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Emotional interference modulates performance monitoring in patients with obsessive–compulsive disorder

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ABSTRACT

Background: Enhanced performance monitoring in patients with obsessive–compulsive disorder (OCD), typically measured by error-related negativity (ERN), provides evidence for the fronto–striatal model of OCD. Here, we examined whether performance monitoring in OCD patients is modulated by emotional interference induced by task-irrelevant emotional stimuli.
Methods: A modified version of the flanker task with emotional face stimuli (fearful vs. neutral faces) was performed by 22 OCD patients and 22 healthy control subjects while electroencephalogram signals were recorded. Response-locked ERN was defined as the mean amplitude from 20 to 120 msec after the response.
Results: During trials with fearful face stimuli, OCD patients showed larger ERN amplitude than control subjects, but there was no difference between groups during trials with neutral face stimuli. Whereas OCD patients exhibited enhanced ERN amplitude in the fearful face condition compared with the neutral face condition, control subjects showed no variation between conditions. OCD patients also exhibited larger correct response negativity amplitude than control subjects in both fearful and neutral face conditions.
Conclusions: These results support the theory that OCD involves overactive performance monitoring and indicate that emotional interference modulates performance monitoring in patients with OCD, thus implying that affective function in the fronto–striatal network forms part of the neural basis of OCD.

1. Introduction

Intrusive thoughts or concerns regarding safety, cleanliness, symmetry, sex, or violence and urges to count or check "to be sure" are commonly experienced by most people to a degree (Belloch et al., 2004; Freeston et al., 1991). However patients with obsessive–compulsive disorder (OCD) have difficulty in controlling unwanted recurrent and persistent thoughts or feelings (i.e., obsession) and repetitive behaviors or mental acts that one feels compelled to perform (i.e., compulsion) and, as a result, experience psychological distress (American Psychiatric Association, 2000). Patients with OCD typically perceive inadequacy and error in everyday activities and as a result experience exaggerated concern, for which ritualistic behavior can compensate (Pitman, 1987). The phenomenology of OCD can thus be characterized as inappropriate or hyperactive performance monitoring (Hajcak and Simons, 2002).

In terms of the neural substrates of OCD, neuroimaging studies (Breiter et al., 1996; Perani et al., 1995; Schwartz et al., 1996) suggest abnormalities in the orbitofrontal cortex, anterior cingulate cortex (ACC), and basal ganglia, which are involved in the control, monitoring, and inhibition of behaviors and thoughts. The orbitofrontal cortex and ACC are connected to the basal ganglia via cortico–striato–thalamo–cortical loops (Saxena et al., 1998; Saxena and Rauch, 2000), dysfunction of which is implicated in OCD pathogenesis (Insel, 1992; Melloni et al., 2012). The theory of inappropriate performance monitoring in OCD patients originates from the cybernetic model of obsessive–compulsive pathophysiology (Pitman, 1987), which maintains that excessive or hyperactive error signals are a common characteristic of OCD. Enhanced performance monitoring and overactive error processing in OCD patients, typically examined by measuring error-related brain activity, provide support for the fronto–striatal model of OCD (Milad and Rauch, 2012). Error-related negativity (ERN) (Gehring et al., 1993) is a frontally maximal negative deflection in the response-locked event-related potential (ERP) that peaks within 100 msec after an incorrect response and that can be induced by errors committed outside of conscious awareness (O'Connell et al., 2007). Increased error-related brain activity in patients with OCD has been consistently demonstrated using ERPs (Endrass et al., 2008; Xiao et al., 2011; Melloni et al., 2012) and functional magnetic resonance imaging (Kiehl et al., 2000). Source localization (Keil et al., 2010) and functional neuroimaging studies (Carter et al., 1998; Holroyd and Coles, 2002) strongly suggest that the

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ACC is one of the principal generators of ERN and an important structure within the error detection system.

Extensive discussion has been devoted to the precise cognitive mechanisms that generate ERN. The principal theories that explain the functional significance of enhanced ERN suggest that such enhancement reflects the detection of a mismatch between representations of actual and intended responses (i.e., mismatch theory) (Falkenstein et al., 1991), conflict monitoring in the ACC arising from multiple simultaneously active response

tendencies (i.e., conflict monitoring theory) (Yeung et al., 2004) or disinhibition of dopaminergic innervations in the ACC, which signal events as worse than anticipated (i.e., reinforcement learning theory) (Holroyd and Coles, 2002). Furthermore, low ERN-like amplitude is sometimes evident in correct response trials and is called correct-related negativity (CRN) (Ford, 1999). Enhanced CRN amplitude in subjects with OCD symptoms (Endrass et al., 2008; Hajcak and Simons, 2002) suggests that OCD may also involve excessive performance monitoring during correct responses.

ERN is considered a potentially suitable endophenotype for OCD in that (1) increased ERN amplitudes have been repeatedly shown in patients with OCD; (2) increased ERN amplitude is substantially heritable as indicated by a twin study (Anokhin et al., 2008); (3) enhanced ERN amplitude may serve as a trait marker due to its constancy despite a reduction in OCD symptoms after therapy (Hajcak et al., 2008); (4) increased ERN amplitude in OCD patients is also observed in their asymptomatic first-degree relatives (Carrasco et al., 2013; Riesel et al., 2011).

