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Neurobiology of Self-Awareness in Schizophrenia: an fMRI Study

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Abstract

Self-awareness (SA) is one of the core domains of higher cortical functions and is frequently compromised in schizophrenia. Deficits in SA have been associated with functional and psychosocial impairment in this patient population. However, despite its clinical significance, only a few studies have examined the neural substrates of self-referential processing in schizophrenia. The aim of this study was to assess self-awareness in schizophrenia using a functional magnetic resonance imaging (fMRI) paradigm designed to elicit judgments of self-reference in a simulated social context. While scanned, volunteers looked at visually-displayed sentences that had the volunteer's own first name (self-directed sentence-stimulus) or an unknown other person's first name (other-directed sentence stimulus) as the grammatical subject of the sentence. The volunteers were asked to discern whether each sentence-stimulus was about the volunteer personally (during a self-referential cue epoch) or asked whether each statement was about someone else (during an other-referential cue epoch). We predicted that individuals with schizophrenia would demonstrate altered functional activation to self- and other-directed sentence-stimuli as compared to controls. Fifteen controls and seventeen schizophrenia volunteers completed clinical assessments and SA fMRI task on a 3T Philips 3.0 T Achieva system. The results showed significantly greater activation in schizophrenia compared to controls for cortical midline structures in response to self- vs. other-directed sentence-stimuli. These findings support results from earlier studies and demonstrate selective alteration in the activation of cortical midline structures associated with evaluations of self-reference in schizophrenia as compared to controls.

Keywords

neurobiology; self-awareness; schizophrenia; fMRI

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1. Introduction

Self-awareness (SA) refers to a higher-order cognitive function required to differentiate between self and non-self cues. It is pivotal to accurately appraise the self in order to accurately represent one's own traits, abilities and attitudes and to understand the behavior of other human beings during interpersonal communications. This ability to self-reflect is impaired in many neuropsychiatric disorders including schizophrenia (Frith, 1992; Sass and Parnas, 2003) and may represent a wide range of behavioral manifestations including impaired insight into illness, lack of empathy (Moriguchi et al. 2007; van der Meer et al. 2010), or an impaired social cognition. Thus, it is not surprising that deficits in SA have been associated with compromised psychosocial and clinical outcomes in schizophrenia subjects (Dassa et al. 2010; Fisher et al. 2008; Kettle et al. 2008; Lysaker et al. 2005 & 2009; Vokeley, 2007).

Despite its clinical significance, few studies have focused on the neurobiological basis of deficits in SA in schizophrenia (Blackwood et al. 2004; Holt et al. 2011; Murphy et al. 2010). The studies by Blackwood et al. (2004) and Holt et al. (2011) observed differences between controls and schizophrenia subjects in the activation of cortical midline structures (CMS) in response to self-versus non-self-related stimuli. However, the study by Murphy et al. (2010) did not observe group differences in the activation of CMS in response to self-relevant stimuli and instead found lesser activation of superior temporal sulcus in early-course schizophrenia than the control subjects.

Regardless of these differences in brain activation, interesting observations can be derived from these studies with regard to self-referential processing in schizophrenia. For example, studies in chronic schizophrenia subjects have revealed greater activation of ventral anterior CMS (medial orbitofrontal or medial prefrontal cortex) and lesser activation of posterior cingulate (posterior CMS) in response to self- and/or other-referential probes in controls than schizophrenia subjects (Blackwood et al. 2004; Holt et al. 2011). These changes in cortical activations have been labeled as an anterior-to-posterior shift in midline cortical activity in schizophrenia during self-reflection (reviewed in Shad et al. 2011).

This paper presents findings from an fMRI study on the neurobiological substrates of SA processing in schizophrenia subjects. An SA fMRI paradigm was developed to examine the differential brain response in controls versus schizophrenia volunteers in response to self-versus other-referential stimuli. We customized each fMRI session so that each volunteer's own first name appeared in relevant probes rather than having volunteers respond to the generic first-person pronoun, a feature of our design intended to increase participants' attention and augment the emotional salience of the self-referential stimuli (Bundesen et al. 1997; Harris et al. 2004; Shapiro et al. 1997) compared to previous studies. In addition, and also in contrast to previous studies, our fMRI paradigm employed only unambiguous uniformly-structured sentences with either positive or negative trait-adjectives for which the latter were chosen to reflect common delusional themes in schizophrenia.

We predicted that the schizophrenia volunteers would reveal altered neuronal response, as assessed by functional blood-oxygen-level-dependent (BOLD) signal changes, in their evaluations of both self- and other-directed sentence-stimuli when contrasted with the corresponding BOLD response of controls. Here we present preliminary findings from 15 healthy controls and 17 schizophrenia volunteers, who completed fMRI and clinical assessments in this study.

2. Materials and Methods

Please refer to the on line supplement for details. The summary of the materials and methods is as follows:

2.1. Participants

The participants in this study included 17 adult volunteers with DSM IV (American Psychiatric Association 1994) based diagnosis of schizophrenia and 15 controls matched for age and premorbid IQ who endorsed having no personal or (first-degree) family history of major psychiatric illness (Table 1). All subjects were right-handed. Although the two groups of volunteers did not differ significantly by age, gender, or by their Intelligence Quotient (IQ) scores, there was a significant group difference in mean education by 1.5 years ($t = 2.33$; $df = 30$; $p = .03$). For further details please see online supplement. Screening details are available in the online supplement.

2.3. Study Assessments

The IQ of controls and the premorbid IQ for schizophrenia volunteers were estimated using the Wechsler Test for Adult Reading (WTAR; Wechsler 2001) and psychopathology was assessed with Positive and Negative Syndrome Scale (PANSS; Kay et al. 1987).

2.4. Self-Awareness (SA) Task

The SA task is an fMRI paradigm designed to distinguish between one's own self-evaluation and inferences of self-reference based on the utterances of others (Flavell, 1967). As can be seen in Figure 1, the task is comprised of two cue-question epochs, "*Are they talking about you?*" during a self-referential cue epoch [SR] or "*Are they talking about someone else?*" during an other-referential cue epoch [OR]. Each epoch is comprised of blocks of four types of visually presented sentence-stimuli equally divided into sentences with positive and negative trait adjectives as follows: 1) Self-directed positive sentence stimulus; 2) Self-directed negative sentence stimulus; 3) Other-directed positive sentence stimulus; and 4) Other-directed negative sentence stimulus. Each study subject is instructed to respond by pressing the right button representing "yes" if he/she think that 'they' are talking about him/her or the left button representing "no" if he/she thinks that 'they' are talking about someone else. The structure and examples of the sentence stimuli can be seen in Figure 1.

During the pre-scan task training (see Appendix A in the online supplement) all subjects undergo a task familiarization activity and interview during which volunteers are first asked to imagine a scenario in which they accidentally overhear a conversation between people and think that they may have heard their name during the conversation but are not sure about hearing their name (see Appendix B in the online supplement). The study subjects are instructed to remember the "overheard" statement, while responding to the sentence stimuli during the scan using the same set of instructions given during the pre-scan training. In addition, a post-scan questionnaire (see Appendix C in the online supplement) is also administered to record whether study subjects based their responses to their names or the cued epochs under the scanner. Each trial of the SA task is comprised of a single visual stimulus presentation, which is the appearance on screen of either a sentence-stimulus (presented for 3.5 s) or a null-trial arrow (randomly pointing left or right presented for 1.75 s). Pseudo-randomly jittered onset timing of trials is scheduled using optseq2 software (<http://surfer.nmr.mgh.harvard.edu/optseq>). The SA task paradigm is implemented over five scanned runs of equal duration, each comprised of two randomly presented cued epochs of SR and OR conditions each lasting 7 s followed by four pseudo-randomly ordered blocks of trials, corresponding to the four core sentence-stimulus types. The order of the blocks is counterbalanced per subject across the five runs. The total duration of one SA task run is

248.5 seconds. The fMRI task is administered using the E-Prime software (Schneider et al. 2002).

2.5. MRI scans

Functional magnetic resonance imaging (fMRI) data are acquired on a Philips 3.0 T Achieva system with a 32 channel receive head coil (Philips Medical Systems, Best, Netherlands). The raw fMRI data acquired from each subject are converted to ANALYZE image format using SPM conversion software (<http://sourceforge.net/projects/r2agui/files/r2agui/>). 3D-SPGR (resolution=1 mm × 1 mm × 1 mm) and Fluid Attenuation Inversion Recovery (FLAIR) scans are also acquired for each subject. Details about pulse sequence and image acquisition are described in the online supplement.

