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Research report

Regional homogeneity of spontaneous brain activity in adult patients with obsessive–compulsive disorder before and after cognitive behavioural therapy

Xiang-Yun Yang [a], Jing Sun [b], Jia Luo [a], Zhao-Xi Zhong [a,1], Ping Li [c], Shu-Min Yao [a], Hong-Fang Xiong [a], Fang-Fang Huang [a], Zhan-Jiang Li [a,*]

[a] Department of Clinical Psychology, Beijing Key Lab of Mental Disorders, Beijing Anding Hospital, Capital Medical University, and Center of Schizophrenia, Beijing Institute for Brain Disorders, Beijing, People's Republic of China
[b] Menzies Health Institute Queensland and School of Medicine, Griffith University, Australia
[c] Department of Psychiatry, Qiqihaer Medical University, Qiqihaer, Heilongjiang, China

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ABSTRACT

Background: Cognitive behavioural therapy (CBT) is an effective treatment for obsessive–compulsive disorder (OCD). Several neuroimaging studies have explored alterations of brain function in OCD patients as they performed tasks after CBT. However, the effects of CBT on the neural activityin OCD during rest remain unknown. Therefore, we investigated changes in regional homogeneity (ReHo) in OCD patients before and after CBT.

Methods: Twenty-two OCD patients and 22 well-matched healthy controls participated in the resting-state functional magnetic resonance imaging scans. We compared differences in ReHo between the OCD and control groups before treatment and investigated the changes of ReHo in 17 OCD patients who responded to CBT.

Results: Compared to healthy controls, OCD patients exhibited higher ReHo in the right orbitofrontal cortex (OFC), bilateral middle frontal cortex, right precuneus, left cerebellum, and vermis, as well as lower ReHo in the bilateral caudate, right calcarine, right posterior cingulate cortex, and right middle temporal cortex. Along with the clinical improvement in OCD patients after CBT, we found decreased ReHo in the right OFC, bilateral middle frontal cortex, left cerebellum and vermis, and increased ReHo in the left caudate. Improvement of OCD symptoms was significantly correlated with the changed ReHo in the right OFC and left cerebellum.

Conclusions: Although these findings are preliminary and need to be replicated in larger samples, they indicate the presence of abnormal spontaneous brain activity of the prefrontal–striatal–cerebellar circuit in OCD patients, and provide evidence that CBT can selectively modulate the spontaneous brain activity of this circuit in OCD patients.

1. Introduction

Obsessive–compulsive disorder (OCD) is a chronic psychiatric disorder characterised by persistent intrusive thoughts (obsessions) and/or repetitive behaviours (compulsions), affecting 2–3% of the general population (Abramowitz et al., 2009; Kessler et al., 2005). Cognitive behavioural therapy (CBT) is a treatment that focuses on patients' dysfunctional thinking, emotions and behaviour. It has been widely adopted in clinical practice and there is compelling evidence that it is an effective treatment for OCD (Prazeres et al., 2007). Approximately 60–70% of OCD patients are responsive to CBT (Abramowitz, 2006), and have lower relapse rates and less adverse side effects than patients who undergo pharmacotherapy (Simpson et al., 2004). Despite these benefits, deleterious residual symptoms and treatment non-response are common among patients who have undergone CBT (Olatunji et al., 2013), and a biological perspective on the mechanisms of CBT in OCD patients remains to be defined.

* Correspondence to: Beijing Anding Hospital, Capital Medical University, No. 5 Ankang Lane, Dewai Avenue, Xicheng District, Beijing 100088, People's Republic of China. Fax: +86 10 58 30 3 004.
E-mail addresses: wysun828@126.com (X.-Y. Yang), j.sun@griffith.edu.au (J. Sun), luojia529@aliyun.com (J. Luo), zzxzzx9268@163.com (Z.-X. Zhong), lipingchxyy@163.com (P. Li), xiongmaoxiehui@163.com (H.-F. Xiong), hff87hff87@163.com (F.-F. Huang), lizhj8@ccmu.edu.cn (Z.-J. Li).
[1] Current workplace: The Second Affiliated Hospital of Xinxiang Medical University, Xinxiang, Henan, People's Republic of China.

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During past decades, with the advent of neuroimaging techniques with high spatial and temporal resolution, it has become increasingly possible to determine the biological consequences of psychotherapeutic interventions. Several neuroimaging studies have indicated that CBT could induce the brain anatomical and functional changes in OCD patients. One study using magnetic resonance imaging (MRI) found that grey matter volume abnormalities in the left putamen were no longer detectable after treatment with either CBT or fluoxetine (Hoexter et al., 2012). Another study by the same group found that pre-treatment grey matter volume in the right medial prefrontal cortex (MPFC) was positively associated with symptom improvement following CBT (Hoexter et al., 2013). Earlier positron emission tomography studies found that, as the metabolic rates of the right anterior cingulate cortex (ACC) increased, the caudate and bilateral thalamic decreased after CBT treatment (Baxter et al., 1992; Saxena et al., 2009). A single-photon emission computed tomography study found that the baseline regional cerebral blood flow in the bilateral orbitofrontal cortex (OFC) was significantly correlated with the change in clinical symptoms after CBT (Yamanishi et al., 2009). These studies demonstrate that CBT-induced anatomical and functional changes in OCD patients are primarily located in the cortico-striato-thalamo-cortical circuitry.

