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Association between subjective well-being and prefrontal function during a cognitive task in schizophrenia: A multi-channel near-infrared spectroscopy study

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ABSTRACT

The purpose of this study was to examine the relationship between subjective well-being and prefrontal function during a cognitive task in schizophrenia. Twenty-four patients with clinically stable schizophrenia participated in the study. We measured the change in hemoglobin concentration in the prefrontal region during a verbal fluency task (VFT) by using 52-channel near-infrared spectroscopy (NIRS). The subjective well-being of participants was assessed using the Subjective Well-being under Neuroleptic drug treatment Short form (SWNS). A significant positive relationship was observed between the SWNS score and frontopolar, left ventrolateral, and bilateral dorsolateral prefrontal function during the VFT. These results suggest that the frontopolar and left ventrolateral and bilateral dorsolateral prefrontal cortical regions are associated with the subjective well-being of clinically stable patients with schizophrenia and that NIRS may be an efficient medical tool for monitoring these characteristics.

1. Introduction

In parallel to the steady improvement in the methods for treatment of patients with schizophrenia, the desired outcome has evolved from symptom management to maximization of quality of life (QOL) and functional recovery (Burns, 2007). Schizophrenia considerably affects the QOL of patients beyond impairing psychosocial functioning through positive and negative symptoms (Hofer et al., 2004).

Earlier research had focused on QOL from a physician's perspective by using suitable questionnaires. Recent interest in the patient's own perspective of QOL has resulted in the development of questionnaires assessing well-being from a patient's perspective.

Recently, new avenues of neuroimaging and electrophysiological research have been initiated to determine the neurobiological substrate of the individual's own experiences in schizophrenia. Striatal dopamine depletion can lead to negative subjective states that frequently impact the QOL, especially the ability of the person to experience pleasure (Voruganti and Awad, 2006). Functional brain imaging has provided empirical evidence for the neural basis of cognitive and affective states, which are known to affect QOL (Kurtz et al., 2008; Kurtz and Tolman, 2011; Tolman and Kurtz, 2012). Recent electrophysiological studies have reported an association between local brain activity (P300) in the superior temporal gyrus and prefrontal cortex (PFC) and functional outcomes, including QOL (Higuchi et al., 2008; Sumiyoshi et al., 2009). To date, only one neuroimaging study has shown an association between QOL and brain activity (Boyer et al., 2012) in patients with schizophrenia, and to our knowledge, no studies have evaluated the relationship between the subjective well-being and brain activity of these patients. A neurobiological understanding of subjective well-being may enhance the scientific foundation of the construct and allow development of appropriate scales and accurate interpretation of data.

A recently developed functional neuroimaging technology, multi-channel near-infrared spectroscopy (NIRS; ETG-4000, Hitachi Medical Co.), enables the noninvasive, restraint-free detection of spatiotemporal characteristics of brain function near the brain surface by using near-infrared light (Strangman et al., 2002a; Boas et al., 2004). NIRS has enabled 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 the changes in the regional cerebral blood volume (rCBV), as shown by simultaneous NIRS and positron emission tomography (PET) measurements (Hock et al., 1997; Villringer et al., 1997; Ohmae et al., 2006).

The Subjective Well-being under Neuroleptic drug treatment scale (SWN) is one of the most useful tools for assessing subjective

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well-being—the major component of QOL. The SWN scale is a questionnaire used to subjectively assess a patient's QOL (Naber, 1995; Naber et al., 2001). This questionnaire has been widely used to assess QOL in patients with schizophrenia (de Haan et al., 2002; Kluge et al., 2005; Naber et al., 2005; Lambert et al., 2006). SWN was developed by Naber, D. in 1995, and was found to be significantly correlated to D2 blockade by the antipsychotic drugs (de Haan et al., 2000; Mizrahi et al., 2009), stronger D2 blockade in ventral striatum leading to lower scores, and also earlier improvement in SWN predicted better long-term outcome (de Haan et al., 2008). SWN Short form (SWNS) was created in 2001. SWNS is a 20-item scale for evaluating a patient's subjective well-being; the reliability and validity of its Japanese version have subsequently been confirmed (Watanabe and Matsumura, 2003). Each item is scored from 1 to 6, corresponding to minimal and maximal subjective well-being, with a total score ranging from 20 to 120. The SWNS consists of 5 subscales: emotional regulation, self-control, mental functioning, social integration, and physical functioning (Naber et al., 2001).

