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Performance monitoring in obsessive-compulsive disorder

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Abstract

Obsessive-compulsive disorder (OCD) is associated with hyperactivity of brain structures involved in performance monitoring. It has been proposed that this pathophysiology results in the generation of inappropriate or excessive internal error signals, giving rise to the characteristic symptoms of OCD. We measured an electrophysiological correlate of performance monitoring, error-related negativity (ERN), to study whether OCD patients exhibit enhanced brain activity associated with errors and negative performance feedback. We found that OCD patients (n=16) and healthy control participants (n=16) did not differ in the amplitude of the ERN associated with errors and negative feedback in a probabilistic learning task. The discrepancy between these results and the results from previous studies is discussed.
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1. Introduction

Obsessive-compulsive disorder (OCD) is a psychiatric condition characterized by recurrent, intrusive and unwanted thoughts and an urge to perform repetitive, ritualistic behaviors to relieve the distress caused by these obsessions. Compulsive behaviors, such as excessive hand washing, ritualistic counting or checking, can be highly time-consuming, interfering with normal psychosocial functioning (American Psychiatric Association, 1994). Here we report the results of an electrophysiological study designed to replicate and extend previous studies suggesting that a critical aspect of this illness may be an overactive mediofrontal action-monitoring system (Gehring et al., 2000; Johannes et al., 2001; Hajcak and Simons, 2002; Ursu et al., 2003).

These previous studies were inspired by an intriguing proposal regarding the neurobiological and functional basis of OCD (Pitman, 1987; Schwartz, 1997). According to this proposal, OCD is charac-

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terized by the generation of inappropriate or hyperactive error-detection signals, manifesting phenomenologically as a feeling that "something is wrong", and thus giving rise to the urge for correction typically observed in OCD. These error-detection signals are thought to be generated by an internal monitoring system when external stimuli or actions are in conflict with the person's goals or representation of the correct action. Two types of observations support the proposal that excessive error-detection activity is a critical aspect of OCD. First, it is consistent with the symptoms of OCD and, in particular, the patients' constant feeling of erroneous or incomplete performance. Second, neuroimaging studies have found that OCD patients exhibit excessive activity of brain structures thought to be associated with performance monitoring, in particular the anterior cingulate cortex, orbitofrontal cortex and structures of the basal ganglia (Carter et al., 1998; Saxena et al., 1998; Swedo et al., 1989; Holroyd and Coles, 2002; Van der Wee et al., 2003).

As an initial test of this hypothesis, Gehring et al. (2000) investigated whether patients with OCD exhibit enhanced electrophysiological brain activity associated with response errors in a speeded two-choice response task. They found that OCD patients show an increased error-related negativity (ERN), a negative-polarity brain potential that peaks approximately 80 ms following incorrect responses (for reviews, see Falkenstein et al., 2000; Holroyd et al., 2004a; Yeung et al., 2004). The ERN has a frontocentral distribution over the scalp, consistent with a generator in or near anterior cingulate cortex (Holroyd et al., 1998; Herrmann et al., 2004). Gehring and colleagues also reported a significant relationship between the patients' ERN magnitude and symptom severity, lending further support to the hypothesis that OCD is characterized by excessive brain activity associated with performance monitoring. Johannes et al. (2001) confirmed the finding of increased ERN amplitudes in OCD patients.

In a subsequent study on obsessive-compulsive undergraduate students, Hajcak and Simons (2002) found increased ERN-like deflections on both error and correct trials. The authors interpreted these data as consistent with OCD symptoms—that is, patients with OCD engage in excessive action monitoring even when an action has been performed correctly. Further support for the generality of excessive action monitoring in OCD comes from a recent functional magnetic resonance imaging study that reported increased anterior cingulate activation in OCD patients in relation to both errors and correct trials high in response conflict (Ursu et al., 2003). Accordingly, although there is a fair amount of support for the notion that OCD is associated with abnormal neurophysiological markers of action monitoring, the precise nature of this abnormality requires further study.

An additional aim of the present study was to investigate brain activity associated with the valence of performance feedback (i.e., positive or negative) in patients with OCD. Recent research has identified an electrophysiological correlate of medial frontal cortex activity in response to feedback: a negative-polarity frontocentrally distributed scalp potential, peaking roughly 250 ms following the feedback, that is more pronounced for unfavorable outcomes than for favorable outcomes (e.g., Miltner et al., 1997; Nieuwenhuis et al., 2004b; for review, see Nieuwenhuis et al., 2004a). The similarity of this brain potential to the response-related ERN has led several groups to suggest that these two components are manifestations of the same functional and neural system for performance monitoring (e.g., Miltner et al., 1997; Holroyd and Coles, 2002). More specifically, Holroyd and Coles (2002) have suggested that both the response ERN and feedback ERN reflect a reward-prediction error signal that indicates that ongoing events are going worse than anticipated (e.g., in case of a response error or unpredicted negative feedback). According to Holroyd and Coles, reward-prediction error signals are computed by the basal ganglia and conveyed by the midbrain dopamine system to the anterior cingulate cortex, where they are used to reinforce behaviors. The ERN reflects the dopaminergic modulation of anterior cingulate activity, volume-conducted to the scalp. In light of the evidence that both the anterior cingulate cortex and basal ganglia are involved in the pathophysiology of OCD, it stands to reason that both the response ERN and feedback ERN should be enhanced in OCD. However, no studies to date have evaluated the feedback ERN in patients with OCD.

