Spontaneous Hemodynamic Activity in Prefrontal Cortex of Depression Patients Assessed with Functional Near-infrared Spectroscopy

Jiangxue Li[1], **Huilin Zhu**[2,*], **Xinge Li**[2,4], **Hongjun Peng**[3], **Jie Xu**[2], **Tingting Cai**[2], **and Sailing He**[2]

[1]The Research Center of Psychological Counseling
South China Normal University (SCNU), 510006, China
[2]Centre for Optical and Electromagnetic Research, South China Academy of Advanced Optoelectronics
South China Normal University (SCNU), Guangzhou 510006, China
[3]The Department of Clinical Psychology, Guangzhou Brain Hospital
(Guangzhou Huiai Hospital, The Affiliated Brain Hospital of Guangzhou Medical School), China
[4]School of Psychology, South China Normal University (SCNU), Guangzhou 510631, China

Abstract— Patients with major depressive disorder (MDD) typically suffered from pervasive depressed mood or anhedonia, accompanied by several cognitive and physical symptoms. In this study, functional near-infrared spectroscopy (fNIRS) was applied to investigate the spontaneous activity of hemodynamic in the prefrontal cortex (PFC) of the brain. 21 patients with MDD (including 12 with antidepressant and 9 without medication) participated in 8-min resting state measurement. By analyzing the interhemispheric correlation and the correlation maps of the PFC, our results indicated that patients with MDD showed significantly reduced interhemispheric correlation in the PFC and disrupted cortical organizations in the PFC. This study showed that fNIRS could be an effective and convenient way to assess neural features of depression.

1. INTRODUCTION

Functional near infrared spectroscopy (fNIRS), as an optical method for brain imaging, measures cerebral hemodynamic parameters reflecting the neural activity of the brain. fNIRS has high temporal resolution (∼ms) and reasonable spatial resolution (∼cm). By providing a non-invasive and convenient imaging environment, it can be easily applied not only in laboratory, but also in clinical studies. During the 20-years' development, fNIRS was considered to have great potential in clinical populations [1], such as patients with depression.

Patients with major depressive disorder (MDD) typically suffered from pervasive depressed mood or anhedonia, accompanied by several cognitive and physical symptoms. Since patients with depressions usually show heterogeneous symptoms (i.e., emotion, cognition, sleep), it has been proposed that depression are associated with dysfunction of a brain network rather than a single area of the brain. As part of the affection network (including the prefrontal cortex, limbic system and so on) of the brain, the prefrontal cortex showed to play an important role in MDD. Many previous neuroimaging studies on depression have reported dysfunctions in the prefrontal cortex (PFC). A study found patients with MDD exhibit reduction of serotonin in the PFC [2]. Functionally, a study revealed that the ventromedial and dorsolateral areas of PFC were associated with depression, although with distinct functions [3]. Also, another study has found that, in order to achieve a similar level of performance with controls, patients with depression showed hyper-activation in the PFC [4]. Besides, by using positron emission tomography (PET) [5, 6], patient with MDD displayed an atypical metabolism pattern in the prefrontal lobe of the brain, manifesting as reduced metabolism in the lateral prefrontal area and a increased metabolism in the medial prefrontal and subgenual cingulate. Increasing studies have confirmed that PFC played a key role in the neural mechanisms of depression.

Recent years, fNIRS has been increasingly applied to investigate the brain function of clinical populations, such as patients with anxiety, major depression (unipolar) and manic-depressive (bipolar) disorder. One fNIRS study [7] has revealed that, in contrast with controls, patients with unipolar and bipolar depression both displayed decreased activation in ventro-lateral, dorsolateral prefrontal and superior frontal cortex. A fNIRS study [8] found that the PFC played a significant role in anxiety and depression: participants with higher anxiety levels showed a more right-dominant PFC activity at resting-state. Another fNIRS study on patients with post-disaster

*Corresponding author: Huilin Zhu (huilin.zhu@coer-scnu.org).

depression showed that there was a correlation between depressivity and the level of right hemisphere oxygenation [9]. By now, there is no report of brain spontaneous activity from patient with MDD using fNIRS. Therefore, the present study proposed to employ fNIRS to investigate the spontaneous hemodynamic activity in the PFC and revealed the specific role of the PFC in the patients with MDD.

