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Abnormal functional connectivity of EEG gamma band in patients with depression during emotional face processing

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HIGHLIGHTS

- Abnormally increased brain functional connectivity was found in patients with depression by calculating EEG coherence.
- The brain networks of both the depressed group and healthy controls in gamma oscillation presented regular network characteristics during emotional processing, but the depressed group showed randomization trends.
- Healthy controls showed significantly negative bias in the gamma band during emotional processing, while the bias was not detected in patients with depression.

ABSTRACT

Objective: This paper evaluates the large-scale structure of functional brain networks using graph theoretical concepts and investigates the difference in brain functional networks between patients with depression and healthy controls while they were processing emotional stimuli.
Methods: Electroencephalography (EEG) activities were recorded from 16 patients with depression and 14 healthy controls when they performed a spatial search task for facial expressions. Correlations between all possible pairs of 59 electrodes were determined by coherence, and the coherence matrices were calculated in delta, theta, alpha, beta, and gamma bands (low gamma: 30–50 Hz and high gamma: 50–80 Hz, respectively). Graph theoretical analysis was applied to these matrices by using two indexes: the clustering coefficient and the characteristic path length.
Results: The global EEG coherence of patients with depression was significantly higher than that of healthy controls in both gamma bands, especially in the high gamma band. The global coherence in both gamma bands from healthy controls appeared higher in negative conditions than in positive conditions. All the brain networks were found to hold a regular and ordered topology during emotion processing. However, the brain network of patients with depression appeared randomized compared with the normal one. The abnormal network topology of patients with depression was detected in both the prefrontal and occipital regions. The negative bias from healthy controls occurred in both gamma bands during emotion processing, while it disappeared in patients with depression.
Conclusions: The proposed work studied abnormally increased connectivity of brain functional networks in patients with depression. By combing the clustering coefficient and the characteristic path length, we found that the brain networks of patients with depression and healthy controls had regular networks during emotion processing. Yet the brain networks of the depressed group presented randomization trends. Moreover, negative bias was detected in the healthy controls during emotion processing, while it was not detected in patients with depression, which might be related to the types of negative stimuli used in this study.
Significance: The brain networks from both patients with depression and healthy controls were found to hold a regular and ordered topology. Yet the brain networks of patients with depression had randomization trends.

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1. Introduction

With more and more research conducted on functional brain imaging in major depressive disorder (MDD), it is indicated that observed psychopathology might be related to the distributed property of large-scale cortical systems with a number of functionally connected cortical regions (Damasio, 1994; LeDoux, 1996; Rippon et al., 2001; Lagopouplos et al., 2012). Recent studies provided further evidence that individuals with MDD tended to have altered brain networks (Berman et al., 2011). Furthermore, emotional processing is also completed by cooperating among different brain regions (Galderisi and Mucci, 2002). However, how MDD, as a disorder characterized by a distinct change of mood, organizes their emotional brain network still remains unclear.

Most studies indicated that the synchronization of oscillations has been used to identify networks of interacting brain regions (Ertl et al., 2013), and scalp electroencephalogram (EEG) is used to investigate neural oscillations generated in cortical brain structures. To date, many EEG studies have revealed that oscillations in different frequency bands have individual connections with emotional processing in different ways (see review of Güntekin and Basar, 2014). In this review, the related studies presented that beta and gamma oscillatory responses reflected fast and automatic processing of negative stimuli, while the alpha band gave inconsistent results from various groups. The authors concluded that the search for functional correlates of brain oscillations has been an important trend in neuroscience. EEG coherence is an efficient method to calculate the linear-dependent interaction of EEG signals between two channels or brain regions on the frequency domain without restrictedly priori assumptions (Andrew and Pfurtscheller, 1996; Pfurtscheller and Andrew, 1999). Compared with other methods such as partial directed coherence and phase synchronization estimating the function connectivity, EEG coherence can be used conveniently to build network frameworks in the EEG frequency domain (Di and Rao, 2007). A report based on an auditory oddball task showed that most patients with schizophrenia had abnormal patterns of coherence in the temporal lobe (Calhoun et al., 2011). Meanwhile, Leuchter pointed out that patients with MDD in the resting state had significantly higher overall coherence than controls in the frequency range of 0.5–20 Hz (Leuchter et al., 2012). Therefore, one may come to a conclusion that coherence is available to characterize the interaction in brain dynamics. On the other hand, EEG coherence only indicates the interconnection between two structures or brain regions, which does not reveal the global network property.

