Progress in Neuro-Psychopharmacology & Biological Psychiatry 58 (2015) 51–58

Contents lists available at ScienceDirect

Progress in Neuro-Psychopharmacology & Biological Psychiatry

Reduced prefrontal activation during a verbal fluency task in Chinese-speaking patients with schizophrenia as measured by near-infrared spectroscopy

Wenxiang Quan [a,b,c,1], Tongning Wu [d,1], Zhaohua Li [e], Yuduo Wang [e], Wentian Dong [a,b,c,*], Bin Lv [d,**]

[a] Peking University Sixth Hospital, Beijing, China
[b] Peking University Institute of Mental Health, Beijing, China
[c] Key Laboratory of Mental Health, Ministry of Health (Peking University), Beijing, China
[d] China Academy of Telecommunication Research of Ministry of Industry and Information Technology, Beijing, China
[e] School of Information and Communication Engineering, Beijing Information Science and Technology University, Beijing, China

ARTICLE INFO

Article history:
Received 12 August 2014
Received in revised form 16 December 2014
Accepted 17 December 2014
Available online 24 December 2014

Keywords:
Chinese version verbal fluency test
Near-infrared spectroscopy (NIRS)
Prefrontal cortex
Schizophrenia

ABSTRACT

Near-infrared spectroscopy (NIRS) has been applied to examine the possible functional alternations during the performance of cognitive tasks in schizophrenia. With this technique, previous studies have observed that patients with schizophrenia are often associated with reduced brain activation in the prefrontal cortex during the verbal fluency task (VFT) of the English version or the Japanese version. However, it remains unclear whether there is a brain functional impairment in Chinese-speaking patients with schizophrenia. In this study, we designed a Chinese version of the VFT and performed a multichannel NIRS study in a large group of patients with schizophrenia and healthy controls. We investigated brain activation during the task period of the Chinese version of the VFT within a schizophrenia group and a healthy group, respectively, and compared the relative changes between the two groups. Our results confirmed that Chinese-speaking patients with schizophrenia had significantly lower brain activation in the prefrontal cortex and superior temporal cortex when compared with healthy controls. Such findings based on the NIRS data provided us reliable evidences about brain functional deficits in the Chinese-speaking patients with schizophrenia.

1. Introduction

Schizophrenia is a psychiatric disorder which is characterized in general by the disruption in cognitive behavior and the incoordination of affective reaction (American Psychiatric Association, 2000). Besides these impairments in external performance, recent neuroimaging studies have demonstrated that patients with schizophrenia are often associated with the abnormalities of brain structure and function, especially in the prefrontal cortex (Lynall et al., 2010; Manoach et al., 2000; Narr et al., 2005; Palaniyappan et al., 2011; Steen et al., 2006; Weiss et al., 2004). With structural magnetic resonance imaging (MRI), converging evidences have revealed the structural changes of prefrontal cortex in schizophrenia including brain volume atrophy (Steen et al., 2006), cortical thickness thinning (Narr et al., 2005) and gyrification reduction (Palaniyappan et al., 2011). In addition, more and more studies have utilized functional neuroimaging technologies, e.g., functional MRI (fMRI), to investigate brain functional activation during the resting state (Lynall et al., 2010) as well as various cognitive tasks (Weiss et al., 2004). These results provided us imaging observation on the dysfunction of prefrontal cortex in patients with schizophrenia.

Near-infrared spectroscopy (NIRS) is another promising and noninvasive functional neuroimaging technique which can measure the concentration changes of oxygenated hemoglobin ([oxy-Hb]) and deoxygenated hemoglobin ([deoxy-Hb]) near the brain surface (Ferrari and Quaresima, 2012). The NIRS signals ([oxy-Hb] and [deoxy-Hb]) are considered to reflect regional cerebral blood volumes and show strong correlations with fMRI signals (Sasai et al., 2012). Compared with fMRI, NIRS is more portable and less sensitive to motion artifacts. These advantages make it more suitable for the assessment of speech related tasks in schizophrenia (Ehlis et al., 2014; Ferrari and Quaresima, 2012). The verbal fluency task (VFT) is a common language

Abbreviations: BA, Brodmann's area; [deoxy-Hb], relative concentration of deoxygenated hemoglobin; FDR, false discovery rate; MRI, magnetic resonance imaging; NIRS, near-infrared spectroscopy; [oxy-Hb], relative concentration of oxygenated hemoglobin; [total-Hb], relative concentration of total hemoglobin; VFT, verbal fluency task

* Correspondence to: W. Dong, Peking University Sixth Hospital. No. 51, Huayuanbei Road, Haidian District, Beijing 100191, China. Tel.: +86 10 82805966; fax: +86 10 62026310.
** Correspondence to: B. Lv, China Academy of Telecommunication Research of Ministry of Industry and Information Technology, No. 52, Huayuanbei Road, Haidian District, Beijing 100191, China. Tel.: +86 10 62304633 2084.
E-mail addresses: dongwentian@bjmu.edu.cn (W. Dong), lvbin@catr.com (B. Lv).
[1] These authors contributed equally to the work.

