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Precentral and inferior prefrontal hypoactivation during facial emotion recognition in patients with schizophrenia: A functional near-infrared spectroscopy study

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ABSTRACT

Although patients with schizophrenia demonstrate abnormal processing of emotional face recognition, the neural substrates underlying this process remain unclear. We previously showed abnormal fronto-temporal function during facial expression of emotions, and cognitive inhibition in patients with schizophrenia using functional near-infrared spectroscopy (fNIRS). The aim of the current study was to use fNIRS to identify which brain regions involved in recognizing emotional faces are impaired in patients with schizophrenia, and to determine the neural substrates underlying the response to emotional facial expressions per se, and to facial expressions with cognitive inhibition. We recruited 19 patients with schizophrenia and 19 healthy controls, statistically matched on age, sex, and premorbid IQ. Brain function was measured by fNIRS during emotional face assessment and face identification tasks. Patients with schizophrenia showed lower activation of the right precentral and inferior frontal areas during the emotional face task compared to controls. Further, patients with schizophrenia were slower and less accurate in completing tasks compared to healthy participants. Decreasing performance was associated with increasing severity of the disease. Our present and prior studies suggest that the impaired behavioral performance in schizophrenia is associated with different mechanisms for processing emotional facial expressions versus facial expressions combined with cognitive inhibition.

1. Introduction

Patients with schizophrenia demonstrate abnormal social cognition including face perception (Mandal et al., 1998; Walker et al., 1984), emotional face recognition (Kohler et al., 2010), and theory of mind (Bora and Pantelis, 2013; Pinkham, 2014). Behavioral and neuroimaging study results suggest that patients with schizophrenia have impairments in the neural network involved in face perception and emotional face recognition (Habel et al., 2010; Li et al., 2012; Mehta et al., 2014; Taylor et al., 2012). However, the neural substrates underlying face recognition in patients with schizophrenia have not been fully elucidated. We previously used functional near-infrared spectroscopy (fNIRS) to demonstrate abnormal fronto-temporal function in schizophrenia, using emotional-cognitive tasks (Egashira et al., 2015). As that study used an emotional go/no-go task, which involved emotional processing and cognitive inhibition, we did not quantify extent to which the emotional processing affected the results. To address this shortcoming, the current study used fNIRS to examine brain activity in patients with schizophrenia in response to facial emotional expressions.

The aim of this study was to identify which brain regions involved in emotional face recognition are impaired in patients with schizophrenia. In combination with the results of our previous study (Egashira et al., 2015), we aimed to determine which neural substrates are implicated in responses to emotional facial expressions and facial expressions with cognitive inhibition. We hypothesized that patients with schizophrenia would show poor behavioral performance and reduced activation of inferior frontal and ventral premotor areas during an emotional

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face expression task, consistent with involvement of the mirror neuron system (Mehta et al., 2014) and the emotional face processing network (Haxby et al., 2002).

2. Materials and methods

2.1. Participants

Nineteen patients with schizophrenia and 19 healthy participants statistically matched on age, sex, and premorbid IQ were studied. All participants were right-handed (Oldfield, 1971). Patients were recruited from Yamguchi University Hospital and Katakura Hospital. All met the schizophrenia criteria in the Diagnostic and Statistical Manual of Mental Disorders IV, Text Revision (DSM-IV-TR; American Psychiatric Association, 2000) as assessed by senior psychiatrists. Diagnoses were confirmed via the Mini-International Neuropsychiatric Interview (MINI., Japanese version 5.0.0; Otsubo et al., 2005) by research psychiatrists and clinical conferences. Healthy participants were recruited from the local community. All patients were medicated. Doses of medication prescribed for the patients at the time of study participation were converted into chlorpromazine-equivalents (CPZ-eq). The Positive and Negative Syndrome Scale (PANSS, Kay et al., 1987) was used to assess psychiatric symptoms. The duration of illness and the duration of untreated psychosis (DUP) were also assessed. Any participant who had a neurological illness, a history of traumatic brain injury with loss of consciousness, alcohol or drug abuse, or any physical illness, such as hepatitis, brain tumor, or epilepsy was excluded from the study. Healthy participants were screened with the MINI and were excluded if they had first- or second-degree relative(s) with a history of psychiatric disorders. Premorbid IQs were estimated using the Japanese version of the National Adult Reading Test (Matsuoka et al., 2006). The Global Assessment of Functioning scale (GAF; American Psychiatric Association, 2000) and socio-economic status (SES; Hollingshead, 1965) were assessed (Table 1). This study was approved by the Institutional Review Board of Yamaguchi University Hospital and the ethics committee of Katakura Hospital. Written informed consent was obtained from all subjects after a complete description of the study was provided.

