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Research report

Regional homogeneity in depression and its relationship with separate depressive symptom clusters: A resting-state fMRI study☆

Zhijian Yao [a,b,*], Li Wang [b], Qing Lu [c], Haiyan Liu [b], Gaojun Teng [a,*]

[a] *Department of Radiology, Zhong Da Hospital, School of Clinical Medicine, Southeast University, Nanjing, Jiangsu, China*
[b] *Department of Psychiatry, Nanjing Brain Hospital, Nanjing Medical University, Nanjing, Jiangsu, China*
[c] *Key Laboratory of Child Development and Learning Science, Ministry of Education Learning Science Research Center, Southeast University, Nanjing, Jiangsu, China*

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Abstract

Background: Using a newly reported regional homogeneity (ReHo) approach, we were to explore the features of brain activity of patients with major depressive disorder (MDD) in resting state, and further to examine the relationship between abnormal brain activity of depressed patients and specific symptom clusters derived from ratings on the Hamilton Rating Scale for Depression (HRSD).

Methods: 22 patients with MDD and 22 gender-, age-, and education-matched healthy subjects participated in the fMRI scans.

Results:

1. Compared with healthy controls, decreased ReHo were found in depressed patients in the right orbitofrontal cortex, the right fusiform gyrus, the right ventral anterior cingulate gyrus, the left dorsal anterior cingulate gyrus, the right posterior cingulate gyrus, the left lentiform nucleus and the right insula ($p<0.005$, uncorrected).
2. Anxiety severity was positively correlated with the ReHo in the right insula; Cognitive disturbance severity was positively correlated with the ReHo in the right orbitofrontal cortex and the left dorsal anterior cingulate gyrus; Retardation severity was positively correlated with the ReHo in the right posterior cingulate gyrus and the right insula; Sleep disturbance severity was positively correlated with the ReHo in the left dorsal anterior cingulate gyrus; Hopelessness severity was positively correlated with the ReHo in the right ventral anterior cingulate gyrus and the right insula ($p<0.05$).

Limitation: The influence of antidepressant medication to the brain activity of depressed patients was not fully excluded.

Conclusions: Our findings indicated abnormal brain activity was distributed extensively in depressed patients during resting state, and some symptom domains of depression are separately related to specific abnormal patterns of brain activity.

Keywords: Depressive disorders; fMRI; Regional homogeneity; Hamilton Rating Scale for Depression; Resting state

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* Corresponding authors. Yao is to be contacted at Department of Psychiatry, Nanjing Brain Hospital, Nanjing Medical University, Guangzhoulu 264, Gulou District, Nanjing 210029, Jiangsu, China. Teng, School of Clinical Medicine, Southeast University, Nanjing, 210009, China. Tel.: +86 25 83700011x6224; fax: +86 25 83719457.

E-mail addresses: yaozhijian@yahoo.cn (Z. Yao), gjteng@vip.sina.com (G. Teng).

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1. Introduction

Major depressive disorder (MDD) is a common mental disorder, which is characterized by persistent depressed mood, anxiety and dysphoria, psychomotor changes, alterations of motivation and social behavior, and sleep abnormalities (American Psychiatric Association, 1994). The pathogenesis of depression, however, remains unclear.

In the last decades, neuroimaging studies have greatly advanced our understanding of the pathogenesis of depression. Structural magnetic resonance imaging (MRI) studies have shown the abnormalities in various brain areas in depression, and it was presumed that there was abnormality of limbic–cortical–striatal–pallidal–thalamic circuit in depression (Sheline, 2003). Positron-emission tomography (PET) and signal photon emission computed tomography (SPECT) studies also identified the engagement of regions in that circuit in depression (Mayberg, 2003; Soares and Mann, 1997) within paradigms examining both emotional processes and cognitive functions such as attention, executive processing, working memory, or during resting state. However, the results of these studies were always, to some extent, different. This may be due to many factors. Among these, the variety of clinical manifestations may be an important factor, as has been indicated in previous studies (Soares and Mann, 1997; Périco et al., 2005). Exploring the relationships between the abnormality of brain activity and specific symptom clusters in depressed patients is necessary to explain the variety of results. More important, this exploration will be helpful in discovering the neural mechanisms underlying the specific symptoms, which may offer some cues for the diagnosis and treatment of depression.

Many studies have examined the association between the brain activities and depressive symptoms induced in normal subjects. Most of these studies paid attention to anxiety and transient sadness which are important symptoms of depression. In these studies, the induced anxiety was found to be associated with increased activity in the anterior cingulate gyrus (Javanmard et al., 1999; Kimbrell et al., 1999), the anterior insula and the inferior frontal gyrus (Kimbrell et al., 1999; Liotti et al., 2000), the anterior temporal lobe (Kimbrell et al., 1999) and the ventral prefrontal cortex (Liotti et al., 2000). In addition, the induced sadness was found to be associated with increased activity in the anterior cingulate gyrus and the insula (Liotti et al., 2000; George et al., 1995), and the ventral prefrontal cortex (Pardo et al., 1993).

Some studies have directly investigated the correlation between the brain activity of depressed patients and the depressive symptoms. Bench et al. (1993) reported a positive correlation between the anxiety severity and the regional cerebral blood flow (rCBF) in the bilateral posterior cingulate gyrus and the inferior parietal lobule, as well as a positive correlation between cognitive performance and the rCBF in the left medial prefrontal cortex; Conversely, depressed mood and psychomotor retardation were correlated negatively with the rCBF in the left dorsolateral prefrontal cortex and the left angular gyrus. Dolan et al. (1994) found a positive correlation between cognitive performance and the rCBF in the bilateral medial prefrontal cortex and the anterior cingulate gyrus. Graff-Guerrero et al. (2004) reported that some items of the Hamilton Rating Scale for Depression (HRSD), widely used to measure depression severity, were correlated with the rCBF of some regions such as the anterior prefrontal cortex, the temporal lobe, the cingulate cortex, and the insula. Périco et al. (2005) reported that depressive mood was correlated negatively with the rCBF in the left amygdala, the lentiform nucleus, and the parahippocampal gyrus, and correlated positively with the rCBF in the right postero-lateral parietal cortex; Anxiety severity was correlated positively with the rCBF in the right antero-lateral orbitofrontal cortex; Insomnia severity was correlated negatively with the rCBF in the right subgenual and the rostral anterior cingulate gyrus, the insula and the claustrum; Cognitive performance was correlated positively with the rCBF in the right postero-medial orbitofrontal cortex and the left lentiform nucleus.

However, the imaging method these studies used was SPCET, and previous resting studies in depression mainly used PET and SPECT, both of which have some significant limitations including exposure to radioactive tracers and poor spatial resolution. FMRI overcomes these limitations to a large extent. Since the first study performed by Biswal et al. (1995), resting-state fMRI has attracted more attention. But to our knowledge, only two resting-state fMRI studies were conducted on depression. Anand et al. (2005) reported cortico-limbic low-frequency blood fluctuations correlations were decreased in depression in resting state. Greicius et al. (2007) reported resting-state subgenual cingulate and thalamic functional connectivity with the default-mode network were higher in depression. The method for data analysis these studies used was correlation analysis which can only measure the correlation of time series between brain areas. When correlation was found abnormal, one couldn't determine which area was out of norm. Also, no study has yet investigated the relationship between brain activity and depressive symptom clusters in resting state using fMRI.