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Research report

Frequency-dependent alterations in regional homogeneity in major depression

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HIGHLIGHTS

- We investigated spontaneous neural activity in MDD patients in the special frequency band.
- The MDD patients showed increased ReHo in the MOG in the slow-4 band.
- The MDD patients showed decreased ReHo in the ACC, IFG, SFG, and bilateral thalamus in the slow-4 band.
- The MDD patients showed increased ReHo in the mPFC in the slow-5 band.

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ABSTRACT

Previous studies using resting-state functional magnetic resonance imaging (fMRI) have found abnormal spontaneous neural activity in patients with major depressive disorder (MDD). Yet, the frequency-dependent neural activity in MDD is largely unknown. Here, we used resting-state fMRI and regional homogeneity (ReHo) methods to investigate spontaneous neural activity in specific frequency bands of 31 MDD patients and 31 age-, gender- and education-matched healthy controls. We examined spontaneous neural activity in three frequency bands: slow-4 (0.027–0.073 Hz), slow-5 (0.010–0.027 Hz), and the typical band (0.01–0.08 Hz). Compared to controls, MDD patients showed increased ReHo in the middle frontal gyrus (MFG) and decreased ReHo in the fusiform and postcentral gyrus at the typical band. Importantly, MDD patients showed increased ReHo in the middle occipital gyrus (MOG) and decreased ReHo in the anterior cingulate cortex (ACC), inferior frontal gyrus (IFG), superior frontal gyrus (SFG) and the bilateral thalamus in the slow-4 band, while they showed increased ReHo in the medial prefrontal cortex (mPFC) in the slow-5 band. Our results suggest that the abnormality of ReHo in MDD is associated with the frequency band and that future studies should take frequency band effect into account when examining spontaneous neural activity.

1. Introduction

Major depressive disorder (MDD) is a common mental disorder that is characterized by persistent depressed mood, anxiety and dysphoria, psychomotor changes, alterations of motivation and social behavior, and sleep abnormalities [3]. MDD is often accompanied by deficits in cognitive control and abnormal emotional processing [5]. Advanced noninvasive neuroimaging technology, such as functional magnetic resonance imaging (fMRI), allows us to observe the functional brain abnormalities associated with MDD, and resting-state fMRI has been widely used in recent years to investigate abnormal spontaneous neural activity in MDD [6,9,11,19,29,40].

In contrast to task-based fMRI, resting-state fMRI does not require complex experimental designs that can remove some stimuli or task-related confounds. It provides a reliable measure of "baseline" brain activity and connectivity [14]. Regional homogeneity (ReHo) has been shown to be an effective index to measure

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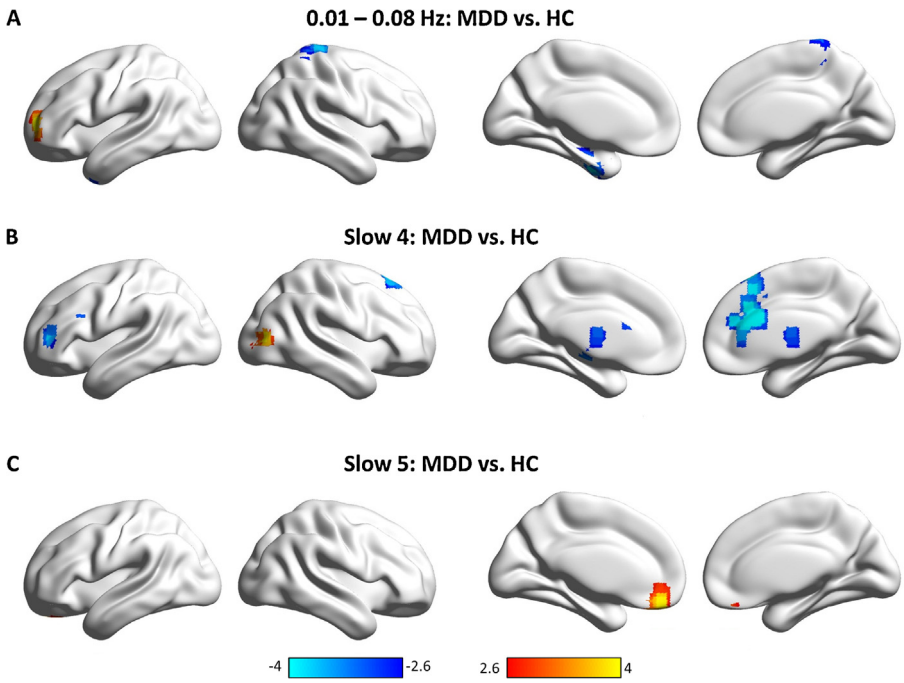