2.2. Emotional face recognition task

We created a task that evaluated the assessment of facial emotions and one that evaluated face perception. A geometric shape task was inserted between the two face tasks as a reference (Fig. 1). In each task, the subject was required to choose which of the two figures in the lower panel matched the figure in the upper panel. In the emotional face task, the matching was to the facial emotion shown in the upper panel. Facial emotions consisted of sadness, anger, and fear. In the identification task, matching was to the sex of the faces in the upper panel. Faces were selected from The Japanese and Caucasian Facial Expressions of Emotion and Neutral Faces (Matsumoto and Ekman, 1988). The baseline task involved selecting the geometric figure in the lower panel that matched that in the upper panel. Figures were a circle, triangle, or square. This figure-matching task was used to cancel sensorimotor artifacts due to finger and body movements from the fNIRS signal change during the emotion- and face-matching tasks.

The task was administered using Presentation software (https://www.neurobs.com/). There were 12 trials, for a total duration of 300 s. The duration of one block was 60 s for the emotional face task and the identification task. The presentation of stimuli, choice of target stimuli, and emotional and identification task order were administered in a counterbalanced order across subjects. Behavioral performance was assessed by the accuracies and mean reaction times (MRT) for each task. Participants completed task training in advance of the main task, and were confirmed to have fully learned the task before the study proper commenced (Table 2).

Table 1
Demographic and clinical characteristics of patients with schizophrenia and healthy participants.

	Schizophrenia (n = 19)	Healthy (n = 19)	p-Value[a]
Age (years)	40.58 (10.13)[b]	40.53 (8.29)	N.S.
Gender (male/female)	9/10	9/10	N.S.
Education (years)	13.26 (2.47)	15.84 (1.66)	<0.01
Handedness	88.42 (20.55)	89.21 (10.44)	N.S.
tIQ	100.96 (11.20)	100.10 (5.88)	N.S.
SES	18.84 (8.37)	41.84 (5.32)	<0.01
GAF	45.74 (19.89)	98.53 (2.54)	<0.01
DUP[c]	9.68 (15.22)		
Duration of illness (months)	256.63 (139.62)		
PANSS[d] positive factor	10.53 (3.36)		
PANSS negative factor	19.68 (7.91)		
PANSS general psychopathology	23.47 (4.89)		
Chlorpromazine equivalent (mg/day)	975.22 (610.84)		

[a] Student's t-test.
[b] Data are represented as means (SD).
[c] DUP, duration of untreated psychosis.
[d] PANSS, positive and negative syndrome scale.

2.3. fNIRS

Details of the NIRS system have been described in our previous studies (Egashira et al., 2015; Matsubara et al., 2014). In brief, we used a continuous-wave NIRS system (ETG-4000, Hitachi Medical Co., Japan) to collect fNIRS data. Relative changes in the concentrations of oxygenated and deoxygenated hemoglobin ([oxy-Hb] and [deoxy-Hb], respectively) were monitored. As in prior NIRS studies (Egashira et al., 2015; Takizawa et al., 2008), we measured the frontal and temporal areas via 31 channels (channels #22 to 52), anatomically identified by a virtual registration method with automated anatomical labeling (Tzourio-Mazoyer et al., 2002) that enables NIRS channel positions to be registered in the standard brain space (Tsuzuki et al., 2007).

2.4. Statistical analysis

2.4.1. Behavioral performance

We first used repeated measures analysis of variance (ANOVA) with two within-subjects factors: condition (MRT and accuracy) and task (identification and emotional), and one between-subjects factor (diagnosis), with age, sex, and IQ as covariates. Then, if there was a significant interaction between condition, task, and diagnosis, we carried out separate repeated-measures ANOVAs using accuracy and MRT as the dependent variables, with one within-subjects factor (task) and one between-subjects factor (diagnosis), with age, sex, and IQ as covariates. Third, if there was a significant task-by-diagnosis interaction, we implemented separate ANOVAs for the dependent variables accuracy of identification, accuracy of emotion selection, MRT of identification, and MRT of emotion, with one between-subjects factor (diagnosis), and age, sex, and IQ as covariates in each case.

We also examined the partial correlations between task performance and clinical variables, with age, sex, and IQ as covariates. The clinical variables consisted of DUP, duration of illness, the number of hospitalizations, mean duration of hospitalizations, GAF scores, PANSS total scores and subscale scores for positive and negative symptoms, and CPZ-eq. We used SPSS Statistics version 20 for Windows (IBM, Chicago, IL) for all analyses. Differences were considered significant at $p < 0.05$.

2.4.2. fNIRS

We used the mean [oxy-Hb] change during the task as an outcome measure for statistical analyses because [oxy-Hb] in fNIRS is thought to reflect the activation of gray matter in the brain (Sato et al., 2013). Consistent with the statistical analysis of behavioral data, we first examined repeated-measures ANOVAs using mean [oxy-Hb] change as the

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