Although a predominantly cognitive view of performance monitoring has received much support, recent work suggests that such theoretical models may provide an incomplete picture of ERN because they do not account for affective components. Researchers (Luck and Kappenman, 2011) emphasize that affective and cognitive processes underlying ERN are not mutually exclusive but could modulate each other. Moreover, research on the relationship between affective states and the neural indices of error monitoring provide mixed results. Several studies suggest that after affective distress induced by music (Larson et al., 2013) or the presentation of a spider (Moser et al., 2005), ERN remains unaltered and individuals are less oriented toward errors. These findings are consistent with studies (Tops et al., 2006) showing that ERN is related to trait measures such as behavioral shame proneness and agreeableness but not to affective states such as depression, anger, and tension. By contrast, changes in affect stimulated by emotionally salient images alter the neural indices of performance monitoring. For instance, Larson and colleagues (Larson et al., 2006) presented a flanker stimulus superimposed on neutral, unpleasant, or pleasant pictures. They demonstrated that a larger ERN amplitude occurred in response to background pictures that were pleasant than to those that were neutral or unpleasant. Another report (van Wouwe et al., 2011) demonstrated smaller ERN amplitude following exposure to positive video clips compared with neutral video clips. By contrast, Wisewede and colleagues (Wiswede et al., 2009) showed that unpleasant pictures preceding a performance error increased ERN amplitude more than neutral or pleasant pictures. Furthermore, with the use of emotionally valent face stimuli, larger enhancements in ERN amplitude occurred during evaluations on negative expressions than those on pleasant expressions (Boksem et al., 2011).

Although affective dysregulation is a prominent feature of OCD (Kang et al., 2012; Murphy et al., 2013), to the best of our knowledge, no ERN study with OCD patients has employed affective modulation or emotional interference. In the present study, we used ERPs to investigate how task-irrelevant emotional interference affects attention-demanding cognitive task performance and ERN in OCD patients. Because OCD patients show enhanced brain responsiveness when processing fearful faces (Cardoner et al., 2011) we modified a previous version of the flanker task (Richter et al., 2011) that features fearful versus neutral faces as irrelevant emotional distracters. We hypothesized that ERN is larger in OCD patients than in healthy control subjects regardless of the emotional stimulus. We also hypothesized that OCD patients would show a more distinct increase in ERN amplitude after the presentation of fearful faces than healthy controls. Furthermore, we investigated the relationship between ERN and various clinical correlates.

2. Material and methods

2.1. Participants and clinical assessments

Twenty-two OCD patients and 22 healthy control subjects, aged 18–65 years, were interviewed by two trained psychiatrists using all source of information according to Diagnostic and Statistical Manual of Mental Disorders (DSM)-IV-TR (American Psychiatric Association, 2000) criteria; no history of head trauma or neurological disease was reported. Participants were carefully matched in terms of age and gender (Table 1). Patients were recruited from the outpatient unit of a university psychiatric hospital and satisfied the DSM-IV criteria for OCD as their primary diagnosis. OCD patients with current or previous psychotic disorders, bipolar disorder, or alcohol or substance abuse as defined by the criteria outlined in the DSM-IV were excluded from the study. Diagnostic verification was performed by a senior psychiatrist at the rank of full professor through discussion with two psychiatrists in regular research meetings. Healthy controls were recruited through a local advertisement and reported no family history of OCD and no past or present signs of psychiatric disease. The study protocol was approved by the institutional review board (IRB) at Severance Mental Health Hospital. All participants provided written informed consent.

Psychopathological symptoms of patients with OCD were assessed by a psychiatrist using the Yale-Brown Obsessive–Compulsive Scale (Y-BOCS) (Goodman et al., 1989), Hamilton Anxiety Scale (HAM-A) (Hamilton, 1959), and Hamilton Rating Scale for Depression (HAM-D) (Hamilton, 1960). Other clinical symptoms of all participants were assessed with self-report questionnaires, including the Obsessive–Compulsive Inventory-Revised (OCI-R) (Foa et al., 2002), Dimensional Obsessive–Compulsive Scale (DOCS) (Abramowitz et al., 2010), Beck Depression Inventory (BDI) (Beck et al., 1961) and State–Trait Anxiety Inventory (STAI) (Spielberger and Lushene, 1966).

2.2. Experimental paradigm

A modified previous version of the flanker task (Richter et al., 2011) with task-irrelevant emotional and neutral distracters (Fig. 1) was presented to participants using Stim 2 software (Compumedics, Inc., El Paso, TX, USA). Participants were instructed to respond with their left or right index finger in accordance with the direction of the target arrow, which was the center arrow in a set of arrows. Half of the trials were congruent (i.e., the target and flanker arrows were pointed in

Table 1
Demographic and clinical characteristics of OCD patients and healthy controls.

	OCD patients (n = 22)		Healthy controls (n = 22)		t/χ^2	p-Value
Age, years	34.4	±10.0			0.048	0.962
Gender					0.000	1.000
Male	10	(45.5)	10	(45.5)		
Female	12	(54.5)	12	(54.5)		
Education, years	15.1	±2.1	15.9	±2.1	1.944	0.055
Age at onset, years	21.0	±6.1	–	–	–	–
Medication status						
Antidepressants[a]	22	(100.0)	–	–	–	–
Benzodiazepine	15	(68.2)	–	–	–	–
Antipsychotics	6	(27.3)	–	–	–	–

Values are mean ± standard deviation or n (%).
[a] Antidepressants include clomipramine, fluoxetine, escitalopram, duloxetine, sertraline, and buproprion.