Fig. 1. Brain regions with abnormal ReHo in MDD. Red represents higher ReHo in the MDD patients than in the healthy controls, whereas blue represents lower ReHo. (A) Brain regions showing abnormal ReHo in the typical band (0.01–0.08HZ). (B) Brain regions showing abnormal ReHo in the slow-4 band. (C) Brain regions showing abnormal ReHo in the slow-5 band. All the clusters survived at $p < 0.05$, alphasim corrected (individual voxel threshold $p < 0.01$ and a minimum cluster size of 40). More details about the brain regions are described in Tables 2–4. (For interpretation of the references to color in this figure legend, the reader is referred to the web version of this article.)

spontaneous neural activity in resting-state fMRI analysis [36]. ReHo reflects the neural coherence of a given voxel with its nearest voxels in a voxel-wise analysis, which has been interpreted as "localized connectivity" [17,19]. Numerous studies that have explored spontaneous brain activity in MDD using the ReHo method have provided some evidence of brain abnormalities in MDD during rest [10–12,19,20,22,29,31,35]. For example, Guo et al. [11] found abnormal ReHo in regions of limbic-cortical networks in MDD, while Liu et al. [22] found decreased ReHo in the insula and cerebellum in MDD. Wu et al. [29] found that MDD patients showed high ReHo within temporo-limbic regions and low ReHo in the frontal, parietal, and fusiform cortex and the caudate. Moreover, a *meta*-analysis by Iwabuchi et al. [17] found that the medial prefrontal cortex (mPFC) showed the most reliable abnormalities in MDD.

Previous resting-state studies have examined MDD-related neural activity in the typical low frequency band (0.01–0.08 Hz). However, whether the abnormal ReHo in MDD is related to a specific frequency band is largely unknown. The aim of the present study was to investigate frequency-dependent alterations in ReHo in MDD. The main reason why we focused on frequency-dependent alterations was that different neural signals within different frequency bands might be generated by distinct oscillators that have specific properties and physiological functions [4,24]. The low frequency band can be subdivided into several bands: slow-5 (0.01–0.027 Hz), slow-4 (0.027–0.073 Hz), slow-3 (0.073–0.198 Hz), and slow-2 (0.198–0.25 Hz)] [4,24]. The slow-2 and slow-3 bands mainly reflect high-frequency physiological noise and white-matter signals, whereas the slow-4 and slow-5 bands reflect gray-matter signals [20,41]. Recently, Xue et al. [30] systematically explored the different characteristics of the slow-4 and slow-5 bands at regional and network levels. They found the slow-4 band exhibited higher ReHo in the superior frontal cortex, anterior cingulate cortex (ACC), the fusiform gyrus, and other areas, and the slow-5 band exhibited higher ReHo in the bilateral inferior frontal gyrus (IFG) and some midline structures, including the medial frontal cortex (mPFC) and the supplementary motor area (SMA). In addition, Wei et al. (2014) found that low frequency fluctuations in specific bands were associated with personality traits, which might imply that spontaneous brain activity is frequency-dependent. On the other hand, using this approach to investigate the neural activity of specific frequency bands (slow-4 and slow-5 bands) has been successful in detecting local abnormalities in different psychiatric disorders, such as Alzheimer's disease [21], schizophrenia [33,34], social anxiety [39], mild cognitive impairment [15], and Parkinson's disease [16,39]. To the best of our knowledge, no study has investigated specific frequency bands in MDD. Therefore, it would be useful to differentiate the frequency band specificity associated with MDD.

We sought to address this issue by examining the frequency-dependent neural activity in MDD during the resting-state. This is the first study, to our knowledge, to use ReHo as an index to investigate the spontaneous neural activity of specific frequency bands (slow-4 and slow-5 band) in MDD. We hypothesized that MDD patients would show abnormal ReHo in regions associated with cognitive control and emotional processing, and that these abnormalities would be associated with specific frequency bands. In addition, we also investigated ReHo in the typical frequency band (0.01–0.08 Hz) to identify potential frequency-dependent changes [34].

2. Materials and methods

2.1. Participants

This investigation recruited thirty-one depressed patients (eighteen female) who were outpatients at a Chongqing Medical University affiliated hospital. Thirty-one age-, gender-, and education-matched healthy subjects were recruited from students, government retirees, hospital staff, logistics staff, and other persons. Detailed demographic and clinical characteristics of the samples are shown in Table 1. All patients were diagnosed as suffer-