2.6. fMRI processing

Processing of the fMRI data is conducted using Statistical Parametric Mapping (SPM5) software from the Wellcome Department of Cognitive Neurology, London, UK, implemented in the Matlab programming environment (Mathworks Inc. Sherborn MA, USA). Preprocessing details are available in the online supplement. A General Linear Model approach is used to specify the design matrix (Friston et al. 1995). High-pass filtering (SPM5 default cut-off of 128 seconds) removes low frequency noise caused by scanner drift. Contrast images of the parameter estimates of interest are computed for each subject during first level of SPM analysis. Then the contrast image for each subject is input into a second level Random Effects comparison between groups. Statistical significance is corrected for multiple comparisons across the voxels within the brain by using the SPM5 Family-Wise Error (FWE)-corrected two-tailed cluster probability value less than 0.05 (Friston et al. 1996). The cluster-defining threshold voxel t is 2.4. Because of two way group comparisons for each cued epoch, the two-tailed probability (P) values were obtained by multiplying by two the corrected one-tailed corrected cluster P-values.

2.7. fMRI statistical analysis

First a two-sample t-test was performed to examine cued epoch x valence x group interaction. Since there was no epoch x valence interaction, the negative and positive sentences were collapsed to enhance the power of the study. This was followed by three separate between-group analyses targeting self- and other-directed sentence-stimuli within and between the differently cued epochs as follows:

1. *WITHIN-EPOCH SR-SR CONTRAST* ($SR_{Self-dir}$ vs. $SR_{Other-dir}$): activation elicited in response to self-directed sentence-stimuli [*Self-dir*, e.g., “(Subject’s first name) is suspicious ”], contrasted with activation associated with other-directed sentence-stimuli [*Other-dir*, e.g., “(Another person’s first name) is suspicious ”], both appearing only within self-referential cued epochs (SR);
2. *BETWEEN-EPOCH SR-OR CONTRAST* ($SR_{Self-dir}$ vs. $OR_{Self-dir}$): activation elicited in response to self-directed sentence-stimuli [*Self-dir*, e.g., “(Subject’s first name) is suspicious ”], as the sentence-stimuli appeared in self-referential cue epochs (SR) in contrast to activation associated with the same *Self-dir* sentence-stimuli appearing in other-referential cue epochs (OR);
3. *BETWEEN-EPOCH SR-OR CONTRAST* ($SR_{Self-dir}$ vs. $OR_{Other-dir}$): activation elicited in response to self-directed sentence-stimuli [*Self-dir*, e.g., “(Subject’s first name) is suspicious ”], appearing within self-referential cue epochs (SR) contrasted with activation elicited by other-directed sentence-stimuli [*Other-dir*, e.g., “(Name other than subject’s) is suspicious ”], appearing within other-referential cue epochs (OR).

For additional *post-hoc* within and between group comparisons please refer to the online supplement.

An SPM5 regression analysis was conducted to examine the effect of psychopathology (using PANSS total scores) and chlorpromazine-equivalent antipsychotic-dosages on functional activation, respectively. Regression analysis was also conducted within each group separately and then combined to examine the effect of education on brain activation.

Approximate anatomical labels for regions of activation were determined using Anatomical Automatic Labeling (Tzourio-Mazoyer et al., 2002). The Talairach Daemon (Lancaster et al., 2000) was also used for anatomical labeling of peak coordinates using the Yale Nonlinear MNI to Talairach Conversion Algorithm (Lacadie et al. 2008).

2.8. Statistical analysis of demographic and behavioral data

Microsoft Excel Statistical Package software was employed to conduct *t*-tests to compare differences between groups for continuous data, and Chi Square test was carried out for categorical data. Differences in behavioral performance were analyzed using repeated-measures ANOVA using SPSS statistical software (version 17).

