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Neuroimaging of psychotherapy for obsessive–compulsive disorder: A systematic review

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ABSTRACT

The symptoms of obsessive–compulsive disorder (OCD) include intrusive thoughts, compulsive behavior, anxiety, and cognitive inflexibility, which are associated with dysfunction in dorsal and ventral corticostriato-thalamocortical (CSTC) circuits. Psychotherapy involving exposure and response prevention has been established as an effective treatment for the affective symptoms, but the impact on the underlying neural circuits is not clear. This systematic review used the Medline, Embase, and PsychINFO databases to investigate how successful therapy may affect neural substrates of OCD. Sixteen studies measuring neural changes after therapy were included in the review. The studies indicate that dysfunctions in neural function and structure are partly reversible and state-dependent for affective symptoms, which may also apply to cognitive symptoms. This is supported by post-treatment decreases of symptoms and activity in the ventral circuits during symptom provocation, as well as mainly increased activity in dorsal circuits during cognitive processing. These effects appear to be common to both psychotherapy and medication approaches. Although neural findings were not consistent across all studies, these findings indicate that people with OCD may experience functional, symptomatic, and neural recovery after successful treatment.

1. Introduction

Obsessive–compulsive disorder (OCD) is characterized by obsessive thoughts and compulsive acts, which are associated with anxiety, reduced quality of life and functional impairment, as described in current nosologies (World Health Organization, 1993; American Psychiatric Association, 2013). Recommended treatments for OCD include cognitive-behavioral therapy (CBT) with exposure and response prevention and pharmacological treatment by selective serotonin reuptake inhibitors (SSRIs), with eventual adjuvant atypical antipsychotic medication in treatment-resistant cases (Abramowitz, 1997; Bloch et al., 2006; Gava et al., 2007). There is also burgeoning evidence for the effectiveness of other forms of cognitive therapy and psychotherapy (Fairfax, 2008; Calkins et al., 2013). Three decades of neuroimaging research in OCD have provided a better understanding of the underlying neural mechanisms. Future neuroimaging research in OCD might be valuable in addressing mediators of treatment outcome, which may lead to better personalized treatment (Lennox, 2009; Linden and Fallgatter, 2009).

The neurobiology of OCD is associated with dysfunction within the parallel corticostriato-thalamocortical (CSTC) circuits. Early literature mainly focused on the role of the orbitofrontal cortex (OFC), anterior cingulate cortex (ACC) and striatum (Saxena and Rauch, 2000; Whiteside et al., 2004; Menzies et al., 2008). Recent research, however, also suggests the importance of the amygdala, cerebellum, anterior insula/operculum, hippocampus, parietal cortex, and dorsolateral prefrontal cortex, as well as the structural and functional connectivity of the implicated neural networks (Husted et al., 2006; Menzies et al., 2008; Rotge et al., 2008; Harrison et al., 2009, 2013; Milad and Rauch, 2012; Piras et al., 2013; Anticevic et al., 2014).

A better understanding of OCD as a heterogeneous condition has emerged from the use of dimensional approaches (e.g,. Leckman et al., 1997; Mataix-Cols et al., 2005), which also allows for the exploration of common and symptom-specific neural substrates (Mataix-Cols et al., 2004; van den Heuvel et al., 2009; Harrison et al., 2013; de Wit et al., 2014; Radua et al., 2014). The diversity in symptom profiles seems to be represented by the diversity of implicated neural circuits. Symptoms of anxiety, disgust, contamination fear and harm sensitivity (such as in checking) seem to be strongly

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related to the limbic circuit and the saliency network. Cognitive rigidity, impaired response inhibition, compulsivity and symmetry/ordering behaviors seem to be mainly related to an imbalance between a hyperactive ventral frontal–striatal circuit and impaired top-down cognitive control from dorsal frontal–striatal and fronto-parietal circuits. (Friedlander and Desrocher, 2006; Mataix-Cols and van den Heuvel, 2006; Kwon et al., 2009). The direction of the altered frontal–striatal activation during cognitive tasks in OCD is dependent on the task level, co-morbidity, capacity to compensate, and level of limbic interference, as shown by two recent functional magnetic resonance imaging (fMRI) studies using the visuo-spatial n-back task (de Vries et al., 2014) and the stop-signal task (de Wit et al., 2012).

Although a complete overview of the neural abnormalities in OCD is outside the scope of this review, it is important to consider how they generate hypotheses on potential brain changes during psychotherapy. One hypothesis is that efficacious psychotherapy can normalize function and structure in the areas activated during the experimental tasks, which would support the notion of state-dependent abnormalities in function and structure, rather than a trait perspective of OCD symptoms and cognitive deficits. Another hypothesis is that psychotherapy enhances the compensatory mechanisms while leaving the trait vulnerability untouched. In both cases, one might expect these functional changes to involve altered functional and structural connectivity within the implicated brain circuits.

The aim of this review is to examine the evidence for neural changes after psychotherapy in OCD. The reviewed studies are examined in the context of both research on neuroimaging and psychotherapy, in order to describe an integrated perspective on the treatment of OCD.

