Asian Journal of Psychiatry 45 (2019) 53–60

Contents lists available at ScienceDirect

Asian Journal of Psychiatry

journal homepage: www.elsevier.com/locate/ajp

Altered neural basis of self-reflective processing in schizophrenia: An fMRI study

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ARTICLE INFO

Keywords:
fMRI
Neural circuitry
Schizophrenia
Self-reflection
Other-reflection

ABSTRACT

Background: Impaired self-awareness has often been described in schizophrenia. Recent neuroimaging studies examining the self-reflection processes in schizophrenia have produced inconsistent results.
Method: We examined the self-reflective neural network using self- and other-evaluation tasks in schizophrenia. Fifteen schizophrenia patients and fifteen age- and sex-matched healthy subjects underwent functional magnetic resonance imaging. Subjects were required to decide whether the sentence described their own personal trait (self-evaluation) and that of their close friends (other-evaluation).
Results: Unlike normal control subjects, the schizophrenia patients did not have greater activation of the left posterior cingulate gyrus and hippocampus during self-evaluation than during other-evaluation. On the other hand, the schizophrenia patients had higher activation of the right superior frontal and right supramarginal gyri during self-evaluation than control subjects. Only the patient group exhibited hyperactivation in the left hippocampus and right external capsule associated with the other-evaluation task.
Conclusions: These findings provide evidence for an altered neural basis of self-reflective processing, which may underlie the self-awareness deficits in schizophrenia.

1. Introduction

Impaired self-awareness is a core feature of schizophrenia, which is related to the classical clinical symptoms and deficits in social functioning (Sass and Parnas, 2003). In particular, most first-rank symptoms of schizophrenia identified by Schneider (1959), which involve an alienated sense of one's own mental or physical activity (Kurachi, 2003), can be interpreted as a representation of compromised core self-awareness [i.e., self-monitoring ability or 'minimal' self (Nelson et al., 2014)] (Sass and Parnas, 2003; Frith, 2005) that may be more perceptual than conceptual (Tacikowski et al., 2017). On the other hand, impaired insight in schizophrenia is considered to reflect deficits in more conceptual self-awareness (Lysaker et al., 2005), especially for metacognition associated with self-reflection processes or 'narrative' self (Nelson et al., 2014). Empirical studies have revealed disruptions of these different levels of self-awareness in schizophrenia (Keefe et al., 2002; Lysaker et al., 2005; Pauly et al., 2011; Wang et al., 2011), and disruption of self-monitoring may affect self-reflection processes (Nelson et al., 2014).

Previous functional neuroimaging studies on healthy subjects demonstrated significant activation of the cortical midline structures (CMS), such as the medial prefrontal cortex (MPFC) and cingulate regions, during conceptual self-reflection tasks such as asking whether sentences describing traits, abilities, or attitudes apply to the subject (reviewed by van der Meer et al., 2010). However, functional magnetic resonance imaging (fMRI) studies examining self-reflection processes in schizophrenia have produced inconsistent results with increased (Shad et al., 2012; Liu et al., 2014), normal (Murphy et al., 2010), or even reduced (Tan et al., 2015; Pankow et al., 2016) CMS activation during self-reflection. These studies also reported increased activation in the lateral prefrontal (Liu et al., 2014) and parietal (Shad et al., 2012) regions, in addition to reduced temporal activation (Pauly et al., 2014) in

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https://doi.org/10.1016/j.ajp.2019.08.007
Received 15 January 2019; Received in revised form 22 August 2019; Accepted 22 August 2019

Table 1
Demographic and clinical data for each group.

	Healthy subjects n = 15	Schizophrenia patients n = 15
Male / female	8 / 7	8 / 7
Age (years)	27.5 (4.3)	27.0 (5.3)
Height (cm)	164.8 (9.6)	164.3 (10.3)
Education (years)	15.9 (0.4)	14.0 (1.9)[b]
Parental education (years)	12.5 (1.5)	12.4 (1.1)
Age at onset (years)	–	22.1 (4.7)
Duration of illness (years)	–	4.9 (6.1)[c]
Duration of medication (years)	–	3.1 (4.9)
Drug dose (mg/day, haloperidol equivalent)[a]	–	9.0 (6.1)
Total SAPS score	–	20.8 (20.4)
Total SANS score	–	30.6 (14.1)

Values represent means (SD).
[a] Neuroleptic dosages of different classes of antipsychotic drugs were converted into haloperidol equivalents using the guidelines by Toru (2008).
[b] Significant at $p < 0.001$.
[c] Median 2.8 years.

the patients during the tasks. These discrepancies may be due, in part, to illness chronicity and/or medication because most of these previous studies employed chronic schizophrenia groups (Shad et al., 2012; Liu et al., 2014; Pauly et al., 2014; Tan et al., 2015; Pankow et al., 2016).