To further address the relationship between performance monitoring and OCD, we used a probabilistic learning task previously employed to investigate

brain activity associated with both response errors and performance feedback (Holroyd and Coles, 2002; Nieuwenhuis et al., 2002; Holroyd et al., 2004b). In this task, participants were required to press one of two buttons in response to each of a series of stimuli. The participants were told to infer the stimulus-response mappings by trial-and-error, using the information provided by a positive or negative feedback stimulus presented at the end of each trial. A critical aspect of the task was that the six possible stimuli differed in the degree to which the response was predictive of the value of the feedback (50%, 80% or 100%). Thus, for some stimuli, the value of the feedback was uncorrelated with the selected response, whereas for other stimuli the participant could, to varying degrees, learn to control the value of the feedback by acquiring the stimulus-response mapping.

Previous research has demonstrated that, in this task, the ERN is elicited by the earliest predictor of negative outcome (Holroyd and Coles, 2002; Nieuwenhuis et al., 2002). Thus, feedback ERNs are elicited when the negative feedback stimulus itself is not (or only partly) predicted by earlier events. For example, when the stimulus-response mappings have not yet been learned, the feedback cannot be predicted on the basis of the response; in such cases, feedback ERNs are elicited by negative feedback. However, as the participant gradually learns the mappings, the ERN "propagates back in time" and is elicited as soon as an incorrect response is executed. These results are consistent with the theory that the ERN reflects a reward-prediction error signal (Holroyd and Coles, 2002). As further evidence for this theory, it has been found that ERN amplitude scales with the size of the prediction error, being largest if ongoing events are suddenly worse than expected (e.g., negative feedback to a response that is usually associated with positive feedback; e.g., Holroyd et al., 2003).

We had no specific expectations about whether the predicted group effect on ERN amplitudes would differ between the various task conditions (i.e., the type of stimulus-response mapping). However, any group by condition interactions that we might obtain would be helpful in putting constraints on possible explanations for increased ERN amplitudes in OCD patients. Furthermore, although the reward-prediction theory of Holroyd and Coles (2002) would seem to predict faster learning of stimulus-response mappings in case of increased ERN amplitudes, increased ERN signals in OCD are probably dysfunctional and unlikely to lead to better task performance. Moreover, we are not aware of any literature that would suggest that OCD is characterized by improved associative learning.

To summarize, in the present study, we recorded the event-related potentials (ERPs) associated with errors and negative feedback from a group of OCD patients and a group of healthy control participants performing a probabilistic learning task. One major aim was to verify whether we could replicate previous findings of an enhanced response ERN in OCD patients. The second major aim was to determine whether OCD would also be associated with an enhanced feedback ERN. Evidence addressing these questions would provide important clues about performance-monitoring dysfunction in OCD.

2. Methods

2.1. Participants

Sixteen adult patients and 16 healthy adults participated in the experiment. Details about the composition of the two groups are provided in Table 1. The patients were all diagnosed as having OCD according to DSM-IV criteria (American Psychiatric Association, 1994). This diagnosis was confirmed around the time of testing using the Structured Clinical Interview for DSM-IV Axis I Disorders (SCID-I/P; administered by M.N.). In addition, OCD symptom severity was assessed with the Yale-Brown Obsessive-Compulsive Scale (YBOCS; Goodman et al., 1989). Ten of the patients were medicated at the time of the study (see Table 1 for details). Four OCD patients received psychotherapy around the time of testing (3 cognitive therapy, 1 behavioral therapy). Average age of onset of OCD symptoms was 13.8 years. The healthy adults served as a control group and were carefully matched with the patients with respect to age, education and sex. Both groups completed the Hamilton Rating Scale for Depression (HRSD; Hamilton, 1960). Study exclusion criteria were (i) history of a psychotic episode, (ii) systemic or neurological illness, (iii) head injury, and (iv) alcohol

Table 1
Group characteristics of the obsessive-compulsive disorder (OCD) group and the control group

Characteristics	Group	
	OCD group[a,b]	Control group
Number of males, females	6, 10	6, 10
Age (years)	30.9 (8.5; 21–49)	30.9 (7.6; 20–42)
Education[c]	4.3 (0.4; 4–5)	4.6 (0.6; 4–6)
Handedness (right, left)	14, 2	14, 2
HRSD[d]	9.0 (5.5; 0–19)	2.0 (1.5; 0–5)
YBOCS (total)[d]	19.6 (6.3; 8–29)	–
YBOCS (obsessions)	10.2 (3.2; 4–15)	–
YBOCS (compulsions)	9.3 (4.6; 0–15)	–

Group means are reported, with standard deviation and range in parentheses. HRSD=Hamilton Rating Scale for Depression. YBOCS=Yale-Brown Obsessive-Compulsive Scale.

