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Temporal lobe and inferior frontal gyrus dysfunction in patients with schizophrenia during face-to-face conversation: A near-infrared spectroscopy study

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ABSTRACT

Schizophrenia (SC) is marked by poor social-role performance and social-skill deficits that are well reflected in daily conversation. Although the mechanism underlying these impairments has been investigated by functional neuroimaging, technical limitations have prevented the investigation of brain activation during conversation in typical clinical situations. To fill this research gap, this study investigated and compared frontal and temporal lobe activation in patients with SC during face-to-face conversation. Frontal and temporal lobe activation in 29 patients and 31 normal controls (NC) ($n = 60$) were measured during 180-s conversation periods by using near-infrared spectroscopy (NIRS). The grand average values of oxyhemoglobin concentration ([oxy-Hb]) changes during task performance were analyzed to determine their correlation with clinical variables and Positive and Negative Syndrome Scale (PANSS) subscores. Compared to NCs, patients with SC exhibited decreased performance in the conversation task and decreased activation in both the temporal lobes and the right inferior frontal gyrus (IFG) during task performance, as indicated by the grand average of [oxy-Hb] changes. The decreased activation in the left temporal lobe was negatively correlated with the PANSS disorganization and negative symptoms subscores and that in the right IFG was negatively correlated with illness duration, PANSS disorganization, and negative symptom subscores. These findings indicate that brain dysfunction in SC during conversation is related to functional deficits in both the temporal lobes and the right IFG and manifests primarily in the form of disorganized thinking and negative symptomatology.

1. Introduction

Schizophrenia (SC) is marked by poor social performance, which is a complex phenomenon influenced by many affective, motivational, and environmental factors. Deficiency in *social skills*, a behavioral construct reflecting the smooth application of several specific verbal and nonverbal abilities and cognitive capacities involved in daily conversation, is a critical component of SC. Typically, clinicians diagnose SC on the basis of behavioral observation and analysis of speech content, attitude, and emotional response during interviews. Neuropsychological testing and functional neuroimaging have confirmed that patients with SC have basic cognitive deficits, such as deficits in working and verbal memory and attention (Mohamed et al., 1999; Riley et al., 2000), which are related to impairment in various brain regions, primarily the frontal and temporal lobes, and contribute to their social-skill deficits.

Social cognition is one of the crucial factors necessary for having a conversation. The mainstream of social cognition studies is mental-state attribution, i.e., "theory of mind" (ToM) or "mentalizing," which involves the ability to assume the intentions, beliefs, wishes, feelings, and knowledge states of other individuals based on either observational input ("mental-state decoding") or inferential processes ("mental-state reasoning") (Brune and Schaub, 2012). Many recent studies have reported that the reduced volume and/or reduced activation of gray matter in specific brain regions, mainly the temporal lobe, ventromedial prefrontal cortex (PFC), and cingulate cortex, are associated with the ToM deficits shown by patients with SC (Benedetti et al., 2009; Hooker et al., 2011; Sugranyes et al., 2011). Although the mechanism underlying this phenomenon has been investigated by functional neuroimaging, technical limitations have prevented the investigation of brain activation during conversation in typical clinical situations.

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Therefore, the manner of brain functioning and the consequent integration of various cognitive functions during conversation remain unclear.

Near-infrared spectroscopy (NIRS) has the advantage that brain activation can be evaluated in a naturalistic environment. Several recent studies reported use of NIRS during face-to-face interaction (Costantini et al., 2013; Cui et al., 2012; Konvalinka and Roepstorff, 2012). However, few studies have investigated its application during face-to-face conversation (Suda et al., 2010, 2011).

In this study, we used NIRS to investigate frontal and temporal lobe activation in patients with SC during conversation. Because SC characteristics are well reflected in conversation, we hypothesized that (i) patients with SC and NCs exhibit differences in frontal and temporal lobe activation during conversation, (ii) patients with SC and NCs exhibit differences in behavior during conversation, and (iii) alterations in frontal and temporal lobe activations correlate with clinical symptoms and/or behavior.

2. Materials and methods

2.1. Participants

We recruited 29 patients with SC and 31 NCs ($n = 60$) from the Department of Psychiatry and Neuroscience, Gunma University Hospital, Japan (Table 1). SC diagnosis was based on the Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition (DSM-IV) criteria. Patients older than 60 were not included, to eliminate the possible interference of additional pathophysiological factors, such as aging and cerebrovascular changes. All patients were taking medications, including antipsychotics, mood stabilizers, antidepressants, anxiolytics, hypnotics, and/or antiparkinsonian drugs. The chlorpromazine equivalent dose of antipsychotics, imipramine equivalent dose of antidepressants, diazepam equivalent dose of anxiolytics, and flunitrazepam equivalent dose of hypnotics were calculated for each patient (Inagaki, 2006). All patients were clinically stable, as indicated by their scores on the Positive and Negative Syndrome Scale (PANSS), which assesses the 5 psychiatric factors of positive symptomatology, negative symptomatology, disorganization, excitement, and emotional distress (Kay et al., 1987; van der Gaag et al., 2006). NCs had no history of major psychiatric or physical illness or took any medications. All subjects were right-handed and native Japanese speakers. The exclusion criteria for both groups included clear abnormality in brain magnetic resonance imaging (MRI) results, neurological illness, traumatic brain injury with any of the known cognitive consequences or loss of consciousness for more than 5 min, substance use or addiction, and presence of hearing or vision impairment. This study was performed in accordance with the Helsinki Declaration, as revised in 1989, and was approved by the Institutional Review Board of the Gunma University Hospital. Written informed consent was obtained from all subjects before study initiation. If a patient was younger than 20 years or had been forcibly committed to hospitalization, written informed consent was obtained from his/her legal representative. Because we could not obtain behavioral data of conversations from subjects who had not provided consent for videotape recording, we describe the clinical characteristics of all subjects using the behavioral data listed in Table 1.

2.2. Activation tasks

Two types of activation tasks, a conversation and a control task, were used to assess brain activation during conversation (Fig. 1).

Table 1
Subject characteristics. The data presented on the left side (groups of total subjects) indicate the characteristics of the subjects who participated in this study, whereas the data presented on the right side (subgroups of subjects with behavioral data) indicate the characteristics of the subgroup of subjects with behavioral data. Antipsychotics, chlorpromazine equivalent dose; antidepressants, imipramine equivalent dose; anxiolytics, diazepam equivalent dose; and hypnotics, flunitrazepam equivalent dose. M, male; F, female; SC, schizophrenic subjects; NC, normal controls; ST, speaking time score; RS, receiving aspect score; SS, sending aspect score; GAF, Global Assessment of Functioning; PANSS, Positive and Negative Symptom Scale.

	Groups of total subjects				Subgroups of subjects with behavioral data			
	SC ($n = 29$)		NC ($n = 31$)		SC ($n = 15$)		NC ($n = 28$)	
	M	F	M	F	M	F	M	F
Sex	19	10	20	11	9	6	18	11
	Mean	SD	Mean	SD	Mean	SD	Mean	SD
Age (year)	35.4	11.9	33.5	10	34.3	12.1	32.6	9.7
Age range (year)	19–58		23–58		19–57		23–58	
Age of onset (year)	23.6	7.3			24.3	8.4		
Illness duration (year)	11.6	8.8			10.2	7.9		
GAF					55.8	13.0		
PANSS five-factor model	Mean	SD			Mean	SD		
Positive symptoms	11.6	4.1			10.3	3.3		
Negative symptoms	21.4	8.4			19.8	5.9		
Disorganization	10	4.2			8.1	1.7		
Excitement	6.6	3.1			5.3	1.5		
Emotional distress	8.5	2.7			8.0	2.6		
Medications	Mean	SD	*n*		Mean	SD	*n*	
Antipsychotic (mg/day)	621.9	574.1	26/29		471.8	435.5	14/15	
Antipsychotic (mg/day)	51.8	65.7	4/29		60.7	77.5	3/15	
Anxiolytic (mg/day)	7.4	6.3	10/29		6.0	6.2	5/15	
Hypnotic (mg/day)	1.9	1.1	10/29		1.8	1.0	4/15	
Behavioral data					Mean	SD	Mean	SD
Time (s)					70.3	9.9	77.7	4.9
RS					3.0	0.9	4.0	0.2
SS					2.6	1.0	3.4	0.9