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Neural correlates of symptom reduction after CBT in obsessive-compulsive washers—An fMRI symptom provocation study ☆

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ABSTRACT

There is little knowledge about the neurofunctional changes associated with symptom reduction in obsessive-compulsive disorder (OCD). This functional Magnetic Resonance Imaging (fMRI) study explores changes in responses towards symptom provocation after psychotherapy.

Twelve patients with washing compulsions and twelve case-by-case matched healthy controls participated in a symptom provocation fMRI experiment. All participants were confronted with pictures of standardized and individualized OCD triggers. The experiment was performed before and after an individual ambulatory cognitive-behavioral therapy (CBT).

Post-treatment, OCD patients compared to healthy controls displayed reduced activity in key regions of the fronto-striatal network. While individualized symptom provocation demonstrated reductions in nucleus accumbens and posterior supramarginal gyrus, standardized symptom provocation showed reductions in orbitofrontal cortex, nucleus caudatus, ventrolateral prefrontal cortex, and anterior supramarginal gyrus. OCD patients showed significantly reduced symptoms after treatment, with a large effect size.

These post-treatment reductions are discussed in the light of the current research on OCD, CBT, and the functional roles of the respective brain regions. The present study provides evidence for changes in the processing of disorder-relevant material, reflecting different aspects of psychotherapy-induced normalizations of neurofunctional dysregulations associated with OCD.

1. Introduction

In the past decades, major advances have been achieved in OCD research. On the one hand, psychotherapeutic interventions have greatly improved in their ability to effectively reduce OCD symptoms (Stobie, Taylor, Quigley, Ewing, & Salkovskis, 2007). On the other hand, neuroimaging studies have contributed strongly to an understanding of the neurobiological correlates of OCD. Yet, there is only very little knowledge about how psychotherapy affects these neurobiological correlates (Linden, 2006).

The current neurobiological evidence in OCD research has been consolidated in an extended *cortico-striatal network model* (Menzies et al., 2008) stating that OCD symptomatology is mediated particularly by dysregulations of two relatively segregated fronto-striatal loops: the *affective loop* and the *spatial/attentional loop*. Only few studies have investigated how these neurofunctional dysregulations in OCD are subject to change after symptom reduction, e.g. in the context of psychotherapeutic or psychotropic treatment. Resting state studies using positron emission tomography (PET), single photon emission or xenon-enhanced computer tomography (SPECT, XE-CT) reported reduced striatal activity after treatment, mainly in nucleus caudatus (Baxter et al., 1992; Benkelfat et al., 1990; Nakatani et al., 2003; Schwartz, Stoessel, Baxter, Martin, & Phelps, 1996). Saxena et al. (2003, 2009) reported reduced activity in thalamus, vlPFC, and OFC and increased activity in the dorsal ACC. Benkelfat et al. (1990), Baxter et al. (1992) and Schwartz et al. (1996) also reported reduced post-treatment OFC activity. Resting state studies, however, have been discussed to be unsuitable for investigating most anxiety disorders (Liotti et al., 2000), due to the symptomatic states being relatively temporary in nature ("on–off").

Symptom provocation is a direct and clinically relevant approach, in which patients are confronted with disorder-relevant triggers (e.g. visually) and usually give behavioral feedback to report evoked symptoms. Depending on the paradigm and the choice of stimuli, symptom provocation offers high construct validity and is

☆This study was carried out at the Justus Liebig University Giessen, Germany.

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well-suited for assessing neurofunctional changes associated with symptom reduction (Linden, 2006).

However, the results of present functional OCD neuroimaging studies that investigated etiology-related correlates diverge strongly (for reviews see Rotge et al., 2008; Whiteside, Port, & Abramowitz, 2004). This is supposedly due to most of these studies not differentiating between OCD subtypes, although there is growing evidence from structural (van den Heuvel et al., 2009) and functional (Mataix-Cols et al., 2004) neuroimaging studies for a strong variance in the neurobiological representation of each subtype. Epidemiological studies suggest that a large proportion of OCD patients (approximately 46%; Matsunaga, Hayashida, Kiriike, Maebayashi, & Stein, 2010) suffer from contamination obsessions with cleaning/washing compulsions. The inconsistencies in these findings might also stem from differences in the used symptom provocation approaches (Simon, Kaufmann, Müsch, Kischkel, & Kathmann, 2010).

In the current literature, there are two approaches to OCD symptom provocation. Firstly, many symptom provocation studies account for the diversity of OCD phenomenology and the idiosyncrasy of obsessions by using stimuli that are *individualized* to some extent. For instance, this can be accomplished by using an individualized selection of stimuli from a picture pool (Simon et al., 2010) or by creating unique individualized stimuli that actually show the personal triggers of each patient (Schienle, Schäfer, Stark, Walter, & Vaitl, 2005). Individualized stimuli provoke very little symptoms in healthy controls (Schienle et al., 2005; Simon et al., 2010; Simon, Kischkel, Spielberg, & Kathmann, 2012).