[a] Ten patients were medicated: 9 were using various antidepressants, mostly selective serotonin reuptake inhibitors (SSRIs): paroxetine (5), clomipramine (1), citalopram (1), fluvoxamine (1) and venlafaxine (1). One patient used clonazepam, a benzodiazepine.

[b] Consistent with the heterogeneity of OCD, a number of OCD symptom types were represented in the patient group. Obsessions: aggressive (5), contamination (1), somatic (1), 'need-to-know' (2) and mixed (6) (i.e., aggressive with somatic, contamination and/or sexual obsessions). Compulsions: repeating (1), washing (2), repeating and washing (1), checking in combination with ordering, washing and/or repeating (10). Note that the number of participants was too small to allow for meaningful comparisons between the subgroups.

[c] Since the Dutch educational system differentiates after primary school, a coding system in terms of years of education was somewhat inappropriate. Instead, we coded the level of education ranging from 1 (primary school) to 7 (university or graduate school).

[d] Higher scores on the YBOCS and HRSD are indicative of more OCD and depressive symptoms. Maximum score on the YBOCS is 40 (20 for obsessions and 20 for compulsions). Maximum score on the HRSD-17 is 52. A score of 16 is often used as a cutoff, as scores of 16 or higher make the presence of a depression disorder likely.

or substance abuse. All participants provided written informed consent prior to their inclusion in the study, and the experiment was approved by the local research ethics panel. In addition to a fixed payment of €25, all participants received a performance-related bonus, as described below.

2.2. Stimuli

Stimuli were presented in color against a white background on a computer screen placed at a distance of 100 cm from the participant. Each experimental block involved a new set of six imperative stimuli. These stimuli were images of buildings, animals, musical instruments, etc. Images of a head of lettuce and of a carrot served as feedback stimuli indicating to participants that they were rewarded or penalized on that trial. The mappings between reward/punishment and the feedback stimuli were counterbalanced across participants and kept fixed across the experiment. A different feedback stimulus, an image of a cherry, was presented in case a response deadline was missed. All stimuli were part of a public Corel image library and were scaled to a uniform size so that they subtended approximately $5.2^\circ \times 5.2^\circ$ of visual angle.

2.3. Design and procedure

On each trial, the stimulus events consisted of the presentation of an imperative stimulus for 500 ms, followed by a blank screen for 500 ms, followed by the presentation of a feedback stimulus for 500 ms, followed by a blank screen for 500 ms. Thus, the interval between consecutive imperative stimuli was 2 s. Participants were required to make a two-choice decision by pressing one of two buttons within 700 ms after the onset of the imperative stimulus. The response deadline was introduced to ensure that participants made some errors due to premature responding in the 100% mappings even after the mappings had been learned. If a response exceeded the deadline, the cherry stimulus communicated to the participants that they were penalized 2 eurocents on that trial, providing motivation for them to respond more quickly. Otherwise, the feedback stimulus indicated to the participants that they had either earned or were penalized 1 eurocent of bonus money on that trial.

Participants were not informed about the appropriate stimulus-response mappings but were told to infer these mappings by trial and error and to respond in such a way as to increase their bonus by as much as possible. In each block, one of the six stimuli was mapped to the left button, so that participants were rewarded if they pressed the left button and penalized if they pressed the right button. Another stimulus was mapped to the right button in a similar fashion. Following Holroyd and Coles (2002), we refer to these mappings as the 100% condition. For two other

stimuli, feedback was delivered randomly, irrespective of the given response. As a result, participants were rewarded on 50% of the trials and penalized on 50% of the trials, and these mappings are therefore called the 50% condition. Following the same logic, the two remaining stimuli were associated with an 80% condition. That is, one stimulus required a left button press on 80% of the trials (referred to as valid trials) and a right button press on 20% of the trials (invalid trials), and the other stimulus required a right button press on 80% of the trials (valid) and a left button press on 20% of the trials (invalid). We also examined how performance and ERN amplitudes changed over the course of a block of trials. We analyzed such learning effects by comparing the dependent variables in the first and second half of each block.

The experiment involved five blocks of 300 trials each. Each of the six stimuli was presented 50 times in a random order in each block. Valid and invalid trials from the 80% condition were randomly intermixed, the only restriction being that the first 25 trials with each of the two stimuli contained five invalid trials. Before the experimental phase, participants received written instructions and performed one practice block of 150 trials. Before each experimental block, participants were given the opportunity to study the six imperative stimuli used in the upcoming block and to press a key to start the block when ready. At the end of each block, participants were informed about the total amount of bonus money they had earned throughout the experiment. Participants began the experiment with a bonus of €1.