Graph theoretical analysis (GTA) provides a framework for understanding brain global network topology. GTA has been widely used in the research of brain networks (Stam and Reijneveld, 2007; Bullmore and Sporns, 2009). This approach offers an unique window into the balance of local and distributed interactions occurring in the brain (Fingelkurts et al., 2005). The graph theory enables the detection of so-called small-world network architecture, which combines the high clustering of the regular network with short path lengths of the random network (Sporns and Zwi, 2004; Bassett and Bullmore, 2006; Uehara et al., 2013). Reports on many neuropsychiatric diseases, such as Alzheimer's disease (AD) (Stam et al., 2009, 2007), schizophrenia (Jalili and Knyazeva, 2011; van den Heuvel et al., 2010), and epilepsy (Bernhardt et al., 2011; Ponten et al., 2007), as well as on patients with depression have consistently showed a randomization of network topology and a disruption of the small-word network architecture. A report based on a functional magnetic resonance imaging (fMRI) study showed that patients with MDD exhibited reduced negative blood oxygenation level-dependent responses in the core cortical midline regions of the default-mode network during processing of emotion stimuli (Grimm et al., 2009). Further fMRI study demonstrated that both MDD and healthy controls had small-world architecture in resting-state brain networks, while MDD had a shift toward randomization in their brain networks (Zhang et al., 2011). Meanwhile, researchers reported that healthy controls exhibited neuronal networks closer to the ordered part of the rewiring scale, while patients had brain networks closer to the random part of the scale during sleep (Leistedt et al., 2009). However, little evidence is available about whether the complex network connectivity of depression during cognitive tasks has small-word properties.

In addition, studies of facial emotion processing play an important role in the research of emotion and cognition in MDD. Most of the neuroimaging research show abnormalities in patients with MDD in a common face-processing network, indicating mood-congruent processing bias of hyperactivation to negative stimuli and hypoactivation to positive stimuli, particularly in the amygdala, insula, parahippocampal gyrus, fusiform face area, and putamen (see review of Stuhrmann et al., 2011). In particular, *negativity bias*, a well-known concept in psychology, was reported by many theorists in that negative experience or fear of bad events might have a greater impact on people than neutral experiences or even positive experiences might (Baumeister et al., 2001; Vaish et al., 2008). Researchers then assumed that it is the reason for the bias that unpleasant stimuli can produce stronger emotional effects than pleasant stimuli (see review of Olofsson et al., 2008).

Large-scale studies provided a reasonably consistent evidence that *negative response bias* towards sadness existed in individuals with major depression, so that positive (happy), neutral, or ambiguous facial expressions were evaluated as more sad or less happy compared with healthy controls (see review of Bourke et al., 2010). Therefore, we would like to uncover if the underlying attentional bias is different in a healthy person compared to a person with depression. Gotlib et al. (2004) found that patients with depression exhibited specific bias to the emotion of sadness, while not to the angry or happy faces. As both angry faces and sad faces are negative stimuli, the mechanism of negative bias for normal person and participants with depression should be different. However, it is still uncertain whether this bias affects the whole brain networks. In our previous study, we used a face-in-the-crowd task to induce attention-modulation processing in depression, and we found hypoactivity in response to the positive face in the left frontal region and hyperactivity in response to the negative one in the right frontal region (Tang et al., 2011). However, we could not recognize the stimuli as sadness or anger as schematic faces were used in the study. Therefore, we applied a similar visual search for real facial expressions task for patients with MDD and healthy controls in this study.

In this work, we used EEG coherence to measure the correlations between all pairs of electrodes. The brain functional networks were established in individuals with depression and healthy controls, and the GTA was applied to study the network characteristics. Our hypothesis was that patients with depression, as the other neuropsychiatric diseases, might have an abnormal brain functional connectivity during emotional face processing compared with healthy controls. We therefore investigated the EEG's specific network features in different frequency bands, and we confirmed that the functional brain networks of depression were characterized by a loss of small-world features.

2. Materials and methods

2.1. Participants

The depressed group included 16 right-handed outpatients with depression (male/female = 6/10, 37.75 ± 14.19 years old, 12.06 ± 2.91 years of education) recruited from the Shanghai Mental Health Center (SMHC). All participants with depression