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Contextual and behavioral influences on uncertainty in obsessive-compulsive disorder

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ABSTRACT

Introduction: Behavioral adaptation generally follows the contextual changes arising from the consequences (rewards and punishments) of an action. According to the reciprocal determinism model, there is a mutual influence between external context, cognitive processes and behavior. The maladaptive behaviors observed in obsessive-compulsive disorder (OCD) have been hypothesized to result from the disruption of the interactions between these three entities. For this, we assessed the influence of error signals and checking behavior on prefrontal cortical functions during decision-making in 14 OCD patients and 14 matched healthy participants.

Methods: We used a behavioral task designed to elicit intolerance of uncertainty (IU) followed by the free expression of checking behaviors, which was coupled with functional magnetic resonance imaging.

Results: At the behavioral level, IU intensity was correlated to the number of checking behaviors in both checking OCD patients and healthy controls during decision-making. However, external error signals did not influence checking behaviors in OCD patients, whereas they appeared to trigger checking behaviors in healthy subjects. At the neural level, IU intensity was positively correlated with activation in the orbitofrontal cortex (OFC) in both the OCD and control groups. At the region of interest (ROI) level, error signals increased IU-related OFC activations; in contrast, checking behaviors contributed to

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decreasing these neural activations in the healthy subjects, but no such modulation was observed in the OCD patients.

Conclusions: Our results show that IU-related OFC dysfunctions are not under the influence of the context and the behavioral response in OCD, suggesting that alterations of the dynamic features for this neural network may contribute to the expression of OCD symptoms.

1. Introduction

Obsessive-compulsive disorder (OCD) is a chronic psychiatric affection associated with highly disabling impairments. The hallmark of OCD is the presence of obsessions in the form of intrusive and distressing thoughts and the urge to perform repetitive behaviors, known as compulsions, that aim to reduce the anxiety and distress caused by obsessions (Stein, 2002).

Functional magnetic resonance imaging (fMRI) studies have attempted to investigate the brain alterations involved in the production of OCD symptoms, in particular via the standard symptom provocation task, which entails the presentation of obsessional stimuli. Functional modifications were found primarily within the frontal cortico-subcortical loops encompassing the orbitofrontal cortex (OFC), the anterior cingulate cortex (ACC), or the dorsolateral prefrontal cortex (Rotge et al., 2008a). The symptom provocation task used in fMRI studies is thought to elicit neural patterns of brain activations related to the emergence of obsessive-compulsive symptoms. However, this experimental paradigm suffers from two major limitations. First, it does not allow for behavioral responses to obsessive thoughts, which are the typical drivers of obsessive-compulsive symptoms, as experienced daily by OCD patients. Second, the symptom provocation task involves many cognitive or emotional processes that are unrelated to the mediation of OCD symptoms. In particular, certain brain activations are likely related to the patient's efforts to disregard or to turn their attention away from obsessive and distressing thoughts, especially when a behavioral response is not allowed (Rotge et al., 2008a).

In an attempt to manage these limitations, our research group has developed a delayed matching-to-sample task with the unrestricted possibility of checking a decision [the checking task (CT)] (Rotge et al., 2008b). During the CT, the checking behaviors performed by the OCD patients share similar features with checking compulsions: (i) repetitive checking behaviors are observed in OCD patients, especially when they specifically suffer from checking compulsions, compared with healthy controls; (ii) the checking behaviors are driven by a distressing uncertainty that is enhanced in OCD patients compared with healthy controls; and (iii) the checking behaviors increase throughout the CT in the OCD patients, but not in the healthy controls, in an attempt to reduce the cumulative distress caused by uncertainty (Rotge et al., 2008b; Jaafari et al., 2011).

Checking behavior manifests as the renewal of an action that might be mistaken and be responsible for prejudicial consequences. This behavior allows the subject to obtain more information and provides relief for the uncertainty felt regarding the accuracy of an action. Checking behavior may therefore be viewed as the behavioral output of a perceived uncertainty. Uncertainty, as a state of limited knowledge, may be driven by internal error signals derived from the self-representation of the accuracy of the action, and by external error signals derived from the context. External error signals, as a consequence of an actual mistaken action, may increase the likelihood of feeling uncertainty during the reoccurrence of this action and, therefore, increase the likelihood of performing a checking behavior (Ladouceur et al., 2000; Holaway et al., 2006). This phenomenon illustrates the mutual influence among the external context, cognitive processes and behavior in accordance with the reciprocal determinism model (Bandura, 1986). Indeed, external error signals could trigger uncertainty, whereas checking behaviors appear to be helpful for reducing uncertainty-related distress intolerance of uncertainty (IU). Repetitive and perseverative checking behaviors, as observed in OCD, can be viewed as patterns of disrupted interactions between these three entities. Also, they may result in a reduction of trust in memory, thereby possibly contributing to maintain uncertainty and checking behaviors (Van den Hout and Kindt, 2003).

In this study, we used fMRI while OCD patients and healthy controls performed the CT to explore the cognitive determinants of freely expressed checking behaviors and the influence of external error signals and compulsive behaviors on brain dysfunctions in OCD. We hypothesized that IU and its associated brain dysfunctions would be triggered by error signals and would be relieved in healthy subjects, whereas no such modulation would be observed in OCD patients.

2. Methods

2.1. *Participants*

A group of 16 OCD patients who suffered primarily from checking compulsions were recruited through outpatient clinics in Bordeaux and Poitiers (France), and 16 healthy volunteers were recruited from the local community through notice board advertisements. The groups were matched for age, sex, handedness and educational level.

The OCD patients were diagnosed according to the fourth edition of Diagnostic and Statistic Manual of Mental Disorders (DSM-IV) criteria using the Mini-International Neuropsychiatric Interview (MINI) (APA, 1994; Sheehan et al., 1998). Patients suffering from other current Axis-1 or Axis-2 disorders, as explored with the MINI and the Structured Clinical Interview for DSM-IV Axis-2 personality disorders (SCID-II), were not included (Maffei et al., 1997). The Yale-Brown Obsessive-Compulsive Scale (Y-BOCS) was used to assess

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