http://dx.doi.org/10.1016/j.pnpbp.2014.12.005
0278-5846/

related neuropsychological task and patients with schizophrenia are associated with profound impaired verbal fluency (Dieler et al., 2012). Therefore, we can infer that schizophrenia has a risk of abnormal brain functional activation during the performance of a VFT. By means of NIRS, previous studies have indicated that schizophrenia patients had different changes in [oxy-Hb] than those of healthy controls during the VFT, although the brain regions showing abnormal activation are not always consistent (Koike et al., 2013). Watanabe et al. applied one channel NIRS system to investigate the cerebral hemoglobin response in 62 schizophrenia patients and 31 healthy controls (Watanabe and Kato, 2004). They described for the first time that patients with schizophrenia had reduced [oxy-Hb] in the left prefrontal cortex during the VFT. Till now, their sample size for schizophrenia patient is the largest in related NIRS studies (Koike et al., 2013). Then, Suto et al. described the spatial–temporal patterns of NIRS activation in the prefrontal and temporal cortices using two 24 multichannel NIRS systems (Suto et al., 2004). Their results on 13 schizophrenia patients and 16 healthy controls revealed that schizophrenia patients had lower NIRS activation in the bilateral prefrontal and temporal cortices at the start of the VFT task period. This dysfunction was further confirmed in a relatively large group (including 55 schizophrenia patients and 70 healthy subjects) (Takizawa et al., 2008). In addition, the delayed cortical activation was also detected particularly in the frontopolar region (Takizawa et al., 2008). By comparing the performance of phonological VFT and semantic VFT, the more pronounced cortical activation was observed during the phonological VFT compared to the semantic VFT in both schizophrenia patients and healthy controls, and their induced activations in schizophrenia patients were all significantly reduced than those in healthy controls (Ehlis et al., 2007). These findings demonstrated that it seems a reliable biomarker that patients with schizophrenia had significantly less frontal activation during performance in the VFT. However, most of these NIRS studies were conducted on Japanese-speaking (Suto et al., 2004; Takizawa et al., 2008; Watanabe and Kato, 2004) or English-speaking populations (Ehlis et al., 2007), and few studies have been performed in Chinese-speaking people, even for healthy subjects. A recent study demonstrated the effect of languages on the performance of the VFT using Japanese, Turkish, and English-speaking patients with schizophrenia (Sumiyoshi et al., 2014). Therefore, we need to investigate the response pattern of NIRS activition during the Chinese version VFT in healthy controls and its possible alternation in patients with schizophrenia.

In the present study, we designed a Chinese version VFT and recruited a large group of native Chinese speakers to perform this cognitive task. The group included 140 patients with schizophrenia and 100 healthy controls. Then, a 52 multichannel NIRS system was used to examine the hemodynamic signals in the bilateral prefrontal and superior temporal cortices during the performance of the Chinese version VFT. Our aim was to evaluate the NIRS cerebral response pattern along with the Chinese version VFT and compare the brain activation between patients with schizophrenia and healthy controls. We hypothesized that the Chinese-speaking patients with schizophrenia had an altered brain activation compared to healthy controls during the designed Chinese version VFT.

2. Methods

2.1. Subjects

One hundred and sixty-five schizophrenia patients and 100 healthy comparison subjects took part in this study. 25 schizophrenia patients were excluded from further analysis because of incomplete collection/obvious noise (19 patients) or handedness issue (6 left-handed patients). The final sample comprised 140 schizophrenia patients (male/female: 80/60, age: range 17–62 years, mean 33.81 ± 11.52 years) and 100 healthy subjects (male/female: 65/35, age: range 18–78 years, mean 34.43 ± 12.36 years), and they were all right-handed (Table 1). On education background, the schizophrenia group included 14 graduate degrees, 63 undergraduate degrees and 63 high school degrees, and the healthy group included 20 graduate degrees, 44 undergraduate degrees and 36 high school degrees. All participants were native speakers of the Chinese language and can read the Chinese language.

Schizophrenia patients were recruited from Peking University Sixth Hospital. Each patient was diagnosed independently by two clinical psychiatrists (W.X. Quan and W.T. Dong) according to the Structured Clinical Interview for DSM-IV (American Psychiatric Association, 2000). Their age at onset was 24.25 ± 9.05 years, and the duration of illness was 9.56 ± 7.52 years. The chlorpromazine equivalent doses ranged from 56 mg to 1 575 mg daily (mean dose: 484.06 ± 240.04 mg/day). The healthy subjects were enrolled through the local community. Prior to attending the experiment, they were all interviewed to confirm that they had no history of neurological or psychiatric diseases. All schizophrenic and healthy subjects provided written informed consent after the experimental procedure had been fully explained. This study was approved by the ethics committee of Peking University Sixth Hospital.

2.2. Task description

We designed a Chinese version of phonological VFT which was similar to a previous study (Chan and Chen, 2004). Participants were asked to sit in a comfortable chair with their eyes open and minimize head movements during the measurements. In order to reduce any possible distractions, the experiment needs to be performed under a quiet environment and participants should keep their mood stable for some time prior to the task.

The task paradigm consisted of a 30-s pre-task baseline period, a 60-s task period and a 30-s post-task baseline period. There was a computer screen in front of the participant with a distance of 1 m. Before the pre-task baseline period of the VFT, we provided one Chinese character ('门', which indicates door) as an example to make each participant understand how to perform the experiment. During the pre-

Table 1
Demographic characteristics of study participants in each group.

	Healthy controls	Patients with schizophrenia	Group difference *p*-value
N	100	140	
Age, year	34.43 ± 12.36	33.81 ± 11.52	0.72
Handedness, right-/left-handed	100/0	140/0	
Gender, male/female	65/35	80/60	0.22[a]
Education background, graduate/undergraduate/high school degrees	20/44/36	14/63/63	0.07[a]
Age of onset, year	–	24.25 ± 9.05	
Duration of illness, year	–	9.56 ± 7.52	
Chlorpromazine equivalent dose, (mg/day)	–	484.06 ± 240.04	
VFT performance	11.29 ± 4.50	9.05 ± 3.90	<0.05

[a] Chi-square test was used for testing group difference. Otherwise, *t*-test was used.