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Dysfunctional role of parietal lobe during self-face recognition in schizophrenia

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ABSTRACT

Background: Anomalous sense of self is central to schizophrenia yet difficult to demonstrate empirically. The present study examined the effective neural network connectivity underlying self-face recognition in patients with schizophrenia (SZ) using [^{15}O]H_2O Positron Emission Tomography (PET) and Structural Equation Modeling.
Methods: Eight SZ and eight age-matched healthy controls (CO) underwent six consecutive [^{15}O]H_2O PET scans during self-face (SF) and famous face (FF) recognition blocks, each of which was repeated three times.
Results: There were no behavioral performance differences between the SF and FF blocks in SZ. Moreover, voxel-based analyses of data from SZ revealed no significant differences in the regional cerebral blood flow (rCBF) levels between the SF and FF recognition conditions. Further effective connectivity analyses for SZ also showed a similar pattern of effective connectivity network across the SF and FF recognition. On the other hand, comparison of SF recognition effective connectivity network between SZ and CO demonstrated significantly attenuated effective connectivity strength not only between the right supramarginal gyrus and left inferior temporal gyrus, but also between the cuneus and right medial prefrontal cortex in SZ.
Conclusion: These findings support a conceptual model that posits a causal relationship between disrupted self–other discrimination and attenuated effective connectivity among the right supramarginal gyrus, cuneus, and prefronto-temporal brain areas involved in the SF recognition network of SZ.

1. Introduction

It has been suggested that distorted implicit self-awareness is a core clinical manifestation of schizophrenia (Parnas and Handest, 2003; Thakkar et al., 2011). Empirically, self-processing has been studied most extensively using face stimuli. The face is the most distinctive physical marker of self (Tsakiris, 2008), and the ability to recognize one's own face in a mirror (Platek et al., 2004) or photographs (Butler et al., 2012) has been regarded as a reliable marker of self-awareness. Face-recognition in primates is mediated by a distributed network comprising a posterior "core" and an anterior "extended" network, with multiple regions/patches in each sub-network (Avidan et al., 2013). The initial encoding of facial features and the subsequent perceptual organization occur primarily in the right lateral occipito-temporal areas, such as the occipital face area (OFA) (Pitcher et al., 2011) and fusiform face area (FFA) (Dien, 2009). Distinctive event-related potential waves of P100 (reflecting facial feature extraction) and N170 (reflecting facial configuration detection) peaking over occipito-temporal channels (Rossion and Jacques, 2008) arise from the combined activity of these face-relevant areas. Subsequently, the anterior temporal lobe, associated with identity-related biographical information (Nestor et al., 2011), mediates matching between newly encoded facial representations and previously stored facial structural representation to assess the degree of familiarity. Moreover, the right inferior parietal lobule (IPL) is specifically recruited when one views one's own body compared with a familiar body, and the right supramarginal gyrus (SMG) stores representations of the self-face as part of one's awareness of the self-body; these regions support one's ability to perform self–other discrimination across multiple sensory modalities (Platek et al., 2006; Hodzic et al., 2009). The IPL region contains mirror neurons and maintains self–other distinction during empathic interpersonal face-to-face interactions (Guo et al., 2012). Likewise, a rTMS study of selective inhibition of the right IPL resulted in disrupted performance of a self–other discrimination task (Uddin et al., 2006).

The results of face processing studies in schizophrenia are mixed, depending on the experimental paradigm used. Patients

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with schizophrenia (SZ) show deficits in multiple aspects of face processing including emotion recognition (Goghari et al., 2011), identity and familiarity decision (Sachs et al., 2004). These impairments may derive from deficits in both the magnocellular (Butler et al., 2008) and the ventral visual pathway (Doniger et al., 2002). However, the ability to recognize facial features is relatively preserved in SZ (Joshua and Rossell, 2009) and exposure to face stimuli for longer than 400 ms results in accurate processing in the visual ventral stream, reflected in an intact face inversion effect in schizophrenia (Butler et al., 2008). With respect to self-face processing in SZ, evidence is also mixed. Kircher et al. (2007) found increased self face identification errors but only when the self face was presented to the right hemifield. In contrast, Lee et al. (2007) found intact self-face processing in a visual search task that required participants to detect self-face or famous-face. Thus, to elucidate self-face recognition process in schizophrenia, we must investigate effective connectivity among the nodes of self-face recognition networks in addition to considering the impact of regional functional deficits.

Effective connectivity refers to patterns of directed causal influences and flows of information that manifest as synchronized coherent neural activity between brain areas on time-scales faster than synaptic changes (Friston, 2011; Varela et al., 2001). Even within specifically fixed structural connectivity, effective connectivity patterns are reconfigurable depending on the context and task involved ((Battaglia et al., 2012). Effective functional network for self-face recognition in schizophrenia has not yet been clearly elucidated (Silverstein and Keane, 2011). To explore the neural correlates and effective connectivity network of visual self-face recognition, we used $[^{15}O]H_2O$ Positron Emission Tomography (PET) scans to cover entire brain areas, even in the close quarters of air-filled sinuses (Wilson et al., 2002), and to directly measure hemodynamic regional brain blood flow (rCBF) rather than mere infer about brain activity changes using blood-oxygenation-level-dependent signals (Kudo et al., 2003). We tested the hypothesis that schizophrenia is associated with functional connectivity abnormalities within parietal-centered effective connectivity networks during self-face recognition.

2. Materials and methods

2.1. Participants

Eight male SZ were diagnosed using the Structured Clinical Interview for DSM-IV Axis I Disorders (SCID-I) (First et al., 1997). Eight age-matched male CO were screened for the presence of psychiatric illnesses using the SCID Non-patient version (SCID-NP). Exclusion criteria were a lifetime history of neurological disorders, comorbid Axis-I psychiatric disorders, substance abuse, or general medical illnesses. All subjects were right-handed. The two groups were matched for age ($t(14) = -1.579$, $p = 0.137$)(Table 1). The mean illness duration of SZ was 4.6 years ($SD = 3.5$), and all were medicated (see Supplementary Table 1). This study protocol was approved by the Institutional Review Board of Seoul National University Hospital and written informed consent was obtained from all subjects.

2.2. Face recognition task

All subjects underwent six consecutive $[^{15}O]H_2O$ PET scans under the self-face (SF) and famous-face (FF) recognition experimental conditions. Each of the SF and FF conditions was repeated three times in a random order, and performances were measured in terms of accurate hit rates and reaction times. Under the experimental condition, subjects were asked to respond whenever the correct photograph of one's own or a famous face was presented. Each task consisted of 30 target stimuli of one's own or a famous face (three different photos of the self/famous face repeated 10 times) presented before and after the 60 intervening stranger-face presentations (photos of six strangers repeated 10 times each). Detailed information about the $[^{15}O]H_2O$ PET data acquisition and pre-processing steps are described in the Supplementary material.

Table 1
Demographic, clinical characteristics and task performance of subjects[a].

	Schizophrenia (n = 8; 24 trials)	Control (n = 8; 23 trials)	*t*-Score	*p* value
Demographic data				
Age (year)	24.6 ± 2.3	22.9 ± 2.1	−1.58	.137
Gender (M/F)	8/0	8/0	–	–
Education (year)	11.8 ± 1.6	15.5 ± 1.9	4.26	.001
Estimated IQ	95.1 ± 12.2	125.3 ± 12.6	4.87	<.001
Illness duration (year)	4.6 ± 3.5	–	–	–
Positive and Negative Symptom Scale				
Total	82.4 ± 13.4	–	–	–
Positive	20.8 ± 5.4	–	–	–
Negative	21.6 ± 4.0	–	–	–
General	39.9 ± 6.7	–	–	–
Self-face: inter-group comparison				
Accuracy (%)	99.58 ± 0.55	99.91 ± 0.31	−2.509	.017*
Reaction time (ms)	571.61 ± 43.60	526.86 ± 75.08	2.525	.016*
Famous face: inter-group comparison				
Accuracy (%)	99.49 ± 0.65	99.90 ± 0.46	−2.505	.016*
Reaction time (ms)	561.76 ± 40.04	552.68 ± 72.67	0.528	.601
Self-face vs. famous face: intra-group comparison				
Accuracy	–	–	0.531	0.598
	–	–	0.035	0.972
Reaction time	–	–	0.815	0.419
	–	–	−1.197	0.238

[a] Data are given as mean ± standard deviation. * $p < .05$.

2.3. Statistical analyses

Demographic data, clinical variables, and behavioral performance were analyzed using SPSS, v20.0. Group comparisons for continuous and discrete variables were performed using independent *t*-tests and *chi*-square tests, respectively. Relationships between face recognition and scores on the Positive and Negative Syndrome Scale (PANSS) (Kay et al., 1987) in SZ were investigated with bivariate correlation analyses.

2.4. Voxel-based analyses

Using the independent *t*-test menu in SPM8, we explored differential patterns of rCBFs as a function of condition (self-face and famous face) in patients with SZ and CO. We also searched for the distinctive regional brain area showing rCBF changes between the SF and the FF recognition condition in each group ($p < 0.05$ (family-wise error), $k > 50$). Additional multiple regression analyses applying the mean reaction time as an independent variable were also performed. Results were visualized with the BrainNet Viewer (http://www.nitrc.org/projects/bnv/).

2.5. Region selection for Structural Equation Modeling

To perform an a priori specification of the effective connectivity analyses, we selected nine 2-mm-diameter regions of interest (ROIs; MNI coordinates in parentheses) centered on the global local maxima from our intergroup-comparison voxel-based analyses to construct SF and FF recognition networks. Degrees of rCBF were extracted using the MarsBaR toolbox (http://marsbar.sourceforge.net). First, we selected two ROIs located in the right visual association cortex (V3; 58, −74, −10) and the left inferior temporal gyrus (ITG; −60, −54, −16)

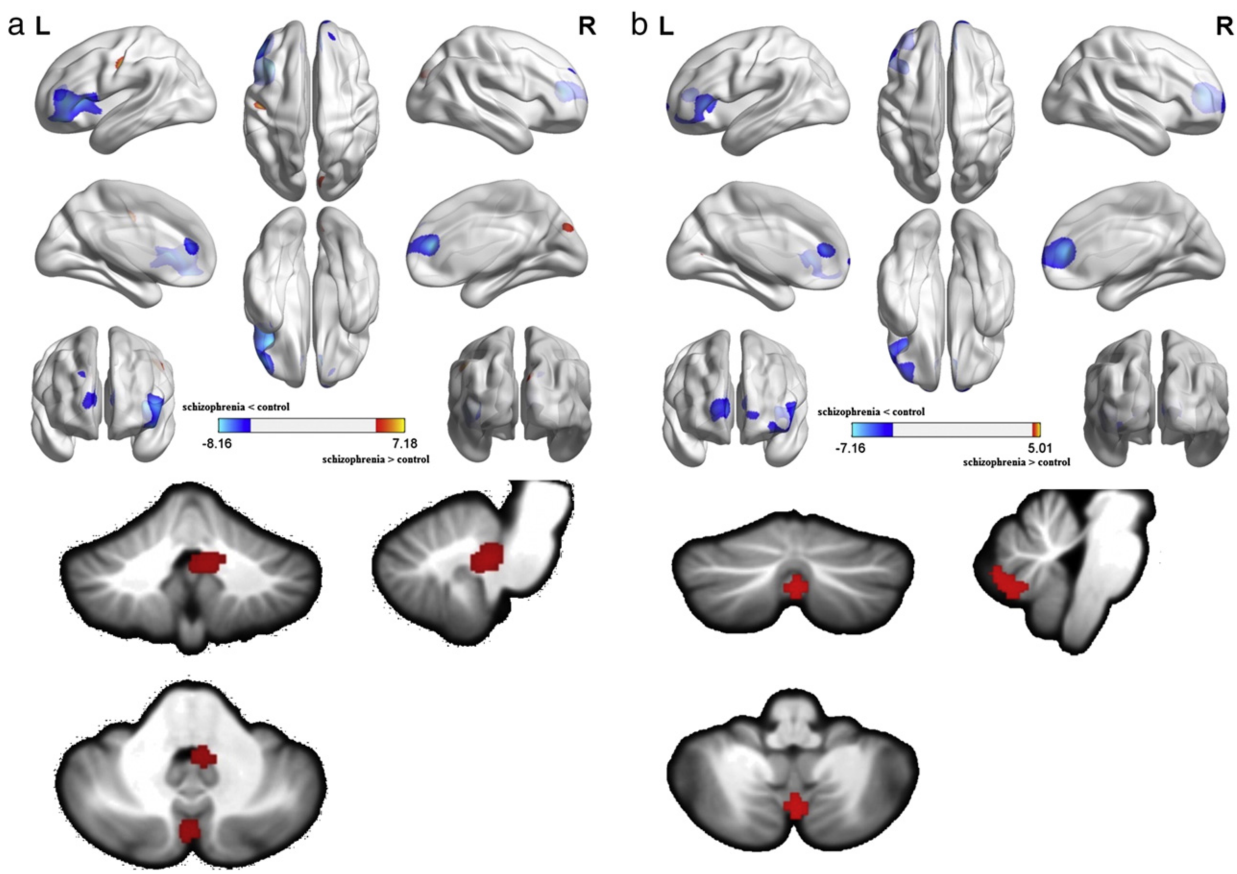

Fig. 1. Significant between-group differences in regional brain activation patterns during (a) self-face recognition tasks and (b) famous-face recognition tasks ($p < 0.05$ (family-wise error), $k > 50$).

overlapping with the temporo-occipital brain areas of the occipital face area (OFA) (Gauthier et al., 2000) and fusiform face area (FFA) (Kanwisher et al., 1997), respectively. Second, we chose the cuneus (8, −84, 30) and the left anterior superior temporal gyrus (STG; −48, −4, −6) as brain regions measuring degree of familiarity (Platek and Kemp, 2009) and supplying facial identity-related information (Nestor et al., 2011). Third, the right SMG (42, −48, 42), as a member of the fronto-parietal self–other discrimination neural network (Decety and Sommerville, 2003) participating in own-body perception, was also selected. Finally, the three prefrontal cortices namely the right medial prefrontal gyrus (MFG; 14, 40, 14), which matches stimuli with inherent self-referential phenotypes (Platek and Kemp, 2009), the left dorsolateral prefrontal cortex (DLPFC; −52, 42, 6), which processes facial feature information and face-related semantic information (Renzi et al., 2013), and the left orbitofrontal cortex (OFC; −44, 44, −16), which extracts information on facial attractiveness (O'Doherty et al., 2003), were chosen. Additionally, the cerebellar vermis (0, −80, −34), which comprises the cerebellar–cortical network that undergoes comparable computations as efferent copies of the process are computed in the prefrontal cortex (Ramnani, 2012), was also included.

2.6. Effective connectivity analyses of the face-recognition network

Path analyses using Structural Equation Modeling implemented in AMOS 20.0 software (IBM Corp., USA, 2011) were used to characterize the differential patterns of the SF and FF recognition networks of SZ and CO. A maximum-likelihood algorithm was adopted to estimate path coefficients and to confirm the most efficient path model from the initial hypothetical model. In testing differences between SF and FF recognition networks, we applied a hierarchical modeling approach (McIntosh and Gonzalez-Lima, 1994; Protzner and Mclintosh, 2006). *Chi*-square statistics for group differences and critical ratios for path coefficients were interpreted as significant at $p < 0.05$ (Labus et al., 2009). We adopted *chi*-square statistics, the comparative fit index (CFI), and the root mean square error of approximation (RMSEA) as measures of fitness for the proposed model (de Jong et al., 2013).

3. Results

3.1. Behavioral performance

As shown in Table 1, the mean accuracy rates of SF recognition were higher than 95% in both groups, rendering intergroup differences negligible. However, the mean reaction time during each trial was significantly longer in the SZ (mean ± *SD*; 571.61 ± 43.60 ms) than in the CO (526.86 ± 75.08 ms; $t(36.930) = 2.525$, $p = 0.016$). The accuracy of both groups in the FF recognition tasks was above 99% ($p = 0.016$). We found no statistically significant difference in reaction times (RTs) ($p = 0.601$) between the two groups. Detailed behavioral data is provided in the Supplementary materials.

3.2. Inter/intra-group differences of rCBF: SF and FF recognition

In the SF condition, rCBFs were reduced in the bilateral superior (BA 10)/medial (BA 9/10) frontal gyri, left middle (BA 11)/inferior (BA 46) frontal cortices, left insula (BA 13), and left postcentral gyrus (BA 2) in SZ. On the other hand, several posterior brain regions of the right middle occipital gyrus (BA 19), cuneus (BA 19), left precentral gyrus (BA 4), and right anterior lobe of the cerebellum demonstrated relatively increased rCBFs in SZ. During the FF condition,

Table 2
Regional brain areas which demonstrated significant difference of activation in relevance to self-face recognition task.

Brain region	Laterality	BA	Peak coordinates (MNI)			*t* score	Z score	*p* value	Cluster size
			x	*y*	*z*			(FWE)	
SF: SCZ < CNT									
Medial prefrontal cortex[a]	R	9	14	40	14	8.16	6.39	<.001	9718
Orbitofrontal cortex[a]	L	11	−44	44	−16	8.04	6.32	<.001	
Dorsolateral prefrontal cortex[a]	L	46	−52	42	6	7.99	6.29	<.001	
Insula	L	13	−38	24	6	7.97	6.29	<.001	
Medial prefrontal cortex[a]	L	10	−12	42	14	6.73	5.58	<.001	
Fronto-polar prefrontal cortex	R	10	14	72	6	5.94	5.09	0.001	
Fronto-polar prefrontal cortex	L	10	−34	64	−6	5.7	4.93	0.003	
Primary somatosensory cortex	L	2	−70	−22	20	6.9	5.69	<.001	137
SF: SCZ > CNT									
Primary motor cortex	L	4	−44	−16	38	7.18	5.85	<.001	322
Anterior lobe, cerebellum[a]	R		8	−44	−32	6.23	5.28	<.001	664
Cerebellar vermis[a]	–		0	−80	−34	5.77	4.98	0.002	309
Visual association cortex (V3)[a]	R	9	58	−74	−10	5.46	4.77	0.005	135
Cuneus	R	19	8	−84	30	5.21	4.6	0.01	144
FF: SCZ < CNT									
Pars triangularis (Broca's area)	L	45	−58	30	2	7.16	5.82	<.001	4092
Orbitofrontal cortex	L	47	−56	32	−2	7.15	5.81	<.001	
Medial prefrontal cortex	R	10	12	44	10	6.5	5.43	<.001	
Insula	L	13	−36	24	8	5.74	4.95	0.002	
Medial prefrontal cortex	L	10	−10	44	12	5.6	4.85	0.003	
Orbitofrontal cortex	L	11	−36	48	−14	5.11	4.52	0.011	
Fronto-polar prefrontal cortex	L	10	−30	62	−6	4.94	4.39	0.018	
FF: SCZ > CNT									
Primary visual cortex	R	17	22	−76	6	5.01	4.44	0.015	53
Inferior semi-lunar lobule (Crus II)	R		2	−74	−42	4.8	4.29	0.027	82

Note. *Z* values, coordinates (*x*, *y*, *z*) in the Talairach and Tournoux stereotactic space, and anatomical names of the regions corresponding to the regional peak *Z* values in the specific clusters.
Abbreviation: BA = Brodmann area; CNT = control subjects; FF = famous face; FWE = family-wise error; SCZ = schizophrenia; SF = self-face.
[a] Brain areas included in the structural equation analyses (SEM) which were described in Supplementary Tables 1 and 2.

the left superior (BA 10/11)/inferior (BA 45/47) frontal cortices, left insula (BA 13), and bilateral MFGs (BA 10) revealed reduced rCBFs in SZ. However, some posterior brain areas of the right cuneus and right inferior semi-lunar lobule of the cerebellum showed increased rCBFs in SZ ($p < 0.05$ (family-wise error), $k > 50$; Fig. 1 and Table 2). No statistically significant differences of rCBF during the SF versus the FF recognition tasks were demonstrated in the intragroup analyses for SZ as well as for CO ($p < 0.05$ (family-wise error), $k > 50$).

Table 3
Reaction time of face-recognition task performances showed negative correlations with these brain areas.

Brain region	Laterality	BA	Peak coordinates (MNI)			*t* score	*Z* score	*p* value	Cluster size
			x	*y*	*z*				
SCZ_SF: reaction time									
Dorsolateral prefrontal cortex	L	9	−46	4	20	6.94	5	0.003	82
CNT_SF: reaction time									
Inferior temporal gyrus[a]	L	20	−60	−54	−16	8.52	5.61	<.001	842
Middle temporal gyrus	L	21	−68	−32	−14	8.24	5.51	<.001	
Tuber (posterior vermis)	–		44	−64	−26	7.94	5.4	0.001	550
Culmen (anterior vermis)	–		44	−48	−20	7.07	5.06	0.003	
Supramarginal gyrus[a]	R	40	42	−48	42	7.5	5.23	0.001	451
Precuneus	R	7	24	−54	52	6.96	5.01	0.003	
Pyramis (vermis)	–		10	−66	−24	7.11	5.07	0.003	478
Culmen (anterior vermis)	–		−6	−50	−12	6.07	4.6	0.018	
Uvula (posterior vermis)	–		−16	−72	−26	6.95	5	0.004	136
Primary sensory motor cortex	L	3	−20	−24	50	5.63	4.38	0.04	100
Superior parietal lobule	L	7	−32	−66	44	6.58	4.84	0.007	94
Primary motor cortex	R	4	18	−24	50	6.31	4.72	0.011	91
SCZ_FF: reaction time									
No significant voxels									
CNT_FF: reaction time									
Superior temporal gyrus[a]	L	22	−48	−4	−6	7.33	5.16	0.001	248
Temporo-polar cortex	L	38	−46	10	−10	5.95	4.54	0.016	
Declive (vermis)	–		18	−70	−16	7.25	5.13	0.002	792

Note. *Z* values, coordinates (*x*, *y*, *z*) in the Talairach and Tournoux stereotactic space, and anatomical names of the regions corresponding to the regional peak *Z* values in the specific clusters.
Abbreviation: BA = Brodmann area; CNT = control subjects; FF = famous face; FWE = family-wise error; SCZ = schizophrenia; SF = self-face.
[a] Brain areas included in the structural equation analyses (SEM) which were described in Supplementary Tables 1 and 2.

3.3. Correlation between rCBFs and face recognition

Multiple regression analysis demonstrated that the degrees of increase in the rCBFs of the left inferior frontal gyrus could successfully predict faster RT of SZ in SF condition. In comparison, faster RTs of CO in SF condition were correlated with increased rCBFs in the left inferior (BA 20)//middle (BA 21) temporal gyri, right IPL (BA 40), right precuneus and superior parietal lobule (BA 7), left postcentral gyrus (BA 3), right precentral gyrus (BA 4), and cerebellar vermis. In the FF condition, the rCBFs of the left STG (BA 22/38) and of the cerebellar vermis could effectively predict faster RTs in CO. In contrast, no regional brain area was significantly correlated with the RTs during the FF condition in SZ (Table 3 and Supplementary Fig. 1).

3.4. Effective connectivity network for self-face recognition

When SZ were engaged in the SF recognition task, the effective connectivity network from V3 to several brain areas of the MFG ($\beta = -0.665$, $p = 0.017$), OFC ($\beta = -0.35$, $p = 0.042$), STG ($\beta = -0.81$, $p = 0.001$), and cerebellar vermis ($\beta = 1.047$, $p < 0.001$) was activated. Likewise, effective connectivity from the ITG to the MFG ($\beta = -0.475$, $p = 0.002$), to SMG ($\beta = -0.52$, $p = 0.002$), and to cerebellar vermis was observed. The STG demonstrated significant effective connectivity to the MFG ($\beta = 0.339$, $p = 0.022$) and to SMG ($\beta = 0.469$, $p = 0.01$). In addition to the STG, the SMG received significant effective connection from the cuneus ($\beta = 0.629$, $p < 0.001$). The OFC projected significant effective connection to the DLPFC ($\beta = 0.429$, $p = 0.001$). This hypothetical SF recognition network in SZ might explain the actual directed relation among these ROIs ($\chi^2(10) = 9.518$, $p = 0.484$, RMSEA < 0.05, CFI > 0.95) (Fig. 2(a) and Supplementary Table 2). Moreover, the hypothetical SF recognition network of CO was also successfully matched with the actual directed causal relations among the nine ROIs ($\chi^2(10) = 5.931$, $p = 0.821$, RMSEA < 0.05, CFI > 0.95) (Fig. 2(b) and Supplementary Table 2), details of which are provided in the Supplementary materials.

As shown in Fig. 3(a) and Supplementary Table 2, *chi*-square difference testing indicated significant differences of SF recognition effective connectivity network between the CO and SZ between the SMG and ITG ($\chi^2(\text{diff}) = 23.211$, $p < 0.001$), between the cuneus and MFG ($\chi^2(\text{diff}) = 7.622$, $p = 0.006$) in terms of the decreased absolute values of path coefficients in SZ. In contrast, the absolute path coefficient of effective connectivity between the STG and V3 was increased in the SZ ($\chi^2(\text{diff}) = 6.541$, $p = 0.011$).

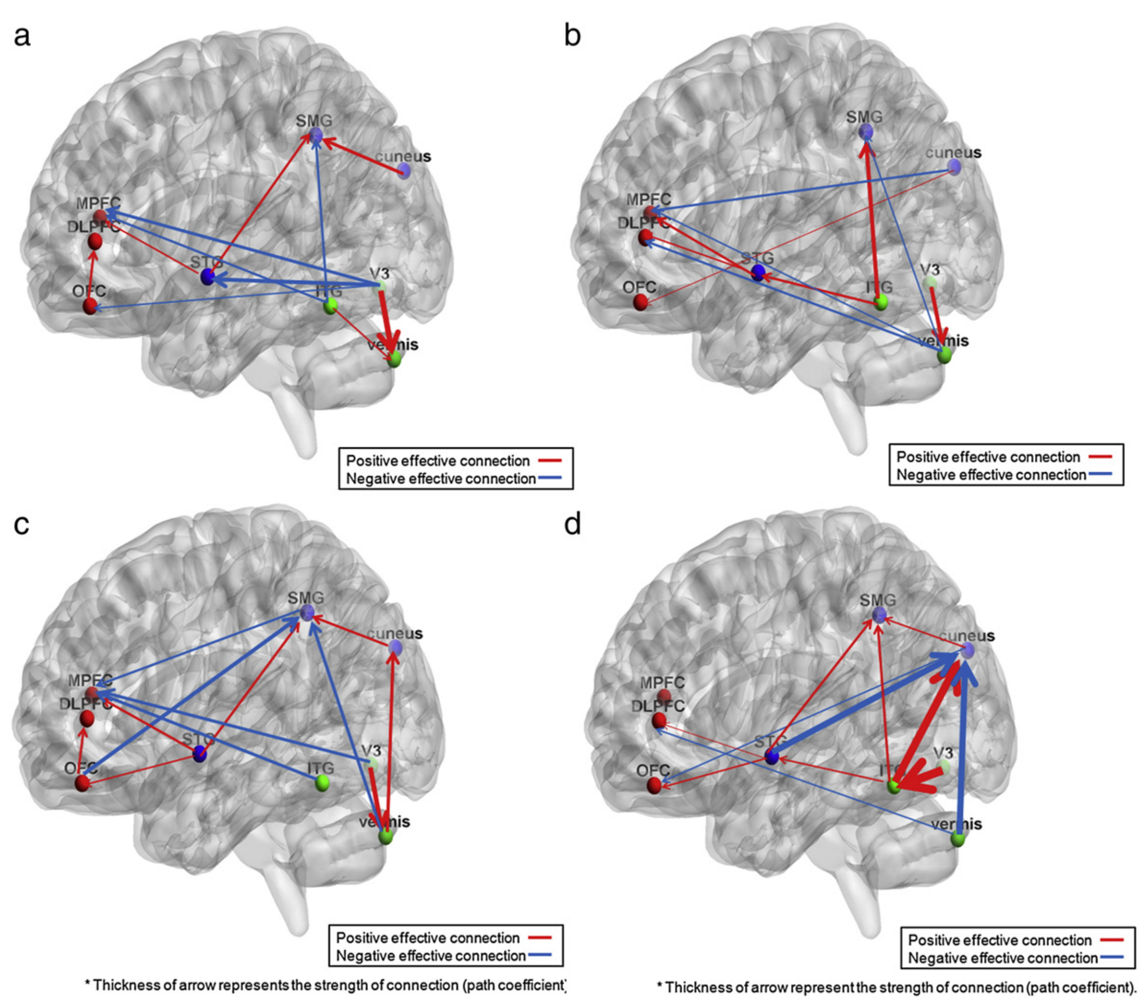

Fig. 2. Schematics of effective connectivity network associated with the schizophrenia patient group and the healthy controls in the self-face recognition condition (a, b) and in the famous face recognition condition (c, d). The regions illustrated in this diagram include: right medial prefrontal cortex (MPFC; BA 9), left dorsolateral prefrontal cortex (DLPFC; BA 46), left orbitofrontal cortex (OFC; BA 11), left superior temporal gyrus (STG; BA 22), left inferior temporal gyrus (ITG; BA 20), right supramarginal gyrus (SMG; BA 40), right cuneus (BA 19), right visual association cortex named V3 (BA 9) and cerebellar vermis. The arrow width for each path represents the magnitude of each connection. Positive path coefficients are represented as red arrows and negative coefficients as blue arrows ($p < 0.05$, two-tailed).

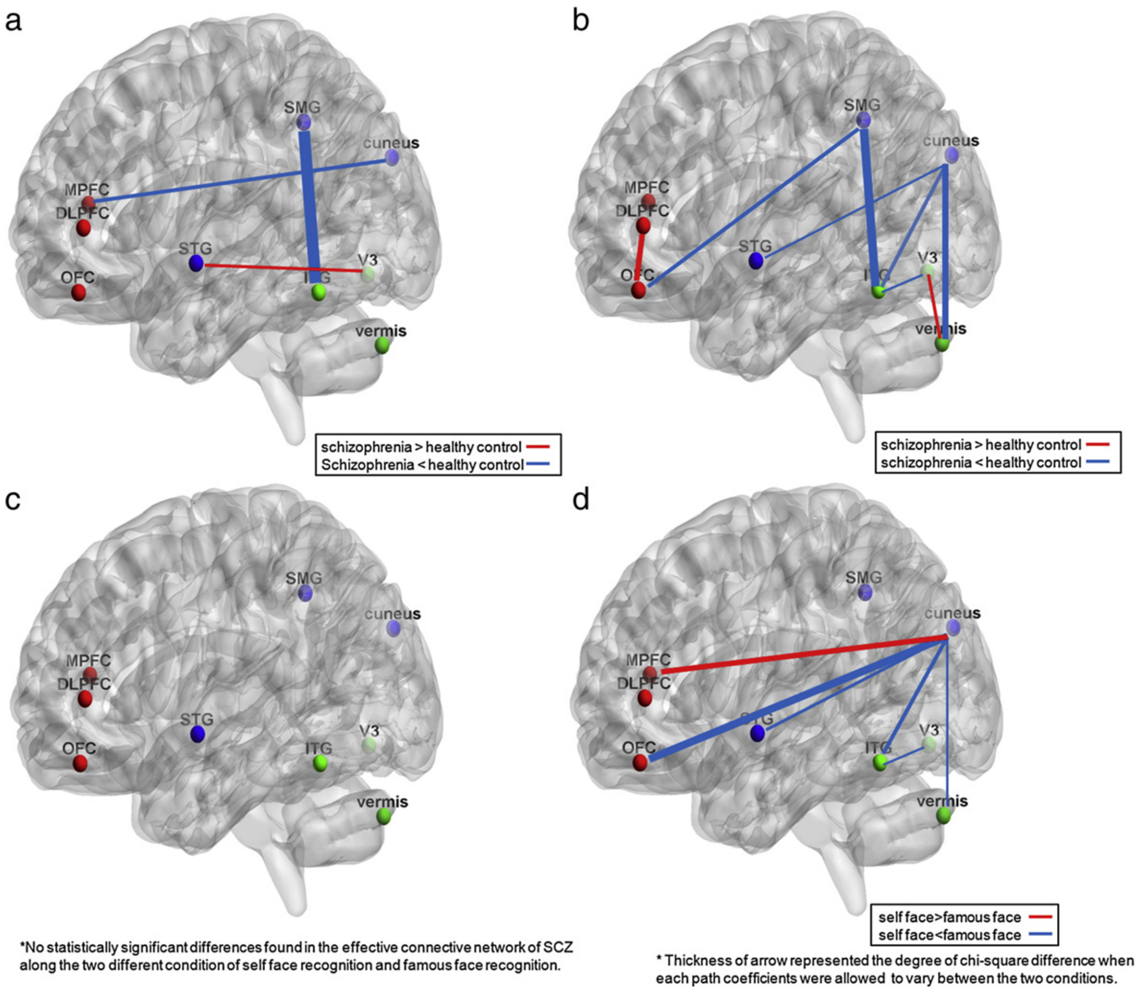

Fig. 3. Effective connectivity differences according to condition: (a) Comparison of self-face recognition networks between the schizophrenia group and healthy controls, (b) comparison of famous face recognition networks between the schizophrenia group and healthy controls, (c) comparison of self-face versus famous face recognition networks of the schizophrenia group, and (d) comparison of self-face versus famous face recognition networks of healthy controls. The regions illustrated in this diagram include: right medial prefrontal cortex (MPFC; BA 9), left dorsolateral prefrontal cortex (DLPFC; BA 46), left orbitofrontal cortex (OFC; BA 11), left superior temporal gyrus (STG; BA 22), left inferior temporal gyrus (ITG; BA 20), right supramarginal gyrus (SMG; BA 40), right cuneus (BA 19), right visual association cortex named V3 (BA 9) and cerebellar vermis. The line width for each path represents the degree of *chi*-square difference when each path coefficients were allowed to vary between the two different conditions ($p < 0.05$, two-tailed).

3.5. Effective connectivity network for famous face recognition

The hypothetical model of the FF recognition network demonstrated a statistically significant fit with the actual directed relations between nine ROIs not only in SZ ($\chi^2(10) = 13.600$, $p = 0.192$, RMSEA = 0.125, CFI = 0.96) but also in CO ($\chi^2(10) = 22.073$, $p = 0.015$, RMSEA = 0.229, CFI = 0.903) (Fig. 2(c, d) and Supplementary Table 3). Hierarchical model comparison demonstrated significant differences of FF recognition effective connectivity network between CO and SZ demonstrated as absolute path coefficients (details of which are provided in the Supplementary materials).

3.6. Intra-group comparison between self-face and famous face recognition

Hierarchical model comparison in SZ did not reveal any statistically significant differences between the SF and FF recognition networks (Supplementary Table 4). In contrast, data obtained from CO revealed differences between the FF and SF networks in terms of a statistically significant difference of absolute path coefficients between several brain areas, details of which are presented in the Supplementary material.

4. Discussion

The aim of the present study was to examine the neural basis of self recognition in SZ. Our results revealed no self-related impairments in the behavioral data of SZ. Moreover, we found no significant differences in the rCBF levels of the SZ between SF and FF conditions. Comparison of the SF recognition networks of SZ and CO demonstrated significantly attenuated effective connectivity between the right SMG and left ITG, as well as between cuneus and the right MFG in SZ. However, the effective connectivity network profile for SZ did not differ significantly regardless of whether they were performing the SF or the FF task ($p < 0.05$).

People tend to respond faster to their own face than to familiar (other) faces (Miyakoshi et al., 2010; Tacikowski and Nowicka, 2010) in explicit or incidental face-identification tasks. However, in the present study, we did not observe any advantage for self-face compared with famous faces in SZ. Reduced priority for self-referential stimuli in schizophrenia was observed in the lack of difference between the rCBF patterns for SF versus FF condition. Underlying effective connectivity between inferior parietal lobule of SMG, posteromedial cortex of cuneus and prefronto-temporal cortices, was also abnormal. Face processing involves functional crosstalk among multiple brain areas (Van Belle et al. 2011; Palermo and Rhodes, 2007). The temporo-parietal fiber intersection area including the SMG is one of the critical neural crossroads traversed by seven white matter tracts that connect multiple areas of the ipsilateral and contralateral hemispheres (Martino et al., 2013). The dorsal posterior parietal cortex receives multimodal sensory inputs and participates in bodily self-awareness (Huang et al., 2010). Deviant effective connectivity between the parietal and fronto-temporal regions observed in SZ in the present study might be a manifestation of defective functional connectivity network composed of the SMG, superior parietal gyrus, and precuneus, which predicts schizophrenia with a predictive validity of 68% (Guo et al., 2012).

Recruitment and engagement of alternative neural circuits can aid the performance of SZ to the point that it is comparable to that of CO (Murray et al., 2010). It has been proposed that self-awareness including self recognition develops along with the maturation of the frontal lobe (Giedd et al., 2009; Dumontheil et al., 2010). The DLPFC mediates self-referential, spatial working memory (Ma et al., 2012) and self-organized problem solving (Procyk and Goldman-Rakic, 2006). In our study, SZ showed a relative decrement in bilateral prefrontal cortical activity during face-recognition tasks, and the degree of left DLPFC (BA 9/46) activation predicted faster SF recognition in SZ. Moreover, SZ showed increased rCBF at cerebellar vermis simultaneously with weakened activation of prefrontal regions during SF recognition. GABA-B receptor inhibitory neurotransmission in the DLPFC (Hashimoto et al., 2008) and the defective post-perceptual top-down modulation (Sehatpour et al., 2010) reflected in the *gamma* inhibition deficit (Farzan et al., 2010) of SZ might also influence SF recognition process. The potential role of the cerebellum in the visual self-recognition (Semmes et al., 1963) is also interesting; as the cerebellar vermis is connected to the limbic/paralimbic and to the frontotemporal regions, which regulates emotion and cognition (Stoodley and Schmahmann, 2009; Demirtas-Tatlidede et al., 2010).

There are several limitations. Our sample size is small. However, we applied a stringent statistical threshold ($p < 0.05$ (family-wise error), $k > 50$) in the PET image analyses. Additionally, all patients were medicated and the effects of antipsychotic drugs on self recognition are unknown. Finally, we only included males in our study, which restricts the generalizability of our results but a previous study found no sex difference in SF recognition in SZ (McBain et al., 2010).

Taken together, these results suggest that deviant effective parieto-frontal connectivity may underlie altered experience of self in SZ. Future studies should address the limitations noted above and investigate both hemodynamic and electrophysiological bases of self processing in SZ.

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Contributors

Author Jun Soo Kwon and Tak Youn designed the study and wrote the protocol. Author Je-Yeon Yun managed the literature searches and analyses, undertook the statistical analyses, if wrote and revised the manuscript. Author Jun Soo Kwon, Joon Hwan Jang, Sohee Park, Ji-won Hur, Wi Hoon Jung and Do-Hyung Kang supported the analysis, interpretation and manuscript revision. All authors contributed to and have approved the final manuscript.

Conflict of interest

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

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