2. Methods

Studies using neuroimaging methods to investigate psychotherapy effects for OCD were found using the Medline, Embase and PsycINFO databases, as well as manually searching the references of related publications. The search was designed to include as many methods of imaging as possible, and therefore included the terms “functional magnetic resonance imaging”, “positron emission tomography”, “radionuclide imaging”, “magnetic resonance spectroscopy”, “electroencephalogram”, magnetoencephalogram”, and “magnetic resonance imaging”. Different approaches to psychotherapy were also sought, using the terms “cognitive behavioral therapy”, “behavior therapy”, “cognitive therapy”, and “psychodynamic therapy”. Inclusion criteria for studies were as follows: psychotherapy had to be a form of treatment; neuroimaging had to be used both before and after treatment; and all participants had to be adults.

3. Results

Of the 16 included studies in this review, 12 used functional imaging methods to investigate changes in brain activity. One studied applied electroencephalography (EEG), one used magnetic resonance imaging (MRI) to investigate gray matter volume before and after treatment, while two studies investigated neural metabolites. Tables 1–4 summarizes the methodology and findings of each study, categorized by the method of neuroimaging.

3.1. Resting-state functional imaging

Baxter et al. (1992) investigated changes in glucose metabolism in OCD after treatment using a sample of nine OCD participants receiving behavior therapy, nine receiving fluoxetine, and four healthy controls. On the basis of resting state FDG-PET (^{18}F-fluorodeoxyglucose positron emission tomography), a common finding in both treatment groups was a significant decrease in glucose metabolic rate in the head of the right caudate nucleus. However, drug treatment also resulted in a reduction in metabolic rates in the right ACC and left thalamus, effects that were not evident in those receiving behavioral therapy. Treatment also affected intrahemispheric activity, as seen in a decrease in positive correlations between the right OFC, caudate nucleus and thalamus, as well as an increase in positively correlated activity between the left cingulate cortex and caudate nucleus. A limitation of the study is the small sample size, reducing statistical power, as well as the non-randomization of participants.

Schwartz et al. (1996) aimed to further investigate the effects of behavior therapy (BT) with resting state FDG-PET, by combining data from nine new OCD participants and nine BT-treated OCD participants from a previous study (Baxter et al., 1992). Schwartz and colleagues replicated previous findings of reduced metabolism in the right caudate after treatment. They also reported a decreased post-treatment correlation between activity in the right caudate nucleus, OFC and thalamus, as well as a decrease in left caudate activity when combining data from both studies. The small simple size and the lack of control subjects are major methodological concerns.

Saxena et al. (2009) investigated whether intensive and short-term cognitive behavior therapy (CBT) could produce changes in glucose metabolism in 10 OCD participants, compared with 12 healthy controls. Imaging was performed using FDG-PET with participants in a resting state. OCD participants showed a significant decrease in bilateral thalamic metabolism, along with an increase in right dorsal ACC metabolism, while controls showed a decrease in left dorsal ACC metabolism. Methodological limitations were the small sample size, the fact that six OCD participants were taking SSRIs, and the presence of major depression in one participant.

Apostolova et al. (2010) measured glucose metabolism using FDG-PET in participants under resting conditions. Seven of the OCD participants were receiving paroxetine and nine were receiving CBT. Results showed an increase in right caudate activity after successful treatment, regardless of treatment modality. The study did not include a control group, and participants chose their own form of treatment. In addition, several participants had comorbid diagnoses.

Nakatani et al. (2003) applied xenon-enhanced computed tomography (Xe-CT), under resting conditions, using a sample of 31 OCD participants receiving BT and 31 healthy controls. Due to drop-outs and technical issues, only 22 OCD participants remained for the pre-post-treatment analyses. The authors reported a significant reduction in blood flow in the right head of the caudate in responders to treatment. However, a potential confounder was that 21 of the original 31 OCD participants underwent pharmacological treatment in addition to psychotherapy. Also, the second scan was not given after a fixed interval, but was instead performed after the researchers deemed the OCD participants to have achieved sufficient clinical improvement, an assessment that was not standardized. Furthermore, important methodological shortcomings of the study are the use of Xe-CT, lack of sophisticated software for determining brain regions, and the inclusion of OCD patients with comorbid disorders.

Yamanishi et al. (2009) investigated whether BT could affect regional cerebral blood flow using single photon emission computed tomography (SPECT) carried out under resting conditions in 45 individuals with a diagnosis of OCD who were resistant to treatment with SSRIs. For treatment responders, the authors found significantly decreased regional cerebral blood flow in the left middle frontal gyrus, right medial PFC and right OFC, and increased activation in the right ipsilateral fusiform gyrus, cuneus and angular gyrus, while regional cerebral blood flow was unchanged in non-responders. In addition, decreases in symptom scores correlated to a decrease in OFC activity. Previous or current comorbid mental disorder was an exclusion criterion. The lack of a control group limited the ability to establish specificity of the effects of BT compared with other treatment strategies. This methodological problem is further complicated by the fact that all participants were also taking SSRIs.

In summary, resting state studies comparing regional cerebral blood flow (rCBF) before and after therapy have mostly reported decreased rCBF in areas such as the OFC, ACC, thalamus and