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Research paper

Abnormal small-world brain functional networks in obsessive-compulsive disorder patients with poor insight

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ABSTRACT

Background: There are limited data on neurobiological correlates of poor insight in obsessive-compulsive disorder (OCD). This study explored whether specific changes occur in small-world network (SWN) properties in the brain functional network of OCD patients with poor insight.
Method: Resting-state electroencephalograms (EEGs) were recorded for 12 medication-free OCD patients with poor insight, 50 medication-free OCD patients with good insight, and 36 healthy controls.
Results: Both of the OCD groups exhibited topological alterations in the brain functional network characterized by abnormal small-world parameters at the beta band. However, the alterations at the theta band only existed in the OCD patients with poor insight.
Limitations: A relatively small sample size. Subjects were naïve to medications and those with Axis I comorbidity were excluded, perhaps limiting generalizability.
Conclusions: Disrupted functional integrity at the beta bands of the brain functional network may be related to OCD, while disrupted functional integrity at the theta band may be associated with poor insight in OCD patients, thus this study might provide novel insight into our understanding of the pathophysiology of OCD.

1. Introduction

Individuals with obsessive-compulsive disorder (OCD) exhibit obsessions (repetitive intrusive thoughts) and/or compulsions (repetitive ritualistic behaviors) in their actions. Despite being classified as a unitary nosological entity, OCD is a clinically heterogeneous disorder that is characterized by an insight spectrum by the patient that ranges from full recognition of obsessive-compulsive (OC) symptoms as irrational to acceptance of the symptoms as truly realistic and rational (Solyom et al., 1985). The Diagnostic and Statistical Manual of Mental Disorders 4th edition (DSM-IV) describes a subgroup of OCD patients that are characterized as having "poor insight", and these patients do not recognize their obsessions and compulsions as excessive or unreasonable for the majority of the episodes they experience.

Poor insight has been reported to affect 21–36% of all OCD patients (Catapano et al., 2010; Foa et al., 1995; Matsunaga et al., 2002; Ravi et al., 2004), and it has also been associated with greater severity of OCD symptoms (Catapano et al., 2010; Ravi et al., 2004), an earlier age at onset, a longer duration of illness (Catapano et al., 2010; Matsunaga et al., 2002; Ravi et al., 2004), a higher comorbidity rate with depression (Catapano et al., 2010; Ravi et al., 2004), and body dysmorphic disorder (Eisen et al., 2004), and an insufficient response to behavioral therapy (Himle et al., 2006; Mataix-Cols et al., 2002; Solyom et al., 1985) and pharmacotherapy (Catapano et al., 2010; Erzegovesi et al., 2001; Ravi et al., 2004). Furthermore, different OCD clinical subtypes may be associated with different etiologies, and pathogenic mechanisms.

Neuropsychological studies have reported that OCD patients with

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poor insight exhibit more severe neuropsychological deficits in executive function (Tumkaya et al., 2009) conflict resolution/response inhibition, and verbal memory (Kashyap et al., 2012). A previous neuroimaging study reported that OCD patients with poor insight have a higher frequency of various types of brain structure abnormalities compared with patients with good insight (Aigner et al., 2005). These findings suggest that OCD patients with good insight versus poor insight may possess different neuropsychological and neurobiological characteristics. Nevertheless, very few studies have directly examined the specific neurobiological alterations of OCD patients with poor insight.

Abnormal functional connectivity in the neurocircuitry that comprises the corticostriatal-limbic circuits (Jung et al., 2013) and medial frontal cortex (Fitzgerald et al., 2010) is hypothesized to play an important role in the pathophysiology of OCD. Harrison et al. (2009) found that OCD patients have abnormal and heightened functional connectivity of ventrolimbic corticostriatla regions using resting-state functional magnetic resonance imaging. Furthermore, the abnormalities of functional connectivityis not limited tocortical-striatal-thalamic-cortical circuits and involves abnormalities in additional large-scale brain systems, especially the limbic system (Hou et al., 2014). Additionally, evidence of abnormal functional connectivity in subjects with OCD has been found to include alterations in the small-world network (SWN) properties of the brain functional networks of OCD patients compared with nonclinical individuals (Zhang et al., 2011). However, whether poor insight in OCD patients is related to abnormalities in functional brain connectivity remains unclear.

Based on the previous findings of neuropsychological and neurobiological studies (Aigner et al., 2005; Kashyap et al., 2012), it is hypothesized that OCD patients with poor insight have specific abnormalities in their SWN attributes at several electroencephalogram (EEG) bands. The present study was to explore whether specific changes in the properties of the SWN occur within the whole-brain functional networks of OCD patients with poor insight compared with OCD patients with good insight and healthy controls. To evaluate these potential changes, resting-state EEG and graph theoretical analysis were used to investigate the organization of the overall functional brain connectivity of OCD patients with poor insight and good insight at different EEG bands within the SWN.