The second approach is to use subtype-specific symptom provocation. Mataix-Cols' workgroup published the Maudsley Obsessive-Compulsive Stimuli Set (MOCSS; Mataix-Cols, Lawrence, Wooderson, Speckens, & Phillips, 2009), a *standardized* pictorial stimulus set with subsets for all main OCD subtypes. The MOCSS washing subset is also provocative for healthy subjects and has been discussed to provoke emotion and disgust processing (Mataix-Cols et al., 2004). The authors emphasize a dimensional perspective: The addressed processes are not exclusive for but more pronounced in OCD patients (Mataix-Cols et al., 2003, 2004).

The diverging results from these two research traditions implicate that both approaches provoke (partly) different OCD relevant processes. Given this, we would like to argue that in order to capture the changes of OCD relevant neural processes associated with symptom reduction in more detail, the combined use of both approaches should be highly beneficial. This should increase the external validity and the chances of revealing more of the relevant post-treatment changes.

There is also a particular benefit of combining functional neuroimaging with symptom provocation when investigating psychotherapy-induced effects: It allows depicting psychotherapy-associated changes in the neural *processing* of disorder-relevant material (Linden, 2006). Rather than measuring trait-like dysregulation, it activates and measures pathology-associated states. Yet, to date there is only one fMRI symptom provocation study investigating symptom reduction in OCD (Nakao et al., 2005) and one experimental case report study (Schiepek et al., 2009). Nakao et al. (2005) had only six subjects in the psychotherapy group and a provocation task, where subjects had to "generate words in their minds", making the study rather complicated to compare with the rest of the symptom provocation literature. The authors reported reduced responsiveness towards symptom provocation in OFC, dlPFC and ACC after symptom reduction (pooled psychotherapy and pharmacotherapy).

The current study is part of a larger project. The present study solely reports effects associated with symptom reduction. The experimental set-up has been reported earlier in a symptom provocation study with pre-treatment data only (Baioui et al., 2013). There, as compared to healthy controls, individualized symptom provocation showed stronger activation in the basal ganglia (nucleus accumbens, nucleus caudatus, pallidum), while standardized symptom provocation showed stronger activation in the nucleus caudatus.

The present study was designed to explore the neural correlates of CBT-associated symptom reduction in contamination/washing-related OCD. We concentrated on one subtype only in order to minimize undesired variance. We hypothesized that post-treatment, reduced neural activity would be observable in key regions of the fronto-striatal network, especially in the basal ganglia, the intersection of the affective loop and the spatial/attentional loop.

Two different symptom provocation approaches served as markers for the neurofunctional mechanisms of symptom change, in order to capture post-treatment changes more extensively. All post-treatment neural changes will be interpreted within the frame of the current literature on OCD symptom provocation, neuroimaging of symptom reduction, and the respective brain regions.

2. Methods

2.1. Participants

Twenty-four right-handed subjects participated in the experiment: 12 subjects suffering from OCD with washing symptoms ("OCD patients"; 8 females; M_{age}=32.49; SD_{age}=8.89) and 12 healthy controls (M_{age}=33.19; SD_{age}=8.63) matched by sex, age, and handedness.

None of the participants received psychotherapeutic treatment at the time of the experiment, four patients were completely therapy naïve, five were naïve regarding psychotropic medication, and two were medicated with SSRIs. A detailed description of all inclusion and exclusion criteria can be found in Baioui et al. (2013; Table 1). In short, the most important exclusion criterion in the healthy control group was any current or past psychological disorder (adulthood). Primary inclusion criteria for the OCD group were: OCD as primary diagnosis, "washing" as dominant subtype, a Y-BOCS score greater than 15, an illness duration of at least four months, and if medicated, stable medication dosages for at least 12 weeks prior to the first experimental session and during the study (cf. Abramowitz, Foa, & Franklin, 2003). Primary exclusion criteria for the OCD group comprised: Any F0, F1

Table 1
Overview of clinical data across both groups and both points in time. Pre-treatment (pre) and post-treatment (post) values were contrasted with paired *t*-tests separately for OCD patients (OCD) and healthy controls (HC). Meaningful Y-BOCS scores cannot be obtained from healthy controls. The values in brackets represent standard deviations.

	OCD				HC		
	pre	post	*p*	*d*	pre	post	*p*
Y-BOCS	23.08 (4.79)	15.58 (7.45)	<.001	1.2	–	–	–
OCI-R	28.08 (12.63)	20.50 (12.05)	.005	.61	3.08 (3.60)	2.25 (2.99)	n.s.
OCI-R subscale washing	8.33 (2.74)	6.17 (3.10)	.0198	.74	.25 (.62)	.16 (.38)	n.s.
BDI-II	14.83 (8.75)	13.58 (10.50)	n.s.		3.00 (2.59)	2.50 (3.63)	n.s.
QADS	100.33 (20.29)	92.66 (19.57)	n.s.		76.25 (14.83)	73.33 (20.87)	n.s.
STAI-T	52.58 (11.93)	48.83 (11.96)	n.s.		34.83 (7.73)	33.33 (7.95)	n.s.