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ORIGINAL PAPER

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Social cognition in schizophrenia: similarities and differences of emotional perception from patients with focal frontal lesions

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Abstract The structural and functional abnormalities of the frontal lobes, the region implicated in social information processing, have been suspected to underlie social cognitive impairments in schizophrenia. However, multiple structures, including the limbic/paralimbic areas that are also important for social cognition, have been reported to be abnormal in schizophrenia. The aim of this study is to investigate the extent to which the frontal lobe dysfunction accounts for social cognitive impairments in schizophrenia by comparing with patients who have focal frontal lobe injuries. Social cognitive abilities, focusing on affective aspects, were examined by an emotion intensity recognition task, which is sensitive to the amygdala function, and the emotion attribution tasks, which rely mainly on the frontal lobe function. Individuals with schizophrenia were impaired on the emotion intensity recognition task as well as on the emotion attribution tasks as compared with healthy subjects. By contrast, the frontal lobe-damaged group was defective in the emotion attribution tasks but not in the emotion intensity recognition task. Our results indicated that social cognitive impairments observed in schizophrenia can be accounted for partly by their frontal lobe pathology. Other aspects of social cognitive impairments could also be associated with the extra-frontal pathology, such as the amygdala.

Key words amygdala · empathy · emotion attribution · frontal lobe damage · medial prefrontal cortex

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Introduction

Schizophrenia is a psychiatric disorder characterized by debilitating psychosocial impairments, and one of the defining features of this disorder is supposed to be related to abnormal social cognition [10]. Substantial studies found that patients with schizophrenia show a range of impairments in their social cognitive abilities. These studies contained ample evidence to indicate the altered perception of emotional expressions on faces [27] and impaired mind-reading, i.e., theory of mind (ToM) [9]; however, the neurobiological bases of social cognitive impairments in schizophrenia still need to be determined. Based on human lesion studies and activation studies, neural systems specialized for processing social information have been identified. The amygdala has been verified as a critical region in processing emotional information, such as facial expressions [1], and the orbital and medial frontal cortices are found to be associated with a higher level of social information processing, such as ToM [6, 12, 35]. These regions together with the superior temporal sulcus are the constituents of the "social brain" proposed by Brothers [8]; thus one would hypothesize that the deficits in social cognition in schizophrenia are related to the specific pathology within the "social brain".

In support of this view, i.e., "altered social brain in schizophrenia," structural magnetic resonance imaging (MRI) studies of schizophrenia accumulated evi-

dence of regional volume reductions in the frontal and temporal lobes [22], which includes the findings of the amygdala [15, 21] and the orbital/medial frontal cortices [5, 15, 33] volume reductions.

However, the following critical question must be answered: "how are the abnormalities of these neural structures indeed related to the social cognitive impairments observed in schizophrenia?" Schizophrenia is a disease that affects multiple brain regions. Even when focusing on the structures implicated in social information processing, there are multiple regions that are structurally abnormal in schizophrenia, such as several sectors within the frontal cortex, the amygdala, the superior temporal gyrus, etc. Therefore, it is still to be elucidated which neural structural pathologies of schizophrenia underlie the social cognitive impairments observed in this disorder. Perhaps one straightforward way to resolve this issue would be to apply a lesion model approach investigating patients with focal brain injury, which directly links a specific brain region to a behavior; this should help us to better understand the neural basis of social cognitive impairments in schizophrenia.

In the present study, we compared the social cognitive abilities of patients with schizophrenia with those of patients with focal frontal lesions. We applied two sets of social cognitive tasks that are mainly focused on emotional aspects: the emotion intensity recognition task and the emotion attribution tasks. The former examines the ability to recognize the emotion intensity of basic emotions from facial expressions; it was originally developed by Adolphs et al. [1] for brain-damaged patients. Patients with bilateral amygdala damage have been reported to perform poorly on this task, especially in recognizing fearful facial expressions. Thus this task, which was regarded to be sensitive to the amygdala pathology, would serve as a marker of any amygdala dysfunctions in schizophrenia. The latter tasks test the ability to attribute emotions to other individuals and require a broader range of social cognitive processes, including affective aspects of ToM abilities; impairments of which would serve as a marker of frontal lobe pathology in schizophrenia. Previous studies found that patients with schizophrenia have impairments in the emotion intensity recognition task [29] and in the emotion attribution tasks [13, 37], which were correlated with volume reductions in the amygdala and in the medial frontal lobes, respectively. However, the linkage to the brain pathologies with their poor social cognitive abilities in schizophrenia is yet to be revealed by a direct comparison with individuals who have focal brain lesions. We hypothesized that while patients with schizophrenia would show defective performances on both tasks as demonstrated previously, those with focal frontal lesions would show poor performance only in the emotion attribution tasks.

Materials and methods

Subjects

After a complete description of the study to the subjects, written informed consent was obtained from them. This study was approved by the Committee on Medical Ethics of Kyoto University.

The schizophrenia group comprised 28 outpatients (14 men and 14 women) who were referred to the psychiatric department of Kyoto University. Based on the Structural Clinical Interview for DSM-IV (SCID), each patient fulfilled the DSM-IV criteria for schizophrenia [paranoid (n = 14), disorganized (n = 8), catatonic (n = 2), schizophreniform (n = 3), schizoaffective (n = 1)]. Psychopathology was assessed using the Positive and Negative Syndrome Scale (PANSS [23]). All patients were receiving antipsychotic medication [typical (n = 6), atypical (n = 17), typical and atypical (n = 5)] average 11.7 mg/day in haloperidol equivalents calculated according to Inagaki et al. [20]. All patients were physically healthy at the time of scanning and psychological tests. None had a history of head trauma, neurological illness, serious medical or surgical illness, or substance abuse, or any first relatives who had had psychotic episodes.

The frontal lobe damaged (FL-damaged) group consisted of ten traumatic brain injury (TBI) patients (8 men and 2 women), referred to the psychiatric or the neurological department of Kyoto University. Their lesion sites were identified in the frontal lobe by MRI. All the lesions were mapped onto the standard Montreal Neurological Institute (MNI) brain template using MRIcro (Nottingham UK) software. The overlaps of the lesions in these patients were centered on the bilateral ventromedial prefrontal region (Fig. 1). Apart from this, none of the patients had any obvious neurological or psychiatric illness.

The comparison group comprised 22 healthy individuals (11 men and 11 women) who were matched with the schizophrenia group and the FL-damaged group for age and education level. These subjects were also evaluated on the basis of SCID. None had a history of neurological or psychiatric illness, or any first relatives who had had psychotic episodes.

Table 1 provides the demographic data of these three groups. The estimated verbal and performance IQs were obtained from vocabulary and block design subtasks, respectively, in the Wechsler Adult Intelligence Scale-Revised (WAIS-R) by transforming the scores corrected for age into T scores. There were no significant differences in age, education, estimated verbal IQ (VIQ) and performance IQ (PIQ) between the groups (all comparisons: $P > 0.05$).

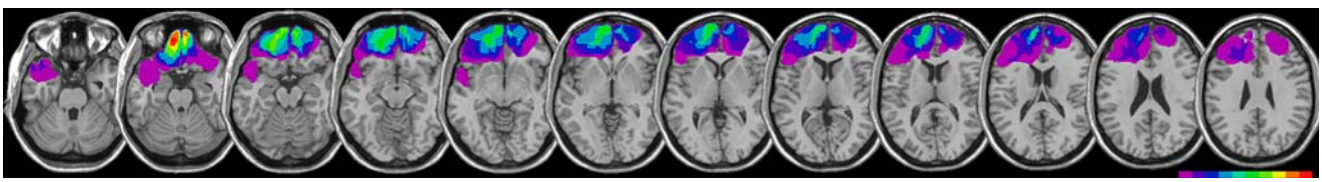

Fig. 1 Lesions of the FL-damaged patients overlaid on the MNI template

Table 1 Demographic and neuropsychological characteristics of subjects

	Healthy (n = 22)		FL-damaged (n = 10)		Schizophrneia (n = 28)	
	Mean	SD	Mean	SD	Mean	SD
Age (years)	40.0	7.5	38.8	13.2	37.8	8.7
Sex (M/F)		11/11		8/2		14/14
Handedness (R/L)		21/1		10/0		27/1
Education years	13.4	2.5	13.5	2.9	13.9	2.7
PANSS positive	–	–	–	–	15.8	6.6
PANSS negative	–	–	–	–	16.1	6.1
PANSS general	–	–	–	–	31.9	9.9
VIQ	107	15.0	94.0	15.8	96.3	14.9
PIQ	108	13.2	104	16.2	98.0	16.1
BFRT	47.5	3.87	43.5	3.63	45.2	5.6

VIQ the estimated verbal IQ obtained from the subtask of vocabulary in the Wechsler Adult Intelligence Scale-Revised (WAIS-R) by transforming scores corrected for age into *T* scores, *PIQ* the estimated performance IQ obtained from the subtask of block design in the WAIS-R by transforming scores corrected for age into *T* scores, *BFRT* Benton facial recognition test

Tasks

Benton facial recognition test

To control the subjects' basic visuoperceptual ability for facial stimuli, a short version of the Benton facial recognition test (BFRT [7]) was administered. Subjects matched the faces of identical individuals from among six choices, which were shown in varying views and light conditions.

Emotion intensity recognition task

The experimental procedure was identical to that of Adolphs et al. [1]. Six faces—each representing happiness, sadness, fear, anger, disgust, and surprise—and three neutral faces were selected from the pictures of facial affect series [11]. Thus there were a total of 39 face stimuli. The set of 39 stimuli were presented in random order in each block with no time limit. This was repeated six times in separate blocks. For each block, one of the six emotion terms was presented, and the patients or comparison subjects had to evaluate the facial expression with regard to the intensity of the given emotion content on a scale of 0 (not at all) to 5 (very much). After rating all the 39 stimuli pertaining to one of the six emotions, the subjects were given other emotion terms to rate in a subsequent block. Thus for each facial stimulus, the subjects rated the intensity of all the six basic emotions.

The accuracy of the task performance was measured using Pearson correlation scores. First, the rating profile given to each face by each participant was correlated with the mean rating profile given to that face by the group of healthy subjects. Correlation coefficients for the healthy subjects were calculated between each healthy individual and the remaining 21 healthy subjects. Thus the correlations near 1 indicate that the participant rated the stimulus normally, and the correlations near 0 (or negative) indicate that the participant rated the stimulus very abnormally. Then, in order to calculate the average correlation for several faces (e.g., the average correlation for all six happy faces), a participant's correlation for each individual face was Fisher Z-transformed, and the Z-transformed correlation was averaged over the six faces that expressed a given emotion; the average was then inverse Z-transformed to obtain the mean correlation for that emotion. The Fisher Z-transformed correlation scores were used in all the parametric statistical analyses. Further details of the task and the analysis have been described elsewhere [1, 2].

Emotion attribution task

To examine the subjects' ability to attribute emotions to facial expressions and to protagonists in complex social situations, we administered the perception of affect task (PAT [30]), identical to that described previously [37]. Briefly, PAT consists of four subtasks. Subtask 1 is a matching between a verbal stimulus and a verbal label. Participants were presented with short stories describing emotional situations and were asked to choose the one that best described the feeling of the main protagonist in each situation from a list of seven emotion labels (happiness, sadness, fear, anger, disgust, surprise, and neutral). Subtask 2 is to match a visual stimulus with a verbal label. Participants were presented with the emotional facial stimuli and were requested to choose the best described label from a list of seven emotions. Subtask 3 is to match a verbal stimulus with a visual label. Participants were again presented with the same short stories as in subtask 1 and were asked to choose the best described facial expression from a seven-emotion list. Subtask 4 is to match a visual stimulus with a visual label. Participants were presented with the emotional facial stimuli and were requested to choose the best described one from seven photographs of social situations, in which human figures represent one of seven emotions. The faces of these figures were erased or not observable. Emotional facial stimuli were selected from the picture of facial affect series [11]. Each subtask consisted of 35 stimuli, five items for each of seven emotions.

Data analysis

Statistical analyses were performed using SPSS v.12.0. Group comparisons for the performances on the emotion intensity recognition task applied two-way analyses of variance (ANOVAs) with groups (schizophrenia, FL-damaged, and healthy subjects) as a between-subject factor and emotion categories (happiness, sadness, fear, anger, disgust, and surprise) as a within-subject factor. Group comparisons for the performances on each of the four subtasks of the perception of affect task (PAT) employed one-way ANOVAs with groups (schizophrenia, FL-damaged, and healthy subjects) as a between-subject factor. The statistical significance was defined as $P < 0.05$.

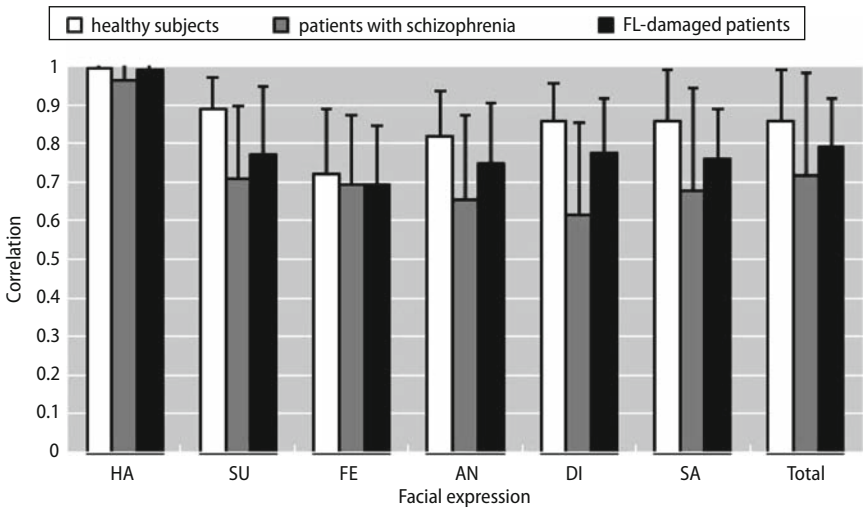

Fig. 2 Performances of the patients with schizophrenia, the FL-damaged patients, and the healthy subjects on the emotion intensity recognition task

Results

Benton facial recognition test

There was no significant difference between the groups in the Benton facial recognition test [$F(2, 57) = 2.804$, $P > 0.05$] (Table 1).

Emotion intensity recognition task

An ANOVA revealed a main effect of group [$F(2, 57) = 9.160$, $P < 0.001$, partial $\eta^2 = 0.24$]. A post hoc comparison confirmed that the schizophrenia group was impaired relative to the healthy comparison group ($P < 0.001$), while there were no differences between the FL-damaged group and the comparison group ($P = 0.344$) or between the FL-damaged group and the schizophrenia group ($P = 0.314$) (Fig. 2). No group by emotion interactions attained statistical significance [$F(5, 146) = 1.328$, $P = 0.254$, partial $\eta^2 = 0.05$].

Emotion attribution task

The performances across subtasks 1–4 were significantly affected by the groups [subtask 1: $F(2, 57) = 4.97$, $P = 0.01$, partial $\eta^2 = 0.15$; subtask 2: $F(2, 57) = 13.551$, $P < 0.001$, partial $\eta^2 = 0.32$; subtask 3: $F(2, 57) = 14.221$, $P < 0.001$, partial $\eta^2 = 0.33$; subtask 4: $F(2, 57) = 7.641$, $P = 0.001$, partial $\eta^2 = 0.21$]. A post hoc comparison revealed that the FL-damaged group performed worse than the healthy subjects across the subtasks (all comparisons: $P < 0.05$), and the schizophrenia group performed worse than the healthy subjects across subtasks 2–4 (all comparisons: $P < 0.05$) with a trend in subtask 1 ($P = 0.063$); however, no significant differences between the FL-damaged group and the schizophrenia group were found across the subtasks (all comparisons: $P > 0.1$) (Fig. 3).

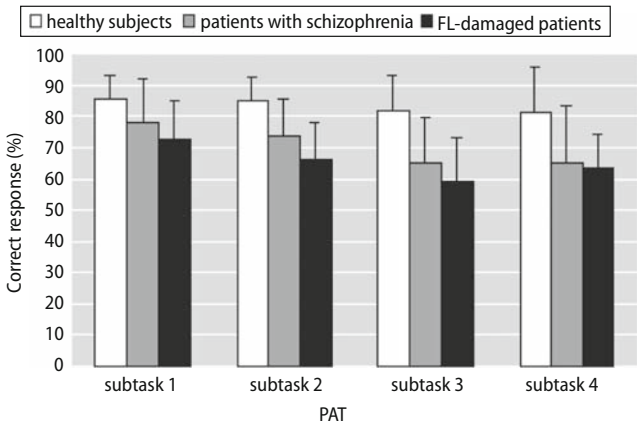

Fig. 3 Performances of the patients with schizophrenia, the FL-damaged patients, and the healthy subjects on the emotion attribution task

Correlation analyses between medication and tasks

To investigate the potential influence of medication on the tasks above, correlation analyses between haloperidol equivalents and task scores were performed in the schizophrenia group. No significant correlations were found (all: $P > 0.05$). Thus the results obtained from social cognitive tasks in schizophrenic patients could be assumed to reflect their abilities themselves, and the influence of medication would be small, if it existed.

Discussion

With this direct comparison of social cognitive performance between the patients with schizophrenia and the FL-damaged patients, we revealed two main findings. The FL-damaged patients performed poorly on the emotion attribution task, but there was no evidence of impairment on the emotion intensity recognition task as compared with normal controls.

On the other hand, the patients with schizophrenia performed poorly on both of these tasks. We first attempt to discern the finding obtained from the FL-damaged patients, followed by the one from the patients with schizophrenia.

The performance on the emotion intensity recognition task of the FL-damaged patients did not differ from that of the healthy subjects. Including the original article of Adolphs et al. [1], patients with damage to the amygdala have been shown to perform poorly on this emotion intensity task [2, 32, but see 17], which suggests that this task relies heavily on the functions of the amygdala. The role of the amygdala in the emotion intensity processing has also been reported by other studies [4, 16, 25, 34], suggesting that the amygdala processes the intensity of emotion in contrast to the recognition of the valence of emotion in the frontal lobes. Thus the insignificant impairment in the processing of emotion intensity from facial expressions in the FL-damaged patients would correspond to their lesion sites that did not extend to the amygdala. This finding should be interpreted carefully, however, because the performance of the FL-damaged patients was also not significantly different from that of schizophrenic patients. In other words, the performance of the FL-damage patients may fall somewhere in between that of the other two groups. The important distinction to make here among the two clinical groups is that the schizophrenic patients are performing significantly worse than the healthy subjects, while the FL-damaged patients are not. Given the high interconnectivity between the amygdala and the frontal lobe [38], it is plausible that the emotion intensity task used in this study is strongly amygdala-dependent, as indicated by previous studies, but not exclusively in a manner that may also be influenced by the medial frontal lobe function, as shown in the present study. This differential deficit issue will be further discussed below.

The emotion attribution tasks applied in the present study comprised different components of social cognition: the recognition of facial expressions, verbal labeling of emotions, empathy and ToM. These types of social cognition have been indicated to incorporate the frontal cortex. Regarding the recognition of facial expressions, a number of imaging studies have reported that the frontal cortex was activated in the explicit recognition of the valence of emotion [41], such as the verbal labeling of emotions to facial expressions. Likewise, neurological patients with damage to the orbitofrontal cortex were reported to fail to label emotions to facial expressions correctly [18]. Consistent with the previous reports, our FL-damaged patients performed poorly on the task of labeling facial expressions as directly indicated in subtask 2.

With respect to the representation of others' mental states, the so-called ToM-related tasks were reported to incorporate the medial frontal cortex in neuroimaging studies [12, 14, 39], and patients with orbital and medial frontal cortices showed poor performances on the ToM-related tasks [26, 35, 36]. In agreement with these previous findings, we found impairments in attributing mental states to others in our FL-damaged patients with lesions centered on the ventromedial frontal cortex. In contrast to the ToM tasks that usually examine cognitive mental attribution, however, our tasks focused to a greater extent on the emotional aspects of mental attribution. Some recent studies attested to the functional and anatomical fraction of cognitive and emotional mental attributions and suggest that emotional aspects are likely to be strongly mediated by the ventral sector of the frontal cortex [3, 19, 24, 40], which also in line with our findings obtained from the emotional mental attribution tasks.