Previous neuroimaging findings from our group suggested a role of limbic-paralimbic atrophy (Suzuki et al., 2005) or increased blood flow in the fronto-parietal regions (Yuasa et al., 1995) in the severity of clinical symptoms related to impaired perceptual self-awareness. These findings are consistent with a recent fMRI study on healthy subjects (Tacikowski et al., 2017) that demonstrated a significant association between perceptual awareness and neural response in the fronto-parietal cortex. However, it remains unclear whether the activation pattern in this region during self-awareness tasks is associated with the symptomatology of schizophrenia.

We examined the neural activities involved in self-reflective processing compared with those in other-reflection processes in schizophrenia patients with a relatively short illness duration and healthy subjects using fMRI. Based on previous observations (e.g., van der Meer et al., 2010; Shad et al., 2012; Liu et al., 2014), including our own structural MRI (Suzuki et al., 2005) and single photon emission computed tomography (SPECT) (Yuasa et al., 1995) findings, we predicted that the subjects would exhibit significant regional activation predominantly in the CMS and fronto-parietal regions during self-reflection, but that the patients and controls would have different activation patterns. We also explored whether the activation pattern during the task was associated with the clinical symptoms of schizophrenia.

2. Methods

2.1. Subjects

Fifteen schizophrenia patients and fifteen healthy control subjects were included. The subjects were right-handed and had normal or corrected-to-normal vision. All subjects were physically healthy at the time of the study, and none had a history of head trauma, neurological illness, substance abuse disorder, or other serious medical illnesses. Demographic and clinical data of the subjects are presented in Table 1; the groups were matched for age, sex, height, and parental education.

The schizophrenia patients fulfilling ICD-10 research criteria (World Health Organization, 1993) were recruited from the inpatient and outpatient clinics of the Department of Neuropsychiatry, Toyama University Hospital. All patients were clinically stable under neuroleptic medication: 11 were receiving atypical neuroleptics, one was being treated using typical neuroleptics, and 3 patients were receiving a combination of atypical and typical neuroleptics. Clinical symptoms were rated at the time of scanning using the Scale for the Assessment of Negative and Positive Symptoms (SANS/SAPS; Andreasen, 1984a, 1984b).

The control subjects consisted of healthy volunteers recruited from among the members of community, hospital staff, and university students. They were given a questionnaire consisting of 15 items concerning their family and past histories; none had a personal or family history of psychiatric illness. They were also screened using the Minnesota Multiphasic Personality Inventory (New Japanese MMPI Committee, 1997) (i.e., excluded if T-score > 70) because their personality traits [e.g., schizotypal (Debbané et al., 2014) and psychopathic (Deming et al., 2018) traits] may have significantly affected self-reflection and related brain activation. The study was approved by the ethics committee of the University of Toyama. Written informed consent was received from all subjects after full explanation of the procedures.

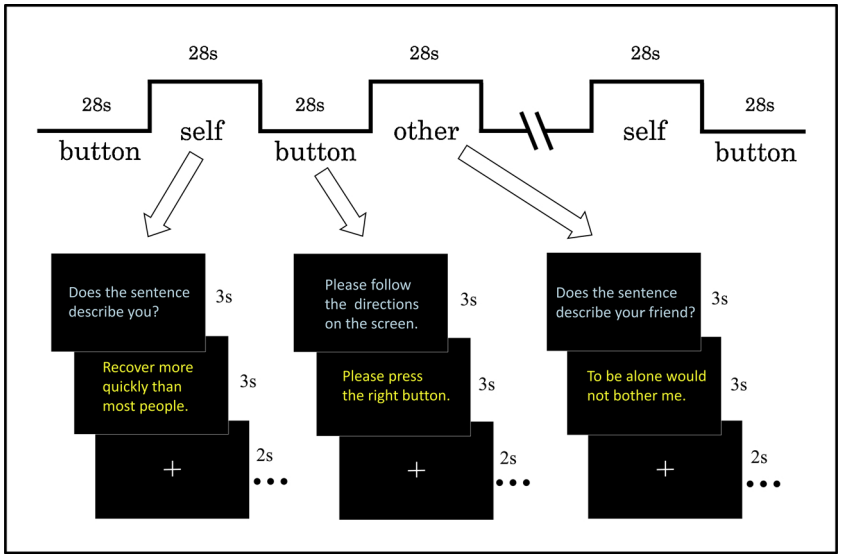

Fig. 1. Examples of experimental stimuli used in the self, other, and button trials. Sentences were presented in Japanese.

