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Amygdala activity in obsessive-compulsive disorder with contamination fear: a study with oxygen-15 water positron emission tomography

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Abstract

Previous imaging studies of obsessive-compulsive symptom states have implicated frontal–striatal and limbic regions in the pathophysiology of obsessive-compulsive disorder (OCD). Functional imaging studies, however, have yielded inconsistent results, presumably due to methodological differences (patient inclusion criteria, stimulus paradigm, imaging technique, and absence of control groups). In the present study, randomized presentation of contamination-related and neutral visual stimuli was used to investigate the neurophysiological correlates of contamination fear in a group of medication-free OCD patients with washing behaviors and healthy controls. A total of 21 subjects (11 OCD patients and 10 healthy controls) were scanned using $H_2^{15}O$ positron emission tomography (PET). Subjects were presented with pictures of clean and dirty surroundings and were requested to make indoor/outdoor decisions to control for attention differences. State anxiety and obsessionality were rated after each scan using visual analogue scales. Main effects of stimulus type (contamination vs. neutral) were found in bilateral occipital cortex in both groups. A significant group interaction effect was observed in the left amygdala reflecting enhanced activity in response to contamination stimuli in OCD patients. Sensitization effects were observed in the right amygdala in the OCD group; these paralleled an increase in levels of distress and obsessionality as well as a decrease in dorsolateral prefrontal activity. The findings of the present study are

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consistent with the hypothesis of decreased frontal–striatal control of limbic structures, specifically the amygdala, resulting in an inadequate fear response in OCD patients with contamination fear.

Keywords: OCD; $H_2^{15}O$; PET; Contamination; Amygdala; Frontal–striatal

1. Introduction

Obsessive-compulsive disorder (OCD) is a common psychiatric disorder, affecting more than 1% of the population (Rasmussen and Eisen, 1992). This chronic disorder generally manifests itself first during adolescence and has a fluctuating course during adult life. OCD is characterized by recurrent intrusive thoughts (obsessions) and repetitive ritualistic behaviors (compulsions). These rituals can be highly time consuming and result in considerable morbidity, whereas concomitant anxiety symptoms often are less prominent at clinical presentation.

Although the pathogenesis of OCD is incompletely understood, a number of neuroimaging studies have reported neuroanatomical and functional abnormalities in OCD, particularly involving prefrontal–striatal and limbic regions. These studies, both volumetric and functional, have not yielded unequivocal results, however. Structural abnormalities in OCD have been described in the caudate nucleus in some studies (Luxenberg et al., 1988; Scarone et al., 1992; Rosenberg et al., 1997), whilst in other studies no differences between OCD patients and normal controls were evident (Kellner et al., 1991; Aylward et al., 1996). Jenike et al. (1996), using magnetic resonance imaging (MRI), found significantly diminished total white matter and increased total cerebral cortex and opercular volumes in OCD patients compared with controls. These results were only partially confirmed by Kim et al. (2001), who found increased gray matter (GM) density in frontal subcortical areas, but decreased GM density in other regions, in particular the cerebellum. In contrast, Szeszko et al. (1999) reported reduced orbitofrontal and amygdala volumes (both GM and white matter), and lack of normal hemispheric asymmetry of the hippocampus–amygdala complex. Although these inconsistencies may reflect various methodological differences such as patient inclusion criteria, imaging modality, and data-analytic techniques, they also suggest that volumetric abnormalities in OCD, if present, are at best subtle.

Early functional imaging studies in OCD have been performed using positron emission tomography (PET), with ^{18}fluoro-deoxyglucose (FDG) as a tracer, assessing resting state glucose metabolism (Baxter et al., 1987, 1988; Nordahl et al., 1989; Swedo et al., 1989). Baxter et al. (1987) reported hypermetabolism of the left orbital gyrus and bilateral caudate nucleus. In addition, striatal hypermetabolism normalized after successful treatment, either pharmacotherapy (Baxter et al., 1992) or behavioral therapy (Schwartz et al., 1996). The normalizing effect of pharmacotherapy on caudate hyperactivity has been replicated by many groups (Benkelfat et al., 1990; Swedo et al., 1992; Saxena et al., 2002; Hansen et al., 2002). In a similar vein, Rauch et al. (2002) found that increased regional cerebral blood flow (rCBF) in orbitofrontal and posterior cingulate cortices before treatment were predictive of response to pharmacotherapy in OCD patients with prominent contamination fear.

To our knowledge, at present, six imaging studies in OCD have been published in which symptom provocation was employed to differentiate between state and trait aspects. In a $H_2^{15}O$ PET study, McGuire et al. (1994) used tactile stimuli (various contaminants sealed in glass tubes) in four medication-free male OCD patients. Symptom scores (and state anxiety) were correlated with increased activity in the right inferior frontal gyrus, basal ganglia, thalamus, left hippocampus and posterior cingulate cortex. Rauch et al. (1994), using $C^{15}O_2$ PET, similarly compared responses to individually tailored provocative vs. neutral stimuli in a sample of eight male OCD patients and found increased relative regional cerebral blood flow during OCD symptom vs. resting state in bilateral orbitofrontal cortex, right