In contrast to the intact emotion intensity recognition in the FL-damaged group, schizophrenic patients performed poorly on this task, which may suggest the presence of dysfunction in the amygdala in these patients. Volumetric studies using high-resolution images have revealed amygdala volume reduction in patients with schizophrenia [15, 21]. More recently, the linkage between the volumes of the amygdala and emotion recognition ability was directly compared [29]. They demonstrated that impaired recognition of sad facial expression in the emotion intensity recognition task was correlated with reduced volumes in left amygdala in schizophrenia.

Patients with schizophrenia were as impaired on the emotion attribution tasks as the FL-damaged patients. There is ample evidence of the FL volume reductions reported in schizophrenia. Among subregions in the FL, in particular, volume reductions in the orbitofrontal and the medial frontal cortex have been demonstrated [5, 15, 33]. Furthermore, our previous study, which directly examined both structural abnormalities and emotion attribution deficits [37], showed the association between volume reductions in the medial prefrontal cortex and poor emotion attribution in schizophrenia. Other studies reported impaired affective inference-making based on the direction of eye gaze [31] and poor understanding of false beliefs [28] in both patients with schizophrenia and those with medial frontal lesions. The present results foster these findings: emotion attribution deficits in schizophrenia may be influenced by abnormalities of the medial prefrontal cortex inasmuch as focal frontal lesions.

Considering the involvement of multiple brain regions in multi-dimensionally construed social cognition, the present study demonstrated that social cognitive impairments in schizophrenia were also manifold and could be associated with pathologies in distinct brain regions, such as the orbital/medial frontal lobes and the amygdala. However, assuming that variability appears to exist in the functional and

anatomical disturbances in schizophrenia and that recent neural network models oppose simplistic localization of function and behavior, it is deemed that a lesion model of social cognitive dysfunction alone would not be sufficient in explaining its occurrence in schizophrenia. Instead, the dysfunction in social cognition may represent abnormalities in the interactions among networks of regions in the social brain or between these regions and their functionally connected cortical and sub-cortical areas. Further studies would elucidate the exact nature of social dysfunction in schizophrenia with a focus on the heterogeneity of schizophrenia. While there appears to be no doubt that these patients exhibit social dysfunction, till date, little attention has been paid to the relationship among social cognition, brain region, and specific schizophrenia subtypes or symptoms. In this regard, future studies may shed light on schizophrenia subtypes that are hypothesized to be associated with social dysfunction; we may then be able to formulate a comprehensive model of the neural basis of social cognitive impairments in schizophrenia.

The present study addresses the important issue about how social cognitive abilities of patients with schizophrenia are similar and dissimilar from those with medial frontal lesions. It should be noted, however, that the emotion processing tasks used in this study were not specifically developed for the identification of differential social cognitive deficits. Although previous studies have indicated differential involvements of neural networks in the two tasks as reviewed above, the psychometric properties, such as the discriminative power, of them are not known. Another possible shortcoming of the present study was the relatively small sample size of the FL-damaged group, which might have yielded the confounding results in the emotion intensity task. This, however, was partially compensated by the close matching of the study groups. Therefore, the findings described above in relation to the amygdala should be viewed with caution, and this study has to be judged preliminary.

In conclusion, by comparing the social cognitive abilities of patients with schizophrenia with those of patients with focal frontal injuries, we demonstrated that patients with schizophrenia performed poorly on the emotion attribution task in ways that were similar to patients with focal frontal injuries; however, only patients with schizophrenia showed impairments on the emotion intensity recognition task. This may suggest that social cognitive impairments in schizophrenia would not be a unified organization but may be multi-dimensionally constructed, some aspects of which would involve the pathology of frontal lobes and the other aspects could be associated with the extra-frontal pathologies, such as the amygdala.

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