More recent studies using functional MRI (fMRI) in combination with cognitive tasks have expanded on earlier findings of the effects of CBT on brain activity in OCD patients. One fMRI study using a probabilistic reversal-learning task found that the caudate nucleus showed increased activity in OCD patients after intensive CBT (Freyer et al., 2011). Further, the anterior temporal pole and amygdala had the strongest association with a better treatment response in OCD patients (Olatunji et al., 2013). In addition, a study using an exposure task fMRI found that the haemodynamic response of the left OFC and ACC to the obsession-inducing images decreased after three months of CBT (Morgieve et al., 2014). These limited studies using different experimental paradigms—such as the Stroop task, reversal-learning task and symptom provocation—suggest that CBT may affect the functions of the brain areas associated with cognitive control, such as the OFC and ACC.

Although these studies have advanced understandings of the mechanisms by which CBT improves OCD symptoms, their experimental designs have focused only on task-related brain regions, and subsequently may have missed other important regions displaying abnormal activity unrelated to the task. Resting brain activity, without any overt behaviour, is recognised as intrinsic spontaneous brain activity (SBA), which can be detected by resting-state fMRI (rs-fMRI) (Biswal et al., 1995). Recent studies on resting state in OCD patients have indicated that OCD is not caused by a single alteration in the brain circuits, but by multiple variations in different circuits, which are associated with the variety of cognitive symptoms and anxiety found in the disorder (Hou et al., 2012; Ping et al., 2013; Leon et al., 2014). Along this line, Zhang constructed a top-down control network of OCD patients at resting state, including 39 regions of interest, such as the PFC, temporal cortex and posterior regions (Zhang et al., 2011). By analysing the topological property of this network, he found an alteration of the architecture of connections between the PFC and other brain areas. Neuropsychological studies have demonstrated that obsessive–compulsive (OC) symptoms are linked to a failure of cognitive control, which may be due to the impairments in the cognitive control system during the resting state (Shin et al., 2014).

Given that important cognitive functions exist at the resting state, CBT may alter the coordination of SBA in the cognitive neural circuits through changing the cognition and behaviour of OCD patients. To the current study's best knowledge, no previous research has investigated the effects of CBT on SBA in OCD patients. To respond to this, this study sought to investigate the coordination of SBA before and after CBT in adult patients with OCD using regional homogeneity (ReHo)—a method of rs-fMRI analysis used to measure local coherence of SBA in neighbouring voxels (Zang et al., 2004). This study hypothesised that alterations in ReHo may be found in the regions of the cognitive control system—such as the OFC, ACC, dorsolateral PFC (DLPFC), caudate and cerebellum—in OCD patients after successful implementation of CBT. It also hypothesised that the alterations of ReHo in specific regions after CBT may be associated with changes in clinical presentation. To test this hypothesis, this study compared the ReHo of the whole brain between OCD patients and healthy controls (HCs) to find the abnormal ReHo in OCD patients, and investigated the changes of abnormal ReHo in OCD patients who responded to CBT. It also examined the correlation between ReHo and symptom improvement.

2. Methods

2.1. Participants

This study was approved by the Research Ethics Committee at Beijing Anding Hospital, Capital Medical University. All participants provided written informed consent. Participants included 22 patients diagnosed with OCD and 22 HCs who matched in terms of age, gender, handedness and education.

Twenty-two outpatients were recruited in Beijing Anding Hospital, Capital Medical University, from August 2011 to October 2013. All patients met the DSM-IV-Text Revision (2000) diagnostic criteria for OCD (diagnosed by four experienced senior psychiatrists using the Structured Clinical Interview for DSM-IV Axis I Disorders). This study included OCD patients who were aged between 18 and 45 years, had a Yale-Brown Obsessive–Compulsive Scale (Y-BOCS) (Goodman et al., 1989) score of 16 or more, had a 17-item Hamilton Depression Rating Scale (HAMD-17) (Hamilton, 1960) score of less than 18, and were right handed. They also had no history of neurological illness or other major physical diseases; no history of Axis I psychiatric disorders other than OCD; and no history of psychoactive substance use, alcohol dependence, and/or alcohol abuse. In addition, they were medication naive or medication free for at least four weeks prior to enrolment.

Of the 22 patients, 10 had never been on any medication for OCD, while the others had been on medications (all had taken serotonin reuptake inhibitors medication for an average of three months). Patients were also excluded if they had previous exposure to any psychotherapy, or were pregnant.

Twenty-two healthy volunteers were recruited from the local community as HCs and were screened using the Structured Clinical Interview for DSM-IV Axis I Disorders—Non-patient Edition. The exclusion criteria included neurological illness, major physical diseases, Axis I psychiatric disorders and a positive family history of major psychiatric disorders. The detailed clinical and demographic data for all participants are shown in Table 1.

2.2. CBT setting

Patients were randomly allocated to a therapist and received a 12-week individual CBT program that consisted of 14 sessions. None of the patients were taking psychoactive medications during the treatment period.

This study compiled a CBT manual based on the researchers' previous CBT trainings and the existing treatment manual of CBT for OCD (Whittal et al., 2005; Wilson and Chambless, 2005). This treatment manual consisted of 14 sessions, with each session lasting 60 min. The sessions entailed the following: