of the VMPFC attenuate the contribution of internally generated goals to behavioral adaptation and make the organism more susceptible to information conveyed by external stimuli as indicated by a compulsive execution of the actions elicited by these stimuli (Bechara *et al.*, 1994; Rudebeck *et al.*, 2008). Located at the confluence of information coding context-specific reward properties, the VMPFC of healthy subjects would be in a key position to identify the emotional and behavioral values of stimuli which indicate an absence of action-relevant information.

A specifically increased response was also found in MCC during negative feedback relative to positive feedback in OCD. Brain imaging

studies on error processing have strongly emphasized the role of the MCC in hyperactive performance monitoring in OCD (Saxena *et al.*, 2009). Enhanced activation of this region during negative feedback presentation is in line with interpretations of increased monitoring of negative outcomes in OCD and can be assumed to be closely linked to OCD psychopathology (Schlosser *et al.*, 2010). Thus, excessive error signals generated by MCC may explain OCD patients' characteristic feeling that something is wrong and that a certain behavioral change is needed to correct the problem. As a consequence, exaggerated MCC activation in response to negative feedback or error commission may constitute the neural basis of a wide range of compulsive behaviors (e.g. repeated checking or exaggerated fear of committing an error).

In conclusion, we found significant alterations in the functional neuroanatomy of OCD patients during feedback processing. Findings indicate that both negative and ambiguous performance feedbacks are associated with abnormal negative emotions and changed brain activation, in particular increased insula activation, while activation in the putamen and VMPFC lacks the normal differential responses depending on feedback type in OCD patients.

Conflict of Interest

None declared.

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