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Association between cognitive insight and prefrontal function during a cognitive task in schizophrenia: A multichannel near-infrared spectroscopy study

Shenghong Pu [a,*], Kazuyuki Nakagome [b], Takeshi Yamada [a], Megumi Itakura [a], Takahiro Satake [a], Hisahito Ishida [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

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ABSTRACT

Insight has been studied mostly from a clinical perspective. Recently, the focus of this research field shifted to cognitive insight or the ability to monitor and correct the erroneous convictions of individuals. In this study, we investigated the relationship between cognitive insight and prefrontal function during a cognitive task in 30 patients with clinically stable schizophrenia and 30 age- and gender-matched healthy controls. We measured the changes in hemoglobin concentration in the prefrontal and temporal cortical regions during a verbal fluency task (VFT) by using 52-channel near-infrared spectroscopy (NIRS). Cognitive insight was measured using the Beck Cognitive Insight Scale (BCIS). Regional hemodynamic changes were significantly smaller in the schizophrenia group than in the control group in prefrontal and temporal regions, and significant positive relationship was observed between the score of the BCIS self-reflectiveness subscale and right ventrolateral prefrontal and right temporal functions during the VFT. These results suggest that the right ventrolateral prefrontal and temporal cortical regions are associated with cognitive insight in clinically stable patients with schizophrenia and that NIRS is an efficient medical tool for monitoring these characteristics.

1. Introduction

Lack of insight (i.e., poor awareness of illness) is a central clinical characteristic of schizophrenia (Carpenter et al., 1973). The clinical concept of insight focuses on the patients' awareness that their symptoms and behavior are abnormal and attributable to a mental disorder, their awareness of the social consequences of the disorder, and the need for treatment (David, 1990; Amador et al., 1993). This form of insight is assessed by observing the behavior of individuals during a clinical examination and is valuable for determining the diagnosis, prognosis, and treatment (Amador and David, 1998; Mintz et al., 2003).

Poor insight may stem from specific neurocognitive deficits (Amador and David, 1998). Among the different neurocognitive functions assessed in studies of insight, only cognitive measures mediated by the prefrontal cortex (PFC), such as perseverative errors and categories completed on the Wisconsin Card Sorting Test, were associated with insight deficits (McEvoy et al., 1996; Lysaker et al., 1998; Marks et al., 2000; Rossell et al., 2003). The evidence linking poor insight to impaired executive function suggests that poor insight may be related specifically to PFC abnormalities (Goldstein et al., 1999; Gur et al., 2000; Hirayasu et al., 2001). Shad et al. (2004) demonstrated that decreased right PFC volume was associated with insight deficits in patients with schizophrenia. The deficits observed in the frontal lobe were associated with impairments in executive functions, such as self-monitoring and conceptual organization, which may be critical for illness awareness (Shad et al., 2004). This suggests that insight deficits may be related to impairments in executive functioning, which are mediated by the PFC (Lysaker et al., 1998; Young et al., 1998). The neural basis of executive function lies in the PFC, which is also involved in other high-level cognitive functions. Considering the significance of insight in patients with schizophrenia, elucidating the relationship between the neural activity in the PFC that underlies executive-function processes and insight in this disease seems worthwhile.

Beck et al. (2004) recently proposed another aspect of insight from the cognitive perspective, namely, cognitive insight, which involves an ability to distance oneself from distorted beliefs and misinterpretations, to reappraise them, and to recognize erroneous conclusions. The Beck Cognitive Insight Scale (BCIS) was developed to measure this aspect of insight (Beck et al., 2004). The initial study by Beck et al. revealed that the BCIS has two components: self-reflectiveness (SR) and self-certainty (SC). The former includes items measuring objectivity, reflectiveness, and openness to feedback, whereas the latter measures the certainty about one's own beliefs or judgment. A composite index

* Corresponding author at: Division of Neuropsychiatry, Department of Brain and Neuroscience, Tottori University Faculty of Medicine, 36-1 Nishi-cho, Yonago, Tottori 683-8504, Japan. Tel.: +81 859 38 6547; fax: +81 859 38 6549.
E-mail address: pshh0517@yahoo.co.jp (S. Pu).

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score (i.e., an estimated measure of overall cognitive insight) is calculated by subtracting the SC subscale score from the SR subscale score. The BCIS is a self-report instrument comprising 15 items rated on a 4-point scale [0 (do not agree at all) to 3 (agree completely)]. The reliability and validity of its Japanese version have been confirmed (Uchida et al., 2009). Cognitive insight is clinically significant because it taps directly into the thinking styles underlying distorted cognitions, which are increasingly acknowledged as targets for intervention (Turkington et al., 2002). Cognitive insight has adequate convergent validity with clinical measures of insight (Beck et al., 2004).

Multi-channel near-infrared spectroscopy (NIRS), a functional neuroimaging technology, enables the noninvasive detection of spatiotemporal characteristics of brain function near the brain surface by using near-infrared light (Strangman et al., 2002a). NIRS has allowed the bedside measurement of the concentration of oxygenated hemoglobin (oxy-Hb) and deoxygenated hemoglobin (deoxy-Hb) in micro blood vessels. Assuming that the hematocrit is constant, the changes in oxy-Hb, deoxy-Hb, and total Hb (the sum of oxy-Hb and deoxy-Hb) are correlated with changes in the regional cerebral blood volume (rCBV), as shown using simultaneous NIRS and positron emission tomography (PET) measurements (Hock et al., 1997; Villringer et al., 1997; Ohmae et al., 2006).