The primary objective of the present study was to investigate the relationship between the hemodynamic response in the PFC and the SWNS total scores in stable schizophrenia, by using a 52-channel NIRS machine. Subjective well-being refers to how people experience the quality of their lives and includes both emotional reactions and cognitive judgments (Diener, 1984). There are electrophysiological measures specifically related to well-being: resting EEG activity in the left PFC has been reported to be higher in individuals with greater eudaimonic and hedonic well-being (Urry et al., 2004). Asymmetrical hemispheric activation in the PFC is perhaps the most studied neural correlate of self-reported well-being (for a review, see Davidson, 2004). Recently, we showed the association of reduced task-related oxy-Hb activation in the PFC region with functional impairment assessed by social adaptation self-evaluation scale scores in major depressive disorder patients (Pu et al., 2008, 2012). These findings suggest that hemodynamic response in the PFC region during a cognitive task may reflect the subjective aspects of their functioning. It is of interest to test whether similar findings could be obtained for other psychiatric disorders, which may indicate universal relevance of the PFC to subjective aspects of functioning. Furthermore, Takizawa et al. (2008) demonstrated the association of reduced oxy-Hb activation in the frontopolar cortex region induced by verbal fluency task with functional impairment assessed by global assessment of functioning scores in schizophrenia patients. Although psychosocial functioning is not necessarily related to subjective well-being in schizophrenia (Brekke et al., 1993; Awad et al., 1997), taking into consideration our findings on patients with depression, we may well hypothesize that the activity in the PFC associated with a cognitive process measured by NIRS is related to subjective well-being in patients with stable schizophrenia.

2. Methods

2.1. Patients

Twenty-four patients with clinically stable schizophrenia participated in the study (Table 1). All the participants were right-handed according to the Edinburgh Handedness Inventory (Oldfield, 1971) and were native Japanese speakers. The patients were recruited from the outpatients at Tottori University Hospital, and were diagnosed using the criteria specified in the fourth edition of the Diagnostic and Statistical Manual of Mental Disorders text revision (DSM-IV-TR, American Psychiatric Association 2000) by an experienced psychiatrist (K.K.). Ten patients were taking aripiprazole, 7 olanzapine, 5 blonanserin, and 2 other atypical antipsychotics (1 risperidone and 1perospirone). On the same day as 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). Prior to NIRS measurement, all participants undertook self-assessment of subjective well-being using the SWNS.

Table 1
Patient demographics and clinical characteristics.

		N = 24 (mean ± SD)
Age, years		33.6 ± 9.72
Gender, women/men		16/8
Handedness		96.5 ± 9.31
Education, years		13.8 ± 2.55
Estimated premorbid IQ		98.2 ± 11.69
Number of words generated		12.0 ± 3.97
Age at onset, years		22.8 ± 8.79
Duration of illness, years		10.8 ± 8.11
PANSS	total	65.1 ± 13.26
	Positive	14.2 ± 3.46
	Negative	18.5 ± 4.38
	General psychopathology	32.4 ± 7.49
SWNS	total	68.3 ± 18.78
	Mental functioning	12.9 ± 4.98
	Self-control	14.7 ± 3.99
	Emotional regulation	12.9 ± 3.92
	Physical functioning	13.9 ± 4.09
	Social integration	13.9 ± 4.04
	Chlorpromazine equivalent dose, mg/day	440.4 ± 232.60

Abbreviations: IQ, Intelligence Quotient; PANSS, Positive and Negative Symptom Scale; SWNS, Subjective well-being under Neuroleptics drug treatment Short form.

The exclusion criteria for this study were 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. All patients gave informed consent before participating in the study, and the protocol was approved by the Ethical Committee of Tottori University.

2.2. Cognitive task

The task procedure in the present study was similar to that of Takizawa et al. (2008). Hb changes were measured during a letter version of the verbal fluency task (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 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, these Hb values include a differential pathlength factor (DPF). In addition, Zhao et al. (2002), using a Monte Carlo simulation, reported that the estimated DPF variation in the forehead region of adult humans was regarded as roughly homogeneous. The distance between pairs of source-detector probes was set at 3 cm, and each measuring area between pairs of source-detector probes was defined as a "channel" (ch). The machine measures points at a depth of 2 to 3 cm below the scalp. This corresponds to the surface of the cerebral cortex (Toronov et al., 2001; Okada and Delpy, 2003). The probes of the NIRS machine were placed on the frontotemporal region of the participant, with the midcolumn of the probe located over Fpz, and the lowest probes were located along the T3–Fp1–Fpz–Fp2–T4 line in accordance with the international 10/20 system for electroencephalography. The arrangement of the probes enabled the measurement of Hb values from both prefrontal and superior temporal cortical surface regions (Fig. 1). The correspondence between the NIRS channels and the measurement points on the cerebral cortex was confirmed by a multi-subject study of anatomical craniocerebral correlation (Okamoto et al., 2004), and