2.2. Stimulus presentation and task

During fMRI scanning, the subjects had visual tasks in three conditions: self-evaluation (SE), other-evaluation (OE), and simple button press (SBP) (Fig. 1). These stimuli were displayed using Presentation software (Neurobehavioral Systems, San Francisco, CA) and viewed on a back-projected screen via a head coil-mounted mirror.

For the SE and OE conditions, the same set of 25 shortened sentences (12 to 26 Japanese characters in *hiragana* and *kanji*) regarding personal traits, abilities, or attitude (e.g., "Good at saving money", "Able to recover quickly from minor illness or stress"), which were from the tridimensional personality questionnaire Japanese version (Takeuchi et al., 1993), were randomly presented and used as visual stimuli. In the SE condition, subjects were required to make a yes/no decision as to whether the sentence described their own personal trait. In the OE condition, subjects were required to decide whether the sentence described one of their close congener friends who had been identified among their classmates or colleagues by each subject prior to

Table 2
Behavioral results.

Reaction time (msec)			
	Self-evaluation	Other-evaluation	Simple button press
Healthy subjects	2045 (422)	2076 (398)	887 (405)
Schizophrenia patients	2524 (403)	2519 (429)	901 (184)

Response type (%)			
	Self-evaluation (% Yes response)	Other-evaluation (% Yes response)	Simple button press (% Correct)
Healthy subjects	47.7 (13.8)	41.1 (14.8)	100.0 (0)
Schizophrenia patients	50.3 (17.8)	49.2 (14.1)	100.0 (0)

Concordance rate (%)		
	Self-evaluation	Other-evaluation
Healthy subjects	96.9 (3.3)	94.2 (6.4)
Schizophrenia patients	87.0 (6.4)	77.1 (13.1)

Values represent means (SD).

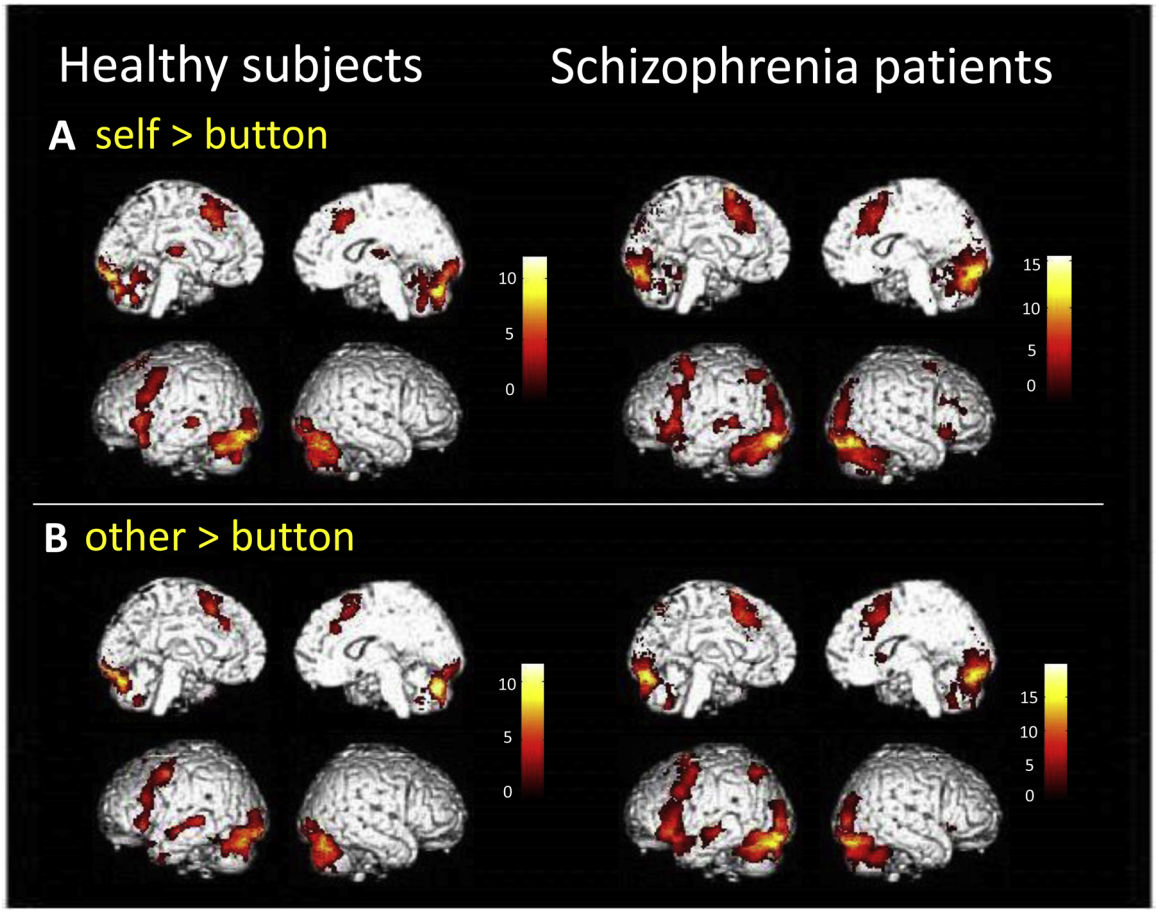

Fig. 2. fMRI results from within-group analysis for self > button (A) and other > button (B) contrasts in each group. All regions were displayed at the $p < 0.001$ uncorrected voxel level and $p < 0.05$ corrected (family wise error) cluster level.