2. Methods

2.1. Participants

Sixty-two (63%) OCD patients and 36 (37%) healthy controls participated in this study. The patients with OCD were recruited from the psychology clinic at Second Xiangya Hospital of Central South University. These patients were diagnosed by two certified psychiatrists using the Structured Clinical Interview for DSM-IV (SCID) and fulfilled criteria for OCD. The exclusion criteria included: (i) patients with comorbid DSM-IV axis I disorders; (ii) patients at specific medical or neurological conditions that would interfere with the evaluation of the study results (e.g., Tourette syndrome, hyperactivity, organic mental diseases, mental retardation, history of psychosurgery, history of epilepsy); and (iii) patients taking prescription of psychoactive medication previously or currently. Accordingly, all patients included in this study were naïve to medications. The patients were subsequently dichotomized into those diagnosed with good insight versus poor insight, with the latter including those who generally did not recognize that their obsessions and compulsions were excessive or unrealistic. The quality of insight (poor/good insight) was rated according to SCID for DSM-IV (kappa = 0.90 for the rating of insight). In addition, the Yale-Brown Obsessive Compulsive Scale (Y-BOCS) was used to assess disease severity for the patients with OCD (Goodman et al., 1989) while the severity of depressive and anxiety symptoms of each subject were separately rated using the Beck Depression Inventory (BDI-II) (Beck et al., 1996) and the State Trait Anxiety Inventory (STAI) (Spielberger, 1983) Each patient underwent an EEG recording prior to the start of any psychiatric treatment.

Healthy controls were recruited from the community and from Central South University by poster advertisements. All of the controls were screened using the Structured Clinical Interview for the DSM-Non-Patient edition (SCID-NP; First et al., 1995) to confirm a lifetime absence of psychiatric and neurologic illness. No history of psychiatric illness was reported in the controls or in any of their first-degree relatives.

This study was conducted in accordance with the Declaration of Helsinki and was approved by the Ethics Committee of the Second Xiangya Hospital of Central South University. All participants provided written informed consent.

2.2. EEG recordings

EEGs were recorded using a 32-channel cap (Easy-cap) with 30 Ag/AgC1 electrodes placed according to the 10/20 system. Electro-oculograms (EOGs) to detect eye movements and blinks were recorded with electrodes placed on the bilateral external canthi and the left infra-orbital and supraorbital areas. Both the EEGs and EOGs were sampled at 1000 Hz with a 0.1–200 Hz band pass of a Neuroscan Nuampls digital amplifier system (Neuroscan Inc., USA). The left mastoid was used as a reference for each recording. Electrode impedances were kept below 5 kΩ. The EEGs were recorded over 180 s when the subjects were sitting in a comfortable fixed chair in a quiet room with their eyes close.

2.3. EEG analysis

During preprocessing, the EEG signals were digitally band-pass filtered at 0.5–70 Hz, while a notch filter was used to remove 50 Hz electrical noise. To reduce the non-zero reference effect, the recordings were re-referenced to REST (zero) to avoid systematic effects that may arise from referencing to a particular channel, particularly in the context of synchronization analysis. The software can be found at (http://www.neuro.uestc.edu.cn/REST/) (Qin et al., 2010). A detrend was subtracted based on the entire time range.

Graph analysis was performed in Matlab (The MathWorks, Inc.) using software written by one of the authors (YC). The EEGs were decomposed to the conventional EEG bands, including delta (1–4 Hz), theta (4–8 Hz), alpha (8–13 Hz), beta (13–30 Hz), and gamma (30–48 Hz) band, using a five-level wavelet filter bank. Functional connectivity was determined by computing the synchronization likelihood (SL) between all pair-wise combinations of channels for the five bands, resulting in a 30 × 30 connectivity matrix. SL is a measure of the dynamic interdependencies between a time series (EEG channel) and one or more other time series. In contrast to some linear technologies, such as coherence, SL is valid for both linear and non-linear interdependencies as a function of time (Stam and van Dijk, 2002), which means that SL could detect more general interaction between dynamic systems. In general, EEG signals may contain both linear and non-linear components. In this work, we firstly tested the nonlinearity of the EEG data with the measure described in the Appendix A. It showed that 72.54%, 72.71%, and 74.35% of the data were identified to be nonlinear for the data set of the OCD patients with good insight, OCD patients with poor insight, and the controls, respectively. Therefore, the synchronization likelihood was chosen as the measure for our research.

The graph theory analysis was performed to reveal the differences among these three groups. Briefly, the SL connectivity matrices were converted into binary matrices through a set of thresholds with a step of 1%. The set of thresholds save the 10–50% strongest links, with their original values while the other links were set to be zero, which make the matric sparser (Liu et al., 2008). For each threshold, the normalized cluster coefficient C_{nml}, which represents the probability that the neighbors of a node are also connected, and the normalized character-