2.4. Psychophysiological recording and data analysis

We recorded the EEG using Ag/AgCl electrodes embedded in a fabric cap (Electro-Cap International), arranged according to the 10–20 system: FP1, FP2, F7, F3, Fz, F4, F8, FT7, FC3, FCz, FC4, FT8, T7, C3, Cz, C4, T8, TP7, CP3, CPz, CP4, TP8, P7, P3, Pz, P4, P8, O1 and O2. During recording, all EEG electrodes were referenced to an electrode placed on the left mastoid. During offline analysis, all signals were re-referenced to linked-mastoid electrodes. The electro-oculogram (EOG) was recorded from electrodes placed above and below the left eye, and from electrodes placed on the outer canthi of each eye. All electrode impedances were kept below 10 kΩ. The EEG signals were amplified (Synamps, bandpass filter 0.1–70 Hz) and digitized at 250 Hz.

Single-trial epochs were extracted offline for a period from 200 ms before until 800 ms after the critical event. Standard Neuroscan (Neurosoft, Sterling VA, USA) analysis procedures were used to correct for EOG artifacts (using the algorithm described in Semlitsch et al., 1986) and to discard trials with recording artifacts (absolute signal value >75 μV; 2.0% for the patient group and 0.9% for the control group). Then, for each participant and each condition, the EEG epochs were averaged with respect to response onset and feedback onset to obtain response-locked and feedback-locked ERPs. A baseline, computed as the average signal activity across the 200 ms prior to the critical event, was subtracted for each ERP. The resulting ERP waveforms were low-pass-filtered (<12 Hz, 48 dB/oct, zero-phase shift). Following previous studies using this paradigm (Holroyd and Coles, 2002; Nieuwenhuis et al., 2002), difference waveforms were created by subtracting the signal elicited on trials with positive feedback from the signal elicited on trials with negative feedback. The scalp distributions of the response ERN and feedback ERN in the difference waveforms showed a typical frontocentral midline focus, and were highly similar for the two groups. The amplitude of the response ERN was defined as the peak negativity of the difference waveform at electrode Cz (where the component had its maximum amplitude) in a window 0–150 ms following the response. The amplitude of the feedback ERN was defined as the peak negativity of the difference waveform at electrode Cz in a window 200–350 ms following feedback onset. Given the potential pitfalls of using difference waves (Van Boxtel, 2004), we confirmed that the same qualitative pattern of results was obtained when the feedback ERN was measured (as a base-to-peak difference) and compared in the separate waveforms associated with correct and incorrect trials. Trials in which no response was generated before the 700-ms deadline were discarded: 2.1% for the patient group and 1.3% for the control group. The average number of remaining trials in each cell of the factorial design is indicated in Table 2. With one notable exception (positive feedback in the 80% invalid condition; see Section 3), the average number of trials contributing to each ERP was larger than 30. Performance

Table 2
Response accuracy and number of trials as a function of group, condition and block half

Condition	Group			
	OCD		Control	
	% Correct	Nr trials	% Correct	Nr trials
100%	74 (9)/79 (11)	245/236	75 (9)/82 (9)	243/239
80% valid	66 (10)/74 (12)	189/193	68 (10)/75 (11)	191/194
50%	50 (3)/50 (4)	241/240	51 (4)/51 (3)	242/237
80% invalid	30 (9)/25 (14)	48/48	30 (11)/25 (11)	48/48

Numbers indicate values in the first/second block half, averaged across trial blocks. Standard deviations are indicated in parentheses. Nr trials=total number of trials included in the ERP analyses.

measures, response-ERN and feedback-ERN amplitudes for each participant were submitted to separate mixed analyses of variance (ANOVAs) with participant group (OCD, control) as the between-subject factor, and condition (100%, 80% valid, 50% and 80% invalid mappings) and block half (trials 1–150, trials 151–300 of each block) as within-subject factors. The Greenhouse–Geisser correction for violations of the ANOVA assumption of sphericity was applied where appropriate.

3. Results

3.1. Behavioral results

Fig. 1A shows behavioral accuracy for individuals with OCD and control participants for each condition, averaged across the first and second halves of each block. The lower-than-chance performance in the 80% invalid condition indicates that participants responded mostly according to the dominant (but here incorrect) mapping. As expected, accuracy differed significantly across conditions, $F(3,90)=174.9$, $P<0.001$. In addition, participants' overall response accuracy improved in the second block half compared with the first block half, $F(1,30)=35.5$, $P<0.001$ (see Table 2). This was due to gradual learning of the stimulus-response mappings in the 100% condition and the 80% condition. In contrast, because participants gradually learned the dominant 80% mapping, response accuracy in the 80% invalid condition decreased as a function of block half. The interaction between condition and block half was highly significant, $F(3,90)=21.2$, $P<0.001$. Errors were associated with significantly faster reaction times than correct responses in the 100% condition (382 ms vs. 427 ms) and in the 80% condition (403 ms vs. 428 ms) but, as expected, not in the 50% condition, resulting in a significant interaction between accuracy and condi-