2. MATERIALS AND METHODS

2.1. Participants and Experiment Protocol

Participants with MDD were 21 adults (8 males, 13 female; mean age 24.29 ± 4.81, mean years of education 14.14±2.22,) recruited from the patients of Guangzhou Brain Hospital. Typical developed participants were 15 demographically similar adults (9 males, 6 females, mean age 25.86 ± 2.90, mean years of education 16.20 ± 0.67,). There was no significant difference in age or sex but significant difference in education. Thus the years of education was used as a covariate in analysis to control its effects on the results. All of the participants were right handed. Participants with MDD were recruited if they met the following criteria: (1) a diagnosis of MDD within 6 months according to the fourth edition of diagnostic and statistical manual (DSM-IV) and administered by experienced psychiatrists; (2) no comorbidity with other disorders in axis-1 of DSM-IV; (3) exclusion from neurological disorder or brain injury by examination with electroencephalo-graph, PET, and MRI for each participant. The diagnosis was confirmed by the Zung Depression Rating Scale (59.92 ± 8.83) [10]. Among the participants with MDD, 12 of whom were in the treatment with antidepressants for minimum 2 weeks (named as MDD 1), 9 of whom were free of psychotropic medication for minimum 6 months (named as MDD2). There was no significant difference between MDD1 and MDD2 in term of the self reported level of depression (scores of Zung Depression Rating Scale). During the experiment, participants were informed to sit still in a comfortable sofa and try to relax and closed eyes without doing or thinking anything particular and moving the head.

2.2. NIRS Measurements

Measurements were performed with a fNIRS system (FOIRE-3000, Shimadzu Corporation, Kyoto, Japan) working at three wavelengths, 780 nm, 805 nm and 830 nm with a sampling rate of 11.764 Hz. The distance between the emitter and detector was fixed at 3 cm. The measured brain regions and channel configurations were shown in Figure 1.

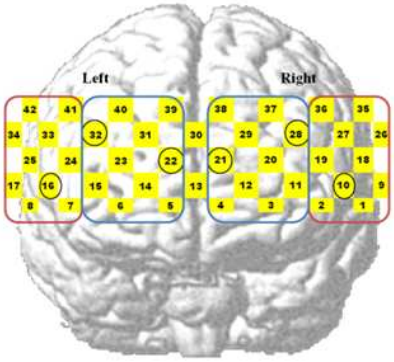

Figure 1: 42 channel covered the prefrontal cortex of the brain. We used the international 10-10 system to locate: Channel 13 and 26 were located in FPZ and APZ, respectively; Channels with black circles were chosen as the seeds for correlation maps. For region of interests (ROI), channels boxed with red lines were mostly located in the bilateral inferior frontal cortex (IFC) and those boxed with blue lines were mostly located in the superior frontal cortex (SFC) and the middle frontal cortex (MFC).

2.3. Data Analysis

Both HbO and Hb data were included in analysis. First of all, a band pass filtered between 0.009 and 0.08 was used to remove physiological noise and signals beyond our study [11]. In terms of interhemispheric correlations, we calculated the Pearson correlation coefficient r between the time course of each channel and the corresponding symmetrical channel in the other hemisphere from the chosen ROI (IFC, SFC & MFC in this study) and then averaged all possible seeds in each ROI. For correlation maps, we chose 6 channels as the seeds (3 seeds in each hemisphere, see Figure 1)

and calculated the correlation coefficient r between the time courses of the seed and the time course of all other channels. Then, the correlation values between the seed and other channels were projected onto the channel geometry and interpolation was employed to fill the blank areas between adjacent channels. The average correlation values for each group were estimated by converting r values to z values with Fisher's r-z transformation for each participant, and then converting back to the averaged z values to obtain the averaged r values. In statistic analysis, we used Bonferroni correction to counteract Type I errors caused by multiple comparisons.

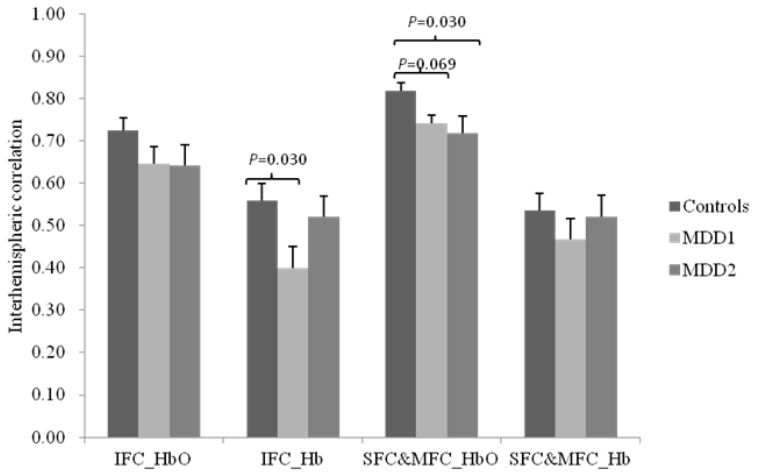

Figure 2: Interhemispheric correlation in ROIs of patients with major depression disorder in treatment with antidepressants (MDD1, $n = 12$), patients with major depression disorder without treatment by any antipsychotic (MDD2, $n = 9$) and controls ($n = 15$). Error bars are standard error of mean across participants. Compared with controls, MDD1 showed significantly reduced interhemispheric correlation in IFC (Hb) and marginally significantly reduces interhemispheric correlation in SFC & MFC (HbO), and MDD2 showed significantly reduced interhemispheric correlation in in SFC & MFC (HbO).

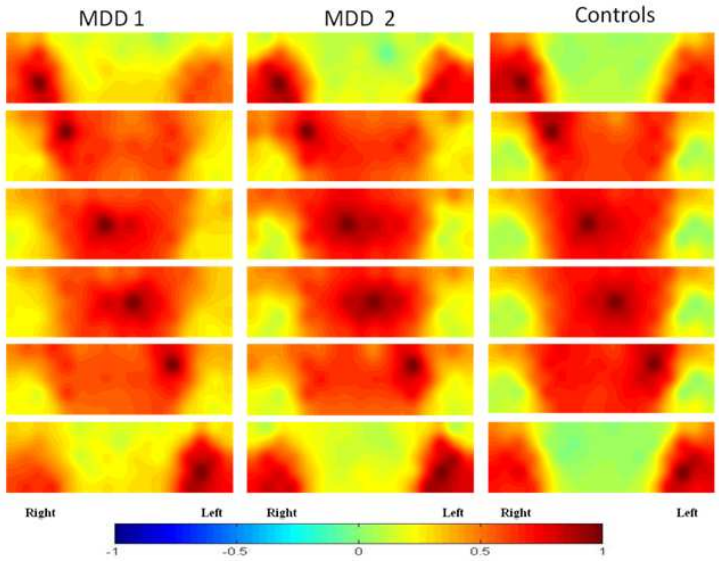

Figure 3: HbO correlation maps (the frontal view of the brain as in Figure 1) for patients with major depressive disorder in treatment with antidepressants (MDD1), patients with major depressive disorder without treatment with any antipsychotic (MDD2) and controls. The selected seeds (Channel 16, Channel 22, Channel 32 in the left hemisphere and Channel 10, Channel 21, Channel 28 in the right hemisphere) could be visually recognized by the maximal red value in each map.

3. RESULTS

Figure 2 shows the averaged interhemispheric correlation for each group. We used a General Linear Model to analyze the effect of groups (between subject factors) on the strength of interhemispheric correlation in the PFC, years of education was used as covariate. Results were shown in Figure 2.

To visualize the results, Figure 3 gives the correlation maps (HbO) for each group, separating by different seeds' locations: 3 seeds in each hemisphere. From Figure 3 (maps for controls), we could see the pattern of cortical organization of the PFC: The bilateral IFC were more functionally connected with each other (Network 1) and the bilateral SFC and the bilateral MFC was more functionally connected with other (Network 2). However, these two networks were mutually independent. Compared with controls, patients with MDD showed obviously disrupted brain network in the prefrontal cortex of the brain. Furthermore, patients with MDD who were in the treatment with antidepressant showed more disorganized brain network than patients with MDD without treatment of any antipsychotic.

4. DISCUSSION

In the present study, we employed fNIRS to detect the spontaneous hemodynamic activity of the PFC of patients with MDD. By analyzing the interhemispheric correlation and maps of functional connectivity, the results revealed that, whether in the treatments of antidepressant or not, patients with MDD showed reduced interhemispheric correlation and a disrupted organization of brain network in the PFC of the brain. In line with previous studies [3], we found the correlation between the function of the PFC and depression. Furthermore, we observed that antidepressant might have effect on the cortical organization of the prefrontal lobe.

In our study, there were two cortical networks in the prefrontal cortex. The ventromedial sectors of the PFC (including the bilateral IFC) were related to the emotion of affection, whereas the dorsolateral sectors of the PFC (including the bilateral SFC and the bilateral MFC) were related to the attention and the executive function. These two sectors of the PFC made up the critical but functionally different substrates underlying depressions [3]. Thus, pattern of the cortical organization of the PFC was an important feature to recognize the neural pathophysiology of the depression.

The limitation of the present study was that we could not clearly distinguish the effect of antidepressant and the effect of the severity of the symptom. Even though the MDD patients with or without medication reported the similar level of depression, the MDD patients in treatment would have more severity of the depression than the MDD patients without treatment. More systematic assessment should be involved in the future studies.

5. CONCLUSION

In summary, by using fNIRS to investigate the spontaneous activity of hemodynamic in the PFC of the brain and analyzing the interhemispheric correlation and the correlation maps of the PFC, we discovered that patients with MDD exhibited significantly reduced interhemispheric correlation and disrupted cortical organizations in the PFC. Our study also suggests that fNIRS is a feasible and effective technique to assess the neural features of depression.

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