3. Results

3.1. Behavioral results during fMRI scanning

The groups did not differ significantly in behavioral responses to the self- or other-referential stimuli in the SA task (Table 2). The percent responses in table 2 represent tendencies to self-attribute self- and/or other-directed sentence stimuli across SR and OR epochs and are not measure of accuracy. In addition, there were no statistical differences in subjects' responses to post-scan questionnaire (see online supplement) and 13 of the 15 controls and 15 of the 17 schizophrenia subjects responded by picking the option, which states that the responses under the scanner were primarily based on whether the subjects see their name as opposed to the cued epoch. Results for the post-hoc within and between group comparisons are documented in the online supplement.

3.3. Comparison of whole-brain BOLD-activation patterns between groups

3.3 A. WITHIN-EPOCH SR-SR CONTRAST: SR_{Self-dir} vs. SR_{Other-dir}—

Significant between group differences were only observed in the schizophrenia > healthy contrast showing a single significant cluster that was found in portions of the postcentral gyrus, inferior parietal lobule and supramarginal gyrus (Table 3).

3.2 B. BETWEEN-EPOCH SR-OR CONTRAST: SR_{Self-dir} vs. OR_{Self-dir}—No significant differences in activation were observed for this or the reverse contrast.

3.3 C. BETWEEN-EPOCH SR-OR CONTRAST: SR_{Self-dir} vs. OR_{Other-dir}—Only schizophrenia > healthy contrast revealed significant group differences yielding a single significant cluster that was found in portions of lingual gyrus, cuneus, precuneus, cerebellum and posterior cingulate cortex (Table 3, Figure 2).

3.3 F. EFFECTS OF EDUCATION: SR_{Self-dir} vs. SR_{Other-dir}—There were no significant correlation between education and activation in either of the groups separately or combined.

3.3 G. EFFECTS OF ANTIPSYCHOTIC MEDICATION AND PSYCHOPATHOLOGY: SR_{Self-dir} vs. SR_{Other-dir}—There were no correlations

between the task-related activation and potential confounds (antipsychotic dose or duration of illness) in the schizophrenia group. However, symptom level (as assessed with PANSS total scores) was positively correlated with SA task-induced activation in portions of thalamus, parahippocampus gyrus, hippocampus, and fusiform (547 voxels; two-tailed FWE corrected cluster $p < .002$; MNI $x, y, z = -24 -27 9$).

4. Discussion

This study revealed differences in task-elicited BOLD activation between schizophrenia and control groups, demonstrated by greater activation in schizophrenia of brain regions previously shown to be involved in self-referential processing. These findings support the study's prediction that processing of self-directed sentence-stimuli would induce an altered brain response in schizophrenia volunteers when compared to activation observed in controls responding to the same conditions.

This is one of the first studies to show significant group differences in activation to self- versus other-directed sentence-stimuli based on a whole-brain voxel-wise comparison. The only study that has reported significant group differences in response to a similar contrast employed a ROI-based approach (Blackwood et al. 2004). While other studies employing a ROI-based (Holt et al. 2011; Murphy et al. 2010) and cortical surface-based (Holt et al. 2011) approaches, observed group differences only when self-reference was contrasted with affective labeling or semantic positivity evaluation. It is possible that using a subject's proper name in this study instead of a first or third person pronoun (i.e., I am or s/he is 'trait adjective') may have enhanced the contrast between self and others due to greater target attention and emotional salience of one's own name (Bundesen et al. 1997; Harris et al. 2004; Shapiro et al. 1997).

The most significant activations between groups were observed in response to contrasts that provided a clear distinction between self- and other (i.e., the contrast between self- vs. other-directed sentence stimuli within the SR epoch and the contrast between self-directed sentence stimuli in the SR epoch vs. other-directed sentence stimuli in the OR epoch). The latter contrast produced most significant activations as it offers least cognitive challenge due to congruence between cued epochs and subjects' names and is consistent with subjects' responses on the post-scan questionnaire in which most subjects based their responses to their names rather than the epochs. This is consistent with lack of significant activation in response to a within group contrast between self-directed stimuli across SR and OR epochs as well as absence of significant group differences in response to a contrast with collapsed self- and other-directed sentence stimuli across the two epochs (based on *post-hoc* comparisons documented in the online supplement).

The contrast between self-directed stimuli in the SR epoch and other-directed stimuli in the OR epoch (SR_{Self-dir} vs. OR_{Other-dir}) resulted in greater activation of lingual gyri, cuneus, precuneus, cerebellum and posterior cingulate cortex in schizophrenