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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)