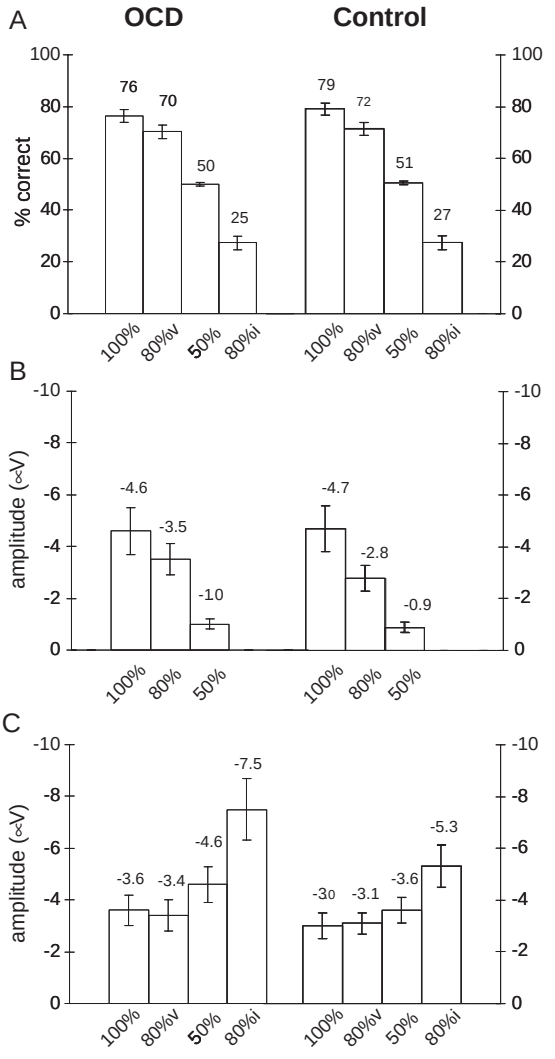

Fig. 1. Average behavioral and ERP results as a function of condition for the OCD group (left panel) and control group (right panel). (A) Response accuracy. (B) Response-locked and (C) feedback-locked ERN amplitudes. Amplitudes reflect the subtraction of amplitude magnitudes associated with negative and positive feedback (see text for more detail). Error bars reflect standard error of the mean. 80%v=80% valid condition; 80%i=80% invalid condition.

tion, $F(3,90)=38.6$, $P<0.001$. Overall, the OCD group was slightly less accurate than the control group, but this difference was not significant, $F(1,30)=1.3$, $P=0.26$. Also, there was no interaction between group and condition or block half, both Fs<1. Similarly, OCD patients responded slightly faster than controls (413 ms vs. 417 ms), but neither the main effect of group nor any of the interaction terms involving group were significant, all Fs<1.

3.2. ERN amplitude

Fig. 2 shows illustrative ERPs, associated with positive and negative feedback for both participant groups and averaged across participants and block halves. Fig. 2A shows the ERNs elicited by the response in the 100% condition, the condition in which the response ERN is largest for both participant groups. Fig. 2B shows the response ERNs in the 80% valid condition. The response ERN is evident as a clear negativity peaking about 60 ms after the response. Fig. 2C shows feedback ERNs in the 50% condition, the only condition in which feedback is not dependent on the given response. In this condition, the ERN is duly elicited primarily by the feedback. In both groups, the feedback ERN peaked roughly 250 ms after the presentation of a negative feedback stimulus. Finally, Fig. 2D shows feedback ERNs in the 80% invalid condition, in which a clear expectancy about the correct response is violated. It should be noted that the average number of trials contributing to the positive feedback ERPs in the 80% invalid condition was small in both groups: 14 and 12 for the first and second block halves, respectively. Because the peak amplitude of ERP components may be increased for small numbers of contributing trials (Polich, 1986), it is possible that the amplitudes of the negativities associated with positive feedback are overestimated.

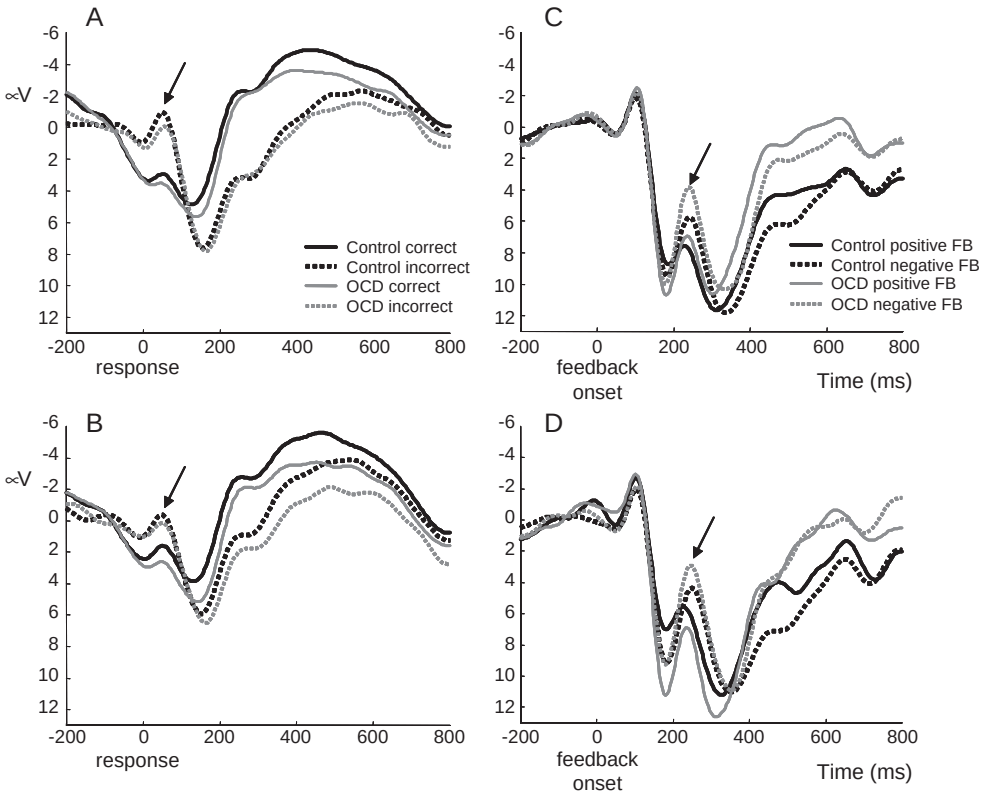

Fig. 2. Grand-average ERP waveforms for the OCD group and the control group from four conditions: The ERN elicited by the response in the 100% condition (A) and the 80% condition (B), and the ERN elicited by the feedback in the 50% condition (C) and 80% invalid condition (D). Waveforms were recorded from Cz where the ERN was largest. Arrows point to the peak of the ERN. FB=feedback.

Fig. 1B shows response-ERN amplitudes as a function of participant group and condition. Note that valid and invalid trials from the 80% condition were pooled, because for the participants these were not distinguishable until the presentation of the feedback stimulus. Note also that the "true" response ERN in the 50% condition should be absent. The negative values reported for this condition in Fig. 1B reflect unsystematic fluctuations of the ERPs associated with negative and positive feedback. Response-ERN amplitudes were of similar amplitude for the two participant groups, $F(1,30)=0.1$, $P=0.73$. Consistent with Holroyd and Coles' (2002) theory, response-locked amplitudes increased with the probability of a correct response in a certain condition, $F(2,60)=29.6$, $P<0.001$, and with block half, $F(1,30)=12.5$, $P<0.005$. These two factors showed a significant interaction, $F(2,60)=8.2$, $P<0.005$. Group interacted significantly only with block half, $F(1,30)=5.0$, $P<0.05$, reflecting the finding that the increase with block half of response-ERN amplitude was more pronounced for the patient group than for the control group.

Fig. 1C shows feedback-ERN amplitudes as a function of participant group and condition. Here, the difference between valid and invalid trials from the 80% condition is clearly important; as predicted by Holroyd and Coles' (2002) theory, the largest feedback ERNs were observed in the 80% invalid condition in which a clear expectation of positive feedback was violated by the actual feedback (cf. Nieuwenhuis et al., 2002). Averaged across conditions, feedback-ERN amplitudes were numerically larger for the OCD patients (group difference = 1.0 μV), but this difference was not statistically reliable, $F(1,30)=2.8$, $P=0.11$. As expected, the main effect of condition was significant, $F(3,90)=10.5$, $P<0.005$, but this effect was of similar magnitude for the two participant groups, $F(3,90)=0.9$, $P=0.4$. Furthermore, post hoc contrasts (ANOVA) revealed that the numerical group differences in the 50% condition ($P=0.25$; see Fig. 2C) and the 80% invalid condition ($P=0.15$; Fig. 2D) were nonsignificant. None of the statistical terms involving block half were significant, all Ps > 0.2.

The number of participants in our experiment (i.e., 16 in both groups) was chosen such that our statistical tests would have high power (>90%) to detect group differences of the size reported in previous studies of the ERN in OCD (i.e., >2 μV; Gehring et al., 2000; Johannes et al., 2001). Contrary to our expectations, the observed main effect of group on feedback-ERN amplitude, although in the expected direction, was substantially smaller (i.e., 1.0 μV). We note that the use of post-experiment power calculations as a guide to interpret nonsignificant test results is inappropriate (e.g., Hoenig and Heisey, 2001). However, we ran simulations to determine the number of participants needed in future studies to detect the observed group difference of 1.0 μV. To detect an effect of this size with reasonable power (70%) and assuming the same intragroup variability as observed in the current study, at least 28 participants per group will be needed.

