Contents lists available at ScienceDirect

Psychiatry Research: Neuroimaging

Self-reported social functioning and prefrontal hemodynamic responses during a cognitive task in schizophrenia

Shenghong Pu [a,*], Kazuyuki Nakagome [b], Masashi Itakura [a], Takehiko Yamanashi [a], Takuya Sugie [a], Akehiko Miura [a], Takahiro Satake [a], Masaaki Iwata [a], Izumi Nagata [a], Koichi Kaneko [a]

[a] Division of Neuropsychiatry, Department of Brain and Neuroscience, Tottori University Faculty of Medicine, 36-1 Nishi-cho, Yonago, Tottori 683-8504, Japan
[b] National Center of Neurology and Psychiatry, 4-1-1 Ogawa-Higashi, Kodaira, Tokyo 187-8551, Japan

ARTICLE INFO

ABSTRACT

Impaired social functioning is a characteristic of schizophrenia that affects patients' quality of life. The aim of the study was to assess prefrontal hemodynamic responses during a cognitive task and establish its influence on psychiatric symptoms, cognitive function, global functioning, and self-reported social functioning in patients with schizophrenia. Thirty-three patients with schizophrenia and 30 age-and sex-matched healthy controls participated in the study. We measured hemodynamic responses in the pre-frontal and superior temporal cortical surface areas with 52-channel near-infrared spectroscopy (NIRS) during a verbal fluency task (VFT). Self-reported social functioning was assessed using the Social Func-tioning Scale (SFS). Regional hemodynamic responses were significantly smaller in the prefrontal and temporal regions in subjects with schizophrenia than in the controls, and prefrontal hemodynamic re-sponses during the VFT showed a strong correlation with SFS total scores. These results suggest an as-sociation between self-reported social functioning and prefrontal activation in subjects with schizo-phrenia. The present study provides evidence that NIRS imaging could be helpful in understanding the neural basis of social functioning.

1. Introduction

Patients with schizophrenia have reduced cognitive function and therefore exhibit impairment in everyday social functioning. This phenomenon was described a century ago in the earliest clinical reports of schizophrenia (Hooley, 2010). Social dysfunction is a hallmark characteristic of schizophrenia that has important implications for the development, course, and outcomes of the disease (Couture et al., 2006). Impaired social functioning often worsens the disease course and contributes to relapse (Pinkham et al., 2003).

Social functioning is instrumental to patient quality of life (QOL), and it requires complex operations of various executive functions, including monitoring, reasoning, organizing, selecting, and plan-ning. The neural basis of executive function lies in the prefrontal cortex (PFC), which is also critical for other high-level cognitive functions. Considering the significance of social functioning im-pairment in subjects with schizophrenia, elucidating the relation-ship between neural activity in the PFC and social functioning is an important goal that could lead to improved patient QOL.

Multichannel near-infrared spectroscopy (NIRS), a functional neuroimaging technology widely used in recent years, can measure the hemodynamics over the surface of the cortices of the bilateral frontotemporal regions (Heinzel et al., 2013; Strangman et al., 2002a). This technique enables the detection of spatiotemporal characteristics of brain function by measuring the concentrations of oxy-hemoglobin (oxy-Hb) and deoxy-hemoglobin (deoxy-Hb), which are assumed to reflect the regional cerebral blood volume as demonstrated by good correlations with functional magnetic re-sonance imaging (fMRI) signals (Sato et al., 2013). NIRS has several advantages over existing imaging techniques, such as positron emission tomography (PET), single photon emission computed to-mography (SPECT), and fMRI, because it is noninvasive, without using any radioactive substances, and is easy to administer, tolerates small movements, is inexpensive, and provides excellent time re-solution (Ferrari and Quaresima, 2012). Meanwhile, it also contains disadvantages such as its poor spatial resolution, and the fact that it could not measure the deeper layer of the brain.

NIRS measurement during a verbal fluency task (VFT) was re-cently approved by the Ministry of Health, Labor, and Welfare of Japan as an advanced medical technology for the aid of differential diagnosis of depressive state psychiatric illnesses and has been

frequently applied in clinical settings in Japan (Takizawa et al., 2014). Additionally, several reports suggest that the mean oxy-Hb changes induced by a VFT in patients with schizophrenia are significantly decreased compared with those observed in controls (Azechi et al., 2010; Ehlis et al., 2007; Kubota et al., 2005; Pu et al., 2013a; Quan et al., 2015; Suto et al., 2004; Takizawa et al., 2008). However, the relationship between hemodynamic responses and clinical characteristics has not been sufficiently clarified.

To date, few NIRS imaging studies have reported an association between global functioning (clinician-ratings) and prefrontal hemodynamic responses during VFT in subjects with schizophrenia (Chou et al., 2015; Kinou et al., 2013; Takizawa et al., 2008). Chou et al. (2015), Kinou et al. (2013), and Takizawa et al. (2008) demonstrated an association between smaller oxy-Hb increase levels in the PFC region induced by VFT and functional impairment as assessed by global assessment of functioning (GAF) scores in patients with schizophrenia (uncorrected $p++ < 0.05$). To our knowledge, no studies have evaluated self-reported social functioning and prefrontal hemodynamic responses during a VFT in subjects with schizophrenia. Although some fMRI studies demonstrated that brain activation during performance of social cognitive task (i.e., theory-of-mind and facial affect perception) was associated with self-reported social functioning (Dodell-Feder et al., 2014; Pinkham et al., 2008), the relationship between the neural activation underlying verbal fluency and self-reported social functioning among schizophrenia subjects has not been examined.

We recently described an association between VFT-related oxy-Hb activation in the PFC and self-reported social functioning in healthy elderly adults (Pu et al., 2014a) and patients with major depressive disorder (MDD) (Pu et al., 2015, 2008). In these studies we used SASS (Social Adaptation Self-Evaluation Scale) for the assessment of social functioning, which is in fact a measure for assessing social motivation and self-perception in patients with depression. It is of interest to determine whether similar findings could be obtained for other psychiatric disorders, which may

indicate universal relevance of the PFC to self-reported social functioning. Psychosocial functioning is not necessarily related to subjective experience in schizophrenia (Awad et al., 1997; Brekke et al., 1993). However, our findings in patients with depression and healthy elderly adults lead us to hypothesize that PFC activity associated with a cognitive process measured by NIRS is strongly related to self-reported social functioning in patients with schizophrenia. Therefore, we used multi-channel NIRS imaging to investigate prefrontal hemodynamic responses during the VFT and the SFS to assess self-reported social functioning in patients with schizophrenia.

2. Material and methods

2.1. Participants

Thirty-three patients with schizophrenia and 30 age- and sex-matched healthy controls participated in the study (Table 1). All patients were recruited between October 2010 and December 2013 based on consecutive referrals. All participants were right-handed according to the Edinburgh Handedness Inventory (Oldfield, 1971) and were native Japanese speakers. The patients were recruited from the outpatient population of the Tottori University Hospital and were diagnosed by an experienced psychiatrist (MI, IN, or KK,) using the criteria specified in the Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition, Text Revision (DSM-IV-TR; American Psychiatric Association 2000). Eleven patients were taking aripiprazole, seven were prescribed olanzapine, six were taking risperidone, five were on blonanserin, two were taking paliperidone, one was prescribed perospirone, and one was on perphenazine. The NIRS data for 23 of 33 patients with schizophrenia have been reported in our previous studies (Pu et al., 2014b, 2013b) but their relationship with social functioning has not been evaluated.

Patients with comorbid neurological illness, previous traumatic

Table 1
Patient demographics and clinical characteristics

	Patients with schizophrenia N=33 (mean ± SD)	Healthy controls N=30 (mean ± SD)	t	df	Group difference P value
Age, years	32.3 ± 8.5	32.4 ± 11.1	-0.026	61	0.980
Gender, women/men	21/12	19/11	$X^2=0$	1	0.980[a]
Handedness	99.6 ± 2.2	97.6 ± 11.1	1.033	61	0.331
Education, years	13.7 ± 2.2	14.7 ± 2.2	-1.831	61	0.072
Estimated premorbid IQ	101.0 ± 10.8	100.2 ± 7.7	0.363	61	0.714
Number of words generated	12.8 ± 4.7	14.2 ± 3.9	-1.303	61	0.197
Age at onset, years	22.5 ± 7.9	NA			
Duration of illness, years	9.8 ± 5.5	NA			
PANSS Total	55.2 ± 24.5	NA			
Positive	12.1 ± 5.8	NA			
Negative	16.2 ± 7.7	NA			
General psychopathology	26.9 ± 12.3	NA			
Composite score of BACS	-1.028 ± 0.783	NA			
GAF	53.3 ± 9.2	NA			
SFS Total	106.2 ± 24.9	NA			
Social engagement	10.1 ± 2.3	NA			
Interpersonal communication	6.4 ± 3.0	NA			
Independence-performance	24.3 ± 7.2	NA			
Recreation	20.1 ± 7.5	NA			
Social activities	9.7 ± 6.6	NA			
Independence-competence	29.8 ± 6.0	NA			
Occupation	5.8 ± 3.5	NA			
Chlorpromazine equivalent dose, mg/day	449.5 ± 231.7	NA			

Abbreviations: IQ, Intelligence Quotient; PANSS, Positive and Negative Symptom Scale;
BACS, Brief Assessment of Cognition in Schizophrenia, Japanese version;
GAF, Global Assessment of Functioning; SFS, Social Functioning Scale;

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