Table 3
Regions of significantly increased activation for within-group analysis.

Brain region	BA	Talairach coordinate x	y	z	Cluster size, voxels.	*T*-value
Healthy subjects						
Self > Button						
L inferior occipital gyrus	18	−18	−95	−2	7646	11.78
L inferior frontal gyrus	44	−42	13	24	1813	8.61
L superior frontal gyrus	6	−5	17	47	1080	7.98
L thalamus		−1	−19	8	236	5.61
L middle temporal gyrus		−48	−35	0	200	5.56
Other > Button						
R cerebellum		15	−71	−21	5859	11.52
L middle frontal gyrus	6	−41	1	43	1264	9.68
L superior frontal gyrus	8	−1	19	47	875	8.03
L middle temporal gyrus	21	−59	−12	−8	523	7.76
L cerebellum		−7	−64	−39	147	7.34
L temporal pole	38	−43	0	−38	206	6.84
(Self > Button) > (Other > Button)						
L hippocampus	54	−23	−21	−10	127	6.68
L posterior cingulate cortex	31	−1	−15	46	138	6.05
(Other > Button) > (Self > Button)						
No significant differences						
Schizophrenia patients						
Self > Button						
L inferior occipital gyrus	18	−22	−93	0	11029	15.55
R superior frontal gyrus	8	4	21	40	4177	10.13
L inferior parietal lobule	39	−34	−57	46	437	6.48
L cerebellum		−3	−43	−13	179	6.33
R insula	13	36	20	−3	395	6.27
L middle temporal gyrus	21	−59	−44	8	373	6.08
R inferior frontal gyrus	44	42	20	22	143	5.02
Other > Button						
L inferior occipital gyrus	18	−28	−87	3	9244	19.81
L inferior frontal gyrus	47	−43	17	−9	4438	10.86
L superior parietal lobule	7	−28	−57	47	473	7.87
L middle temporal gyrus	21	−52	−18	−10	422	6.74
R external capsule		27	19	3	262	6.60
L cerebellum		−3	−62	−36	246	5.19
(Self > Button) > (Other > Button)						
No significant differences						
(Other > Button) > (Self > Button)						
No significant differences						

BA, Brodmann's area; R, right hemisphere; L, left hemisphere. Clusters with significant differences are presented at the threshold of $p < 0.001$ uncorrected voxel level, and $p < 0.05$ corrected (family wise error) cluster level.

scanning. Subjects responded to each sentence with a "yes" (right hand) or "no" (left hand) button press, which was recorded using an MR-compatible keypad. The subjects were asked to remember their responses. For the SBP condition, which was used as baseline data, sentences giving instructions to press the right or left button (e.g., "Please press the left button", which consisted of 13 Japanese characters) were used.

We employed a block design paradigm consisting of 18 blocks within a functional run; the SE, OE, and SBP conditions included 5, 4, and 9 blocks, respectively. The order of the 3 conditions was an ACB-CACBCACBCACBCAC sequence. The blocks started with the instructive sentence (e.g., Does the sentence describe you?) presented for 3 s followed by the stimulus sentence for 3 s. Each block had 5 trials, which were separated by a centered fixation cross that was presented for 2 s. The duration of each block was thus 28 s and the total time for our functional run was 504 s.

Immediately after scanning, the subjects were asked to recall which button they had pressed for each sentence. The concordance rates of the task performance, which reflect the subjects' dedication to the tasks, were calculated based on comparison of online behavioral data with recalled data.

2.3. fMRI data acquisition

Brain imaging was performed using a 1.5-T Magnetom Vision scanner (Siemens Medical System, Erlangen, Germany) with a standard head coil. Foam padding was used to minimize head movement. A T2*-weighted gradient echo planar imaging (EPI) sequence was used to acquire a set of 72 coronal slices of functional images with the following parameters: repetition time = 7000 ms, echo time = 60 ms, flip angle = 90 degrees, 3-mm thickness, no slice gap, field of view = 200 mm, 64 × 64 matrix, voxel size = 3.13 × 3.13 × 3.00 mm. A T1-weighted 3D gradient-echo sequence was used to acquire a set of 160–180 contiguous slices of anatomical images with the following parameters: repetition time = 24 ms; echo time = 5 ms; flip angle = 40°; field of view = 256 mm; and matrix size = 256 × 256 pixels. The voxel size was 1.0 × 1.0 x 1.0 mm.

2.4. fMRI data analysis

Imaging data were preprocessed and analyzed using Statistical Parametric Mapping software (SPM8, Wellcome Department of Imaging Neuroscience, London, UK) on Matlab 7.7.0 (The Mathwork Inc.). The first eight images of each fMRI session were discarded from analysis because the MR signal had not reached the steady state.

Functional images were realigned to the first scan to correct for head movement. The obtained mean EPI image was then co-registered with each subject's anatomical T1 image. After that, images were spatially normalized to the standard anatomical space (voxel size: 2 × 2 × 2 mm) defined by the Montreal Neurological Institute (MNI) template. Normalized images were then spatially smoothed using an 8-mm full-width at half-maximum (FWHM) Gaussian kernel. Low-frequency noise was removed by a high-pass filter (cut-off of 128 s).

For individualized analysis, time series data were analyzed for each subject using a boxcar model convolved with a canonical hemodynamic response function. A general linear model (Friston et al., 1995) was used to compute parameter estimates and *t*-contrast images for each comparison at each voxel (first-level analysis of SE > SBP and OE > SBP). We used an explicit mask of gray matter because we hypothesized that neural activation is restricted to gray matter. To compare neural activity associated with each evaluation condition, we created contrast images showing (SE > SBP) > (OE > SBP) and (OE > SBP) > (SE > SBP).

These individual contrast images were entered into second level analyses using a random effect model. One-sample *t*-tests were performed for each condition in both groups. We then conducted two-sample t-tests with a relatively conservative threshold of $p < 0.001$ for the uncorrected voxel level and $p < 0.05$ for the corrected (family-wise error) cluster level to compare brain activation patterns between the two groups. We specified the activation area of all conditions at the same conservative threshold levels.

SPM spatial coordinates for the standard brain from MNI templates were converted to spatial coordinates of Talairach using a non-linear transform method (http://imaging.mrc-cbu.cam.ac.uk/imaging/MniTalairach). Brain regions and Brodmann areas were identified based on the Atlas by Talairach and Tournoux (1998).

Lastly, using the Spearman rank correlation, we examined correlations between parameter estimates of significant clusters within cortical regions during the SE/OE condition in schizophrenia patients and the total SAPS/SANS score.

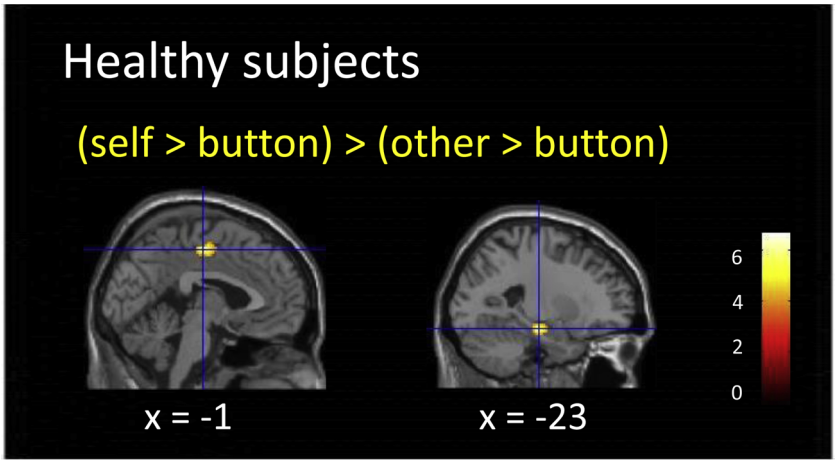

Fig. 3. fMRI results from within-group analysis for the (self > button) > (other > button) contrast in healthy subjects. Displayed at the $p < 0.001$ uncorrected voxel level and $p < 0.05$ corrected (family wise error) cluster level.

3. Results

3.1. Behavioral results

Behavioral data [reaction time, response types (% yes response), and concordance rate], which were available for 28 subjects (13 patients and 15 controls; Table 2), were analyzed using ANOVA with the group as the between-subject factor and the condition as the within-subject factor.

The reaction time was significantly different for the main effects of the group [F (1,26) = 749.4, $p < 0.05$], condition [F (2,52) = 483.7, $p < 0.001$], and group × condition interaction [F (2, 52) = 12.44, $p < 0.001$], in which both groups had a quicker response for the SBP condition than for the SE and OE conditions (all $p < 0.001$). No significant differences were found regarding the response type, but the concordance rate was higher in the SE condition than in the OE condition [F (1,26) = 7.74, $p < 0.05$] and healthy subjects had a higher concordance rate than patients [F (1,26) = 37.4, $p < 0.001$].

3.2. Neuroimaging results

The SE and OE tasks significantly activated multiple brain regions, including the medial and dorsolateral prefrontal cortex, inferior frontal gyrus, and temporal and parietal regions, in both groups (Fig. 2A, B and Table 3). In the controls, the left posterior cingulate cortex (PCC) and left hippocampus were more markedly activated in the SE condition than in the OE condition (see Fig. 3), but no difference was found between the conditions in the patients. No regions had higher activation in the OE condition than in the SE condition.

Compared with the controls, the patient group exhibited higher activation in the right superior frontal and right supramarginal gyri (SMG) in the SE condition, and higher activation in the right external capsule in the OE condition. In addition, the patient group exhibited higher activation in the left hippocampus in the (OE > SBP) > (SE > SBP) contrast, but no group difference was found in the (SE > SBP) > (OE > SBP) contrast (see Table 4 and Fig. 4).

In the patient group, there was no significant correlation between the SAPS/SANS subscale scores and regional activation after Bonferroni correction for multiple comparisons.

4. Discussion

This fMRI study demonstrated that the left PCC and hippocampus were more activated in the SE tasks than in the OE tasks in healthy subjects, whereas these different neural activation patterns in self- and other-reflective processing were disrupted in schizophrenia patients. We also found that schizophrenia patients had higher activation in the superior frontal gyrus and SMG in the right hemisphere during the SE task than healthy subjects. On the other hand, hyperactivation in the left hippocampus and right external capsule was associated with the OE task specifically in schizophrenic patients. The present findings provide evidence of abnormalities in neural circuits, especially fronto-parietal hyperactivation, which may play a role in impaired self-awareness in schizophrenia.

Consistent with previous functional neuroimaging findings in healthy subjects (Seger et al., 2004; Lou et al., 2004; van der Meer et al., 2010) and schizophrenia patients (Murphy et al., 2010), as well as with the hypothesis that the awareness of self and others shares a neural system (Northoff and Bermpohl, 2004), we found similar neural activation of the CMS (e.g., MPFC) and temporo-parietal (Seger et al., 2004; Lou et al., 2004) regions during SE and OE tasks in both healthy and schizophrenic subjects (Fig. 2). These findings are also consistent with

Table 4
Regions of significantly increased activation for between-group analysis.

Brain region	BA	Talairach coordinate			Cluster size, voxels.	
		x	y	z		*T*-value
Healthy subjects > Schizophrenia patients						
Self > Button						
		No significant differences				
Other > Button						
		No significant differences				
(Self > Button) > (Other > Button)						
		No significant differences				
(Other > Button) > (Self > Button)						
		No significant differences				
Schizophrenia patients > Healthy subjects						
Self > Button						
R supramarginal gyrus	40	49	−43	41	351	5.49
R superior frotal gyrus	6	30	15	50	288	5.22
Other > Button						
R external capsule		27	17	3	231	5.28
(Self > Button) > (Other > Button)						
		No significant differences				
(Other > Button) > (Self > Button)						
L hippocampus	54	−23	−21	−10	138	6.21

BA, Brodmann's area; R, right hemisphere; L, left hemisphere. Clusters with significant differences are presented at the threshold of $p < 0.001$ uncorrected voxel level, and $p < 0.05$ corrected (family wise error) cluster level.

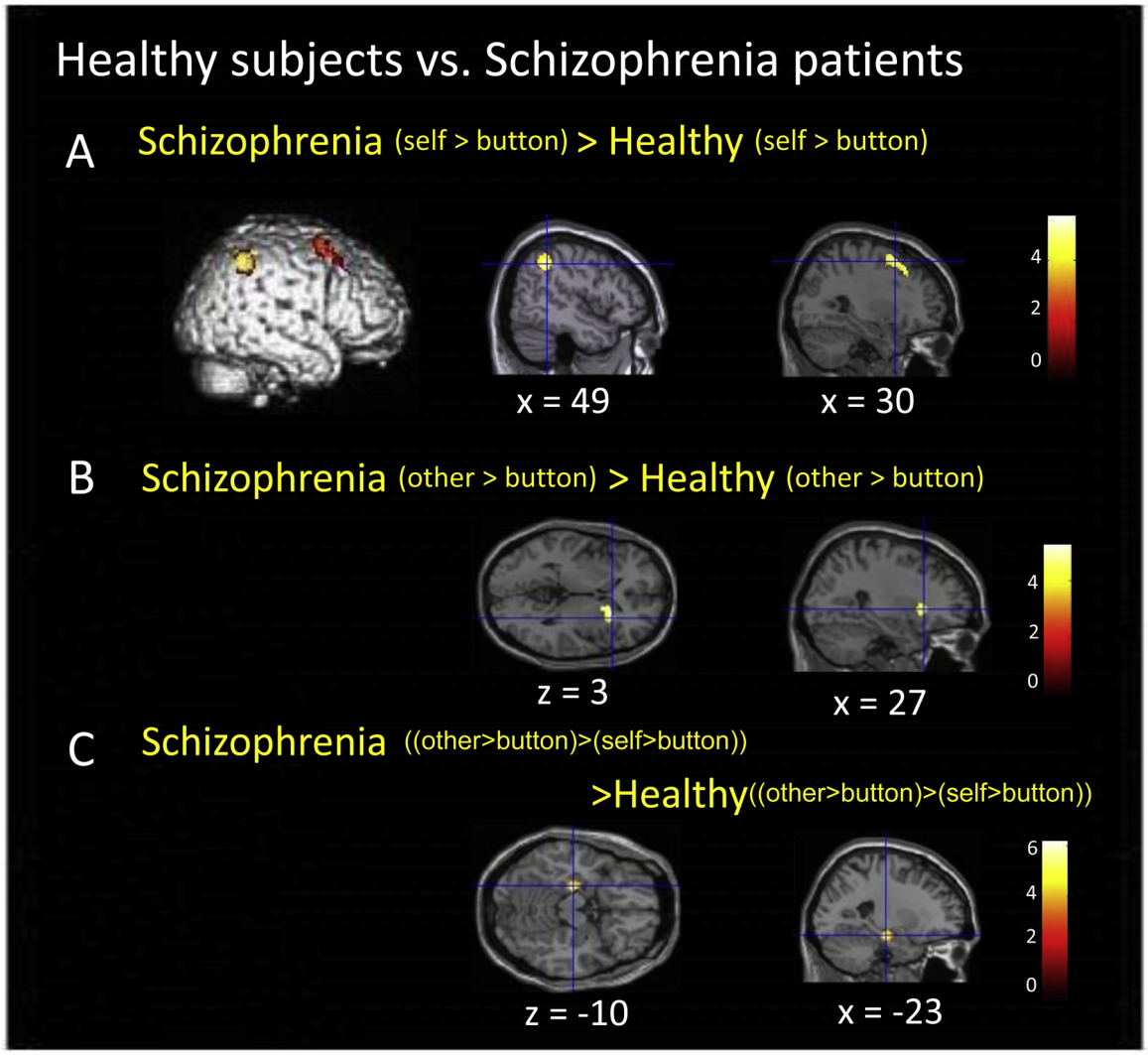

Fig. 4. fMRI results from between-group analysis showing higher activation in schizophrenia patients than in healthy subjects in the self > button contrast (A), other > button contrast (B), and (other > button) > (self > button) contrast (C). Displayed at the $p < 0.001$ uncorrected voxel level and $p < 0.05$ corrected (family wise error) cluster level.

the lack of specific association between the self-reflection processes and MPFC activation in healthy Japanese cohorts (Yoshimura et al., 2008; Yaoi et al., 2009), which suggests a dynamic influence of culture on neural representations underlying the self. Of note, the patients did not exhibit a normal SE > OE contrast of activation in the left PCC and hippocampus (Table 3). The PCC, which has a bidirectional network with the hippocampus through the cingulum (Kubota et al., 2013), is thought to play a key role in self-reflection because it is responsible for the integration of autobiographical and emotional information regarding the self (Northoff et al., 2006; van der Meer et al., 2010). Although direct group comparison revealed no difference in the SE > OE contrast (Table 4), these findings suggest that abnormalities in neural circuits, including the CMS and limbic regions, are involved in impaired conceptual self-awareness in schizophrenia.

In this study, direct group comparison revealed higher activation of the right superior frontal gyrus and SMG during self-evaluation in schizophrenia patients (Fig. 4, Table 3). Although previous fMRI studies of self-reflection processes in schizophrenia had inconsistent results [e.g., frontal hypoactivation (Holt et al., 2011)], potentially due to differences in sample characteristics (e.g., illness duration, medication status, and cultural background) and paradigms used, several fMRI studies have suggested the involvement of fronto-parietal hyperactivation in conceptual self-awareness deficits in schizophrenia (Shad et al., 2012; Liu et al., 2014). Although fronto-parietal hyperactivation has been implicated in more perceptual self-awareness (Tacikowski et al., 2017), as well as the severity of first-rank symptoms in schizophrenia (Yuasa et al., 1995; Spence et al., 1997; Jardri et al., 2011), we found no relationship between the activation pattern in this region during the self-awareness task and symptom severity in schizophrenic patients. These findings may support the notion that disruptions of different levels of self-awareness in schizophrenia are overlapping and/or reciprocally affected (Nelson et al., 2014).