NIRS measurement during a verbal fluency task (VFT) was approved recently by the Ministry of Health, Labour and Welfare of Japan as an advanced medical technology for the differential diagnosis of psychiatric illnesses. Thus, it has been applied frequently in clinical settings in Japan. Additionally, several reports suggest that the mean oxy-Hb changes activated by a VFT in patients with schizophrenia are significantly decreased compared with those observed in control individuals (Suto et al., 2004; Takizawa et al., 2008); however, the relationship between the hemodynamic response and the severity of psychiatric symptoms has not been clarified sufficiently.

We were especially interested in exploring schizophrenia treatment strategies, which should take into account the relationship among cognition, psychiatric symptoms, and cognitive insight. Executive functioning is a cognitive deficit reported in schizophrenia (Kuperberg and Heckers, 2000). As the VFT is one of the executive measures (Burgess et al., 2000; Alvarez and Emory, 2006), it is possible that the hemodynamic response elicited by a VFT may tap the neuronal activity in the PFC, which may be closely linked to cognitive insight.

The primary objective of the present study was to investigate more precisely the relationship between the activity in the PFC and cognitive insight in patients with schizophrenia by using a 52-channel NIRS machine (ETG-4000; Hitachi Medical Co.). We hypothesized that the PFC activity that is associated with the processing of executive function is related to cognitive insight in these patients.

2. Methods

2.1. Participants

Thirty patients with schizophrenia who were clinically stable enough to undergo the assessment and 30 age- and gender-matched healthy controls participated in the study. (Table 1). All the participants were recruited from November 2011 to March 2013 on the basis of 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 (K.K) using the criteria specified in the Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition, Text Revision (DSM-IV-TR; American Psychiatric Association 2000). Nine patients were taking olanzapine; 9, aripiprazole; 6, blonanserin; and 6, other atypical antipsychotics (2 patients each taking risperidone, perospirone, and quetiapine). On the day of the NIRS experiment, psychiatric symptoms were evaluated by the same psychiatrist (K.K.) using the Positive and Negative Syndrome Scale (PANSS) (Kay et al., 1987). Approximately 10–15 min prior to NIRS measurement, all participants performed a self-assessment of cognitive insight using the BCIS.

Table 1
Patient demographics and clinical characteristics.

		Patients with schizophrenia N = 30 (mean ± SD)	Healthy controls N = 30 (mean ± SD)	Group difference *P* value
Age, years		32.1 ± 10.47	32.4 ± 11.11	0.915
Gender, women/men		21/9	19/11	0.584[a]
Handedness		96.5 ± 13.40	97.6 ± 11.11	0.739
Education, years		13.7 ± 2.25	14.7 ± 2.19	0.097
Estimated premorbid IQ		98.7 ± 11.69	100.2 ± 7.72	0.569
Number of words generated		12.1 ± 3.59	14.2 ± 3.86	<0.05
Age at onset, years		21.6 ± 8.15	NA	
Duration of illness, years		10.5 ± 8.20	NA	
BCIS	Self-certainty	5.0 ± 2.82	4.3 ± 2.31	0.320
	Self-reflectiveness	11.3 ± 3.50	11.8 ± 3.15	0.563
	Composite index	6.3 ± 4.54	7.5 ± 4.18	0.305
PANSS	Total	62.6 ± 16.60	NA	
	Positive	13.6 ± 3.98	NA	
	Negative	17.6 ± 5.38	NA	
	General psychopathology	31.4 ± 9.32	NA	
Chlorpromazine equivalent dose, mg/day		513.4 ± 362.98	NA	

Abbreviations: IQ, Intelligence Quotient; PANSS, Positive and Negative Symptom Scale; BCIS, Beck Cognitive Insight Scale

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

Patients with comorbid neurological illness, previous traumatic brain injury with any known cognitive consequences or loss of consciousness for more than 5 min, a history of electroconvulsive therapy, and alcohol/substance abuse or addiction were excluded but for nicotine addiction. Although there is not yet ample evidence about how long the loss of consciousness is necessary to induce postconcussion syndrome, an MRI study that investigated whether unequivocal traumatic lesions might appear in cases of concussion with loss of consciousness of less than 5 min, which is very common, demonstrated that no case with unequivocal intracranial traumatic pathology was detected (Schrader et al, 2009).

Healthy individuals who were appropriate age and gender matches for the schizophrenia patients participated as controls in the present study. Inclusion criteria for controls were similar to those for the patient sample, although controls were additionally required to have no previous or current psychiatric illnesses. Thirty individuals (11 male, 19 female) meeting these criteria were selected to participate in the study. All patients gave informed consent before participating in the study, and the protocol was approved by the Ethics Committee of Tottori University.

2.2. Cognitive task

The task procedure used in the present study was similar to that described by Takizawa et al. (2008) Hb changes were measured during a letter version of the VFT. The patient sat on a comfortable chair and was instructed to minimize movements, such as head movements, jaw clenching, and eye blinking, during the NIRS measurements, to avoid producing artifacts.

2.3. NIRS measurements

The 52-channel NIRS machine measures relative changes in oxy-Hb and deoxy-Hb using 2 wavelengths (695 and 830 nm) of infrared light based on the modified Beer–Lambert law (Yamashita et al., 1996). In this system, the Hb values include a differential pathlength factor (DPF). Zhao et al. (2002), using a Monte Carlo simulation, reported that the estimated DPF variation in the forehead region of adult humans was