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Review Article

Functional Magnetic Resonance Imaging in the Study of Depression: One Side of a Coin

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ABSTRACT

Depression, as one kind of common neuropsychiatric disorder, has made great economic and social burden worldwide. A great number of studies regarding multiple aspects of depression using distinct techniques including positron emission tomography (PET), electroencephalogram (EEG) and the functional magnetic resonance imaging (fMRI) were performed to uncover the pathogenesis of depression, so as to provide valuable evidence for the clinical therapy of depression. Among these distinct techniques, the fMRI, as a relatively powerful approach depending on defining activity in human brain reflected by the changes in regional blood perfusion, blood volume as well as blood oxygenation, becomes popular in the clinical diagnosis of depression in recent years. In this short review, we concisely summarize the advantages of fMRI in characterizing depressive symptoms. It is indicated that the fMRI could be used to distinguish between different types of depression or to identify healthy subjects at risk of depression. In addition, we also strengthen the fact that, just as one side of a coin, the fMRI also has its disadvantages. For example, longitudinal studies of depression involve the collection of fMRI data are costly, time-consuming and also complicated for the data analysis. Moreover, the fMRI is, more or less, still limited in both the temporal and spatial resolution pertaining to data collection. Collectively, it is suggested that though the fMRI is generally considered as a relatively powerful and also a good candidate technique during the diagnosis of depression, much more considerations should be seriously taken into account when using fMRI as a main technique to perform studies regarding depression, and some other research which may also involve the fMRI.

INTRODUCTION

Depression is a common neuropsychiatric disorder and has made huge economic and social burden worldwide [1]. A great number of studies regarding multiple aspects of

depression were performed to uncover the pathogenesis of depression, and in the end, to provide valuable evidence for the clinical therapy of depression [2-12]. It is worthy to note that, in the past few decades, multiple techniques including positron emission tomography (PET) [13], electroencephalogram (EEG) [14] and the functional magnetic resonance imaging (fMRI) [15] have emerged, which has greatly increased the efficiency and acuity in deciphering the mechanism underlying depression. As one of these techniques, the fMRI is a relatively powerful approach in the diagnosis of depression depending on defining activity in human brain reflected by the changes in regional blood perfusion, blood volume as well as blood oxygenation [15]. A plethora of fMRI studies on depression come out in recent years [16-19], which has remarkably promoted the development of fMRI application in the study of neuropsychiatric disorders including depression.

Application of the fMRI in the diagnosis of depression

The fMRI could be used to identify patients with depressive symptoms. In one historic study, ten unmedicated women who had recovered from major depression and eight healthy controls each receives either noxious hot or non-noxious warm stimuli, during which the brain activity is monitored by the fMRI [20]. The result shows that the brain activation exhibits similar patterns during painful stimulation for both patients and healthy controls. In contrast, relative to healthy women, women recovered from depression exhibit a reduced response in the cerebellum during anticipation of the noxious stimulus compared with anticipation of the non-noxious stimulus. This study implies that abnormal cerebellar function could be considered as a marker of vulnerability to recurrent depression. In addition, by performing the fMRI to measure activities in lateral prefrontal cortex (PFC) and parietal brain regions of women with mild to moderate symptoms of depression, it is indicated that impaired engagement of these brain areas are associated with depressive symptoms during cognitive control of emotional information [21]. Thus, studies like this depending on the fMRI could be used to distinguish between different types of depression or to identify healthy subjects at risk of depression. Interesting, it is worthy to be noted that event-related fMRI is commonly used to investigate the interactive and distinct effects of sex and major depressive disorder on neural activity during a facial emotion perception task [22]. The fMRI results identify an interaction between sex and diagnosis for sad and neutral facial expressions in the superior frontal gyrus and left middle temporal gyrus. It also indicates an interaction of sex with diagnosis in the amygdala. These findings, to some extent, further strengthen the relatively strong powerfulness of fMRI in the diagnosis of depressive phenotypes. Another advantage of fMRI in characterizing depressive symptoms is highlighting the abnormal connectivity between different brain regions. One recent study has been performed to examine abnormal cognition connectivity network in major depressive disorder within the whole brain [23]. It is confirmed that there are differences in cognition connectivity network during early stage of major depressive disorder, as identified by increased functional connectivities among part of frontal gyrus, parietal cortex, cingulate cortex, and certain areas with left dorsolateral prefrontal cortex, further suggesting that abnormal connectivities among distinct brain areas might be involved in the underlying mechanisms of cognitive dysfunction in depression. In addition, there is study using fMRI to investigate functional connectivity during reappraisal of a real-life source of stress in depressed and non-depressed adolescents. It shows that reappraisal could similarly reduce negative mood and belief in negative thoughts in both groups. In contrast, compared to non-depressed adolescents, depressed adolescents exhibit greater connectivity between the right frontal pole and numerous subcortical and cortical regions during reappraisal trials [24]. Though the fMRI is generally considered as a relatively powerful and also a good candidate technique during the diagnosis of depression, we should keep in mind that the some aspects should be seriously taken into consideration when performing the fMRI.

Potential considerations when performing depression studies using fMRI

The crucial role of fMRI in the diagnosis of depression is undoubted. However, this is actually only one side of a coin. The other more exciting and meaningful prospect of fMRI will be to tie this technique more closely to therapy development and testing of depression. In fact, longitudinal studies of depression involve the collection of fMRI data at multiple time points have become increasingly popular because they allow scientists/physicians to explore and track changes in brain structure and function over time within individuals. For

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depression patient or people with potential depressive symptoms, longitudinal studies depending on fMRI are actually advantageous in monitoring changes over time and identifying predictors of change, which has a greater ability in distinguishing between and within-individual variation [25]. Though there are great advantages of longitudinal studies regarding depression using fMRI, some factors should be taken into consideration [26]. First, it is costly, time-consuming and also complicated. Second, much more attention is needed to pay on the design of fMRI tasks pertaining to testing depressive symptoms. Last, but not the least, analyses of longitudinal fMRI data regarding depression is complicated because of the nested nature of the data. This implies that combing longitudinal depression studies depending on fMRI with some other cutting edge techniques will be one possible direction deserved to pursue in the future research.

Perspectives of the application of fMRI

In the last few decades following rapid technological advances, great improvements have been made in fMRI in the identification of depressive symptoms, for example, the ultra-high field fMRI makes it possible for investigating correlates of neuronal population activity at an increasing spatial resolution [27]. Though the fMRI can delineate relatively detailed spatial patterns of activity in distinct brain areas, it has tremendously poor temporal resolution [28-30] when compared with electrophysiological recordings. For a great number of depression studies, however, much more still need to be understood about brain function at the neural circuit level as well as the individual neuronal level under the depressive state which, to some extent, the fMRI is still limited in these aspects regarding both the temporal and spatial resolution. Just as a coin has its two sides, the fMRI also has its limitations during the investigation of depression. More efforts are still needed to improve the temporal resolution accompanied with a high spatial resolution, and much more considerations also should be taken into account when performing studies regarding depression, and possibly some other research which may also involve the fMRI.

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