Of note, a significant cluster in the group comparison during self-evaluation was centered in the superior frontal gyrus and extended to the posterior part of the dorsolateral prefrontal cortex (DLPFC), a brain region associated with sustained attention, working memory, and decision-making; dysfunctions in these cognitive functions may play a major role in the pathophysiology of schizophrenia (Stevens et al., 1998; Manoach et al., 1999; Volz et al., 2005). Our finding of fronto-parietal hyperactivation in schizophrenic patients, which suggests that they make a larger cognitive effort than healthy controls during self-evaluation, may partly support a hypothetical model of insight (Shad et al., 2007) that the right DLPFC and/or the parietal region underlie the unawareness of symptoms. The DLPFC is also important for self-other distinction in healthy subjects in close connection with the SMG (Ruby and Decety, 2001; Farrer and Frith, 2002; Blakemore et al.,

2003), an anterior part of the inferior parietal lobule (IPL) that is also implicated in empathy (Silani et al., 2013). Our findings may also support the model by van der Meer et al. (2010) where a deficit in cognitive control caused by DLPFC dysfunction leads to sub-optimal functioning of the CMS and subsequent impairment of self-reflective processing in schizophrenia, and further emphasizes the role of parietal abnormalities in the core features of schizophrenia. Further, the present findings emphasize the role of parietal abnormalities in the core features of schizophrenia, supporting the notion from electrophysiological (Abhishek et al., 2018) and lesion-based connectivity (Narasimha et al., 2019) evidences that abnormalities in the parietal region, which may cause psychotic symptoms, underlie impaired source monitoring in schizophrenia.

In the present study, only the patient group exhibited hyperactivation in the left hippocampus and right external capsule associated with the other-evaluation task. Although previous fMRI of self/other evaluation tasks in schizophrenia patients revealed no such findings (e.g., Murphy et al., 2010; Pankow et al., 2016), the hippocampus plays an essential role in the self-memory system, especially episodic memory (Martinelli et al., 2013), and may have a significant role in impaired self-awareness in neurodegenerative/neuropsychiatric diseases (Chavoix and Insausti, 2017). Recent diffusion tensor image (DTI) studies demonstrated white matter abnormality in the CMS-related area, including the cingulate, hippocampus, and external capsule, in first-episode schizophrenia (Lee et al., 2013; Asmal et al., 2017). Asmal et al. (2017) also reported a significant relationship between these white matter abnormalities and impaired insight in schizophrenia patients, which is considered to reflect conceptual self-awareness. Our findings thus provide important evidence regarding the neural basis of self- and other-reflective processing in schizophrenia.

A few possible confounding factors in this study should be considered. First, as this study included a relatively small sample size, our preliminary results need replication in a larger cohort. Second, the close congener friends in our other-evaluation task were not defined by similarity/dissimilarity with the study participants, which may be a confounding factor because recent fMRI studies on empathy (Beckes et al., 2013; Meyer et al., 2013) suggested that the degree of familiarity with others affects the neural activation pattern. In particular, this may have affected our findings of the SMG, which is specifically involved in the neural circuitry of empathy (Silani et al., 2013). Third, all patients were receiving neuroleptic medication at the time of scanning. Although antipsychotics were reported to have no general effects on the blood-oxygen-level dependence (BOLD) signal in schizophrenia (Röder et al., 2010), an fMRI study by Lui et al. (2010) found short-term effects of antipsychotic treatment on cerebral function in drug-naïve first-episode patients. Lastly, although we hypothesized an association between impaired self-awareness and deficits in social functioning in schizophrenia, cognitive functioning was not comprehensively assessed.

In conclusion, we found that schizophrenia patients exhibited different brain activation patterns for self- and other-reflective processing, especially hyperactivation in the fronto-parietal region associated with conceptual self-reflection, from healthy controls. These findings may partly underlie the self-awareness deficits in schizophrenia that are associated with the core features of the illness.

Funding

This work was supported by JSPS KAKENHI Grant Number JP18K07550 to TT and by the Health and Labour Sciences Research Grants for Comprehensive Research on Persons with Disabilities from the Japan Agency for Medical Research and Development (AMED) Grant Number 16dk0307029h0003 to MS.

Declaration of Competing Interest

There are no conflicts of interest for any of the authors.

Acknowledgments

We are grateful to Mr. Sadanori Ito for his technical assistance on data collection and to Dr. Satoru Yokoyama, Dr. Hiroyuki Tsubomi and Dr. Yukihisa Matsuda for helpful comments on data analysis.

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