3.3. Relationship between ERN amplitude, OCD symptom severity, depressive symptoms and medication

We computed correlations between the patients' symptom severity, as assessed by the YBOCS, and their ERN amplitudes in the conditions in which these were largest. YBOCS scores exhibited a nonsignificant positive correlation with response-ERN amplitude in the 100% condition (Pearson's $r=0.35$, $P=0.18$), indicating smaller ERNs for patients with more severe symptoms. In contrast, YBOCS scores exhibited negative correlations with feedback-ERN amplitude in the 50% condition ($r=-0.31$, $P=0.24$) and 80% invalid condition ($r=-0.49$, $P=0.055$), indicating somewhat larger ERNs for patients with more severe symptoms.

To examine the relationship between symptom severity and ERN amplitude in more detail, we performed a median split on the basis of YBOCS scores and compared ERN amplitudes for the "mild" and "severe" OCD group (average YBOCS scores were 14.6 and 24.6, respectively). Because of the limited number of patients in each subgroup ($n=8$), we conducted no statistical tests; the comparisons were made on a purely exploratory basis. The two subgroups differed in a number of respects. First, depressive symptoms, as assessed by the HRSD, were more pronounced in the severe OCD group than in the mild OCD group (11.5 vs. 6.5). Indeed, there was a large and significant correlation between the patients' YBOCS scores and depressive symptoms ($r=0.70$,

$P<0.01$). Second, the mild OCD group performed better than the severe OCD group (80% vs. 73% correct in the 100% condition; 73% vs. 68% correct in the 80% condition). And third, the mild OCD group exhibited larger response ERNs but smaller feedback ERNs than the severe OCD group (e.g., group differences of 2.2 μV and 1.2 μV for the response ERN in the 100% and 80% conditions; and group differences of 0.6 μV and 3.8 μV for the feedback ERN in the 50% and 80% invalid conditions). We note that this pattern of ERN results is consistent with the finding that the mild OCD group had learned the stimulus-response mappings better than the severe OCD group (cf. Holroyd and Coles, 2002).

Finally, we looked at whether medicated patients ($n=10$; average YBOCS score=17.3; HRSD score=8.7) and unmedicated patients ($n=6$; YBOCS score=23.5; HRSD score=9.5) differed with respect to response-ERN and feedback-ERN amplitude. We found that the differences were small and that, if anything, ERN amplitudes were somewhat larger for medicated patients.

4. Discussion

A number of studies have examined the ERN, an electrophysiological correlate of performance monitoring, in various psychiatrically or neuropsychologically impaired populations (e.g., Kopp and Rist, 1999; Falkenstein et al., 2001; Mathalon et al., 2002). The general notion is that the study of the ERN and error-related behavior in such populations may be informative about the functional deficit underlying the specific cognitive and behavioral manifestations associated with each population. Here we studied the ERN associated with response errors and negative performance feedback in a group of patients with OCD. A major aim of this study was to evaluate the proposal that OCD is characterized by excessive error-detection activity in a brain circuit including the basal ganglia and anterior cingulate (Pitman, 1987; Schwartz, 1997), two brain structures thought to play a critical role in the generation of the ERN. Although we found a trend for larger feedback ERNs in the OCD group, this difference was not statistically reliable. Additionally, we did not find evidence for an enhanced response ERN in the OCD patients. Thus, in contrast to two previous studies (Gehring et al., 2000; Johannes et al., 2001), we did not find solid evidence suggesting action-monitoring abnormalities in patients with OCD.

A key question is why we did not replicate previous findings of an enhanced response ERN in OCD patients (Gehring et al., 2000; Johannes et al., 2001). Although there are obvious difficulties in interpreting null results, the task that we used has previously been shown to be sensitive to group differences in ERN amplitude (Nieuwenhuis et al., 2002), and contains two conditions in which substantial response ERNs have previously been observed, suggesting sufficient measurement space for observing group differences. Furthermore, the number of participants in our study was larger than in previous studies (i.e., 9 in the Gehring study, 10 in the Johannes study). Moreover, the patients in our study had more severe OCD symptoms, which–one would presume–should increase the effect size of any existing differences between the patient group and the control group. Nevertheless, the group effect size was essentially zero, especially in the 100% condition, suggesting that the null effect observed does not simply reflect a lack of statistical power. On the other hand, a potential limitation of our study compared with the study by Johannes et al. (but not the study of Gehring et al.) was that the majority of the patients were medicated. Not surprisingly, some psychopharmacological substances may significantly alter the amplitude of the ERN (De Bruijn et al., 2004). Although the number of patients was too small to allow a rigorous analysis of the effects of medication, a simple comparison indicated that, if anything, ERNs were generally somewhat smaller in unmedicated patients. Thus, despite the fact that some of the methodological aspects of our experiment created favorable conditions for revealing group differences, we did not find such differences.

An alternative explanation for the discrepancy between the current study and previous studies concerns the frequency of performance feedback. In the studies of Gehring et al. and Johannes et al., participants did not receive trial-to-trial feedback about their performance and were only given a summary of their performance at the end of each block of trials. Thus, participants had to rely on self-

monitoring to evaluate the accuracy of their responses. In contrast, in the current experiment, participants received feedback at the end of each trial. It is possible that the OCD patients experienced this as reassuring and considered the feedback as a "check" of their performance, potentially relieving some of the burden placed on the response-monitoring system. This may have somewhat reduced anxiety about the accuracy of their responses, which in turn may have led to smaller response ERNs (cf. Hajcak et al., 2003).

A second alternative interpretation concerns the relatively high average symptom severity of our OCD patients. In particular, an exploratory median-split analysis revealed smaller response-ERN amplitudes for a subgroup of patients with relatively severe OCD than for a subgroup with milder OCD symptoms. The mild OCD group had the same average YBOCS score as the patients tested by Gehring et al. (2000, average YBOCS=14.6). The analysis suggested two possible explanations of why the response ERN of the severe OCD group was reduced in amplitude. First, these patients had more pronounced symptoms of depression, and it has been reported that ERN magnitude varies with depression according to an inverted-U shape (Tucker et al., 2003). These findings suggest that depression may moderate the relationship between OCD severity and the ERN. Second, more severe patients showed relatively impaired performance on the probabilistic learning task. As shown in previous studies (Holroyd and Coles, 2002; Nieuwenhuis et al., 2002), impaired learning of the stimulus-response associations is reflected in smaller ERNs to the response (which is a less reliable predictor of reward) and larger ERNs to the feedback (which has increased predictive value). The empirical results are consistent with this conjecture. On a related note, Gehring et al.'s findings of an enhanced response ERN in OCD patients may, in part, be explained by their better task performance (cf. Yeung, 2004): The patients in Gehring et al.'s study responded more quickly than the control participants while making a similar number of errors.

Finally, it is worth noting that the response-ERN amplitudes observed in the current study were relatively small for both groups. This may be characteristic of the probabilistic learning task, in which error rates and uncertainty about the correct response are generally higher than is the case in the simpler two-alternative forced choice tasks used in previous research. The ERN is known to decrease with increasing uncertainty and error rates (cf. Falkenstein et al., 2000; Holroyd and Coles, 2002), and it is in principle possible that these factors may have affected the probability of detecting group differences in response-ERN amplitude. In this context, it is also noteworthy that the increase of response-ERN amplitudes with block half was more pronounced for the patient group than for the control group. These data suggest that a potential group difference in ERN amplitudes might have been revealed if the experiment had allowed further learning of the stimulus-response mappings to a level characteristic of simple choice reaction time tasks. Existing response-monitoring studies in OCD have utilized tasks in which the stimulus-response mappings are known from the outset. This raises the possibility that the response-monitoring system in OCD only becomes hyperactive once stimulus-response mappings are known.

Thus, several factors may be responsible for the discrepancy between the response-ERN results in the current study and in previous studies: The use of trial-to-trial feedback in the current experiment may have resulted in a decreased response ERN in OCD patients. Furthermore, although more systematic research is needed to investigate the relationship between OCD symptom severity and the ERN, the median-split analysis suggests that the current study might have found larger response ERNs in the overall OCD group if the average symptom severity had been comparable to the patients in the Gehring et al. (2000) study. Finally, the discrepancy may be due to differences between the tasks used in the various studies, another issue that can be addressed in future research.

The second key finding from our study is that we failed to detect a difference in the amplitude of the feedback ERN between individuals with OCD and healthy control participants. Of course, such a null result must be interpreted with caution. If a small difference in ERN amplitude existed between the two populations, our test may have lacked the sensitivity needed to reveal it. Indeed, the results indicated a weak trend towards larger feedback ERNs in the OCD group, especially in the patients with severe OCD symptoms. Interestingly, the patients' feedback ERN was particularly increased in the 80% invalid con-

dition in which a clear expectation of positive feedback was followed by negative feedback. It is possible that the emotional response to this negative expectation violation was stronger for the patient group. Follow-up electrophysiological studies and functional imaging studies are therefore needed to further evaluate the possibility of enhanced medial frontal cortex activity to unfavorable outcomes in OCD.

In sum, we found that OCD patients did not differ from healthy control participants in the amplitude of electrophysiological activity associated with errors and negative feedback. These results are partly inconsistent with previous research and cast doubt on the notion of hyperactive error signals in OCD (Pitman, 1987). In general, our study emphasizes the need for conducting and reporting research aimed at replicating between-group studies of the ERN, especially if this research involves psychiatrically or neuropsychologically impaired groups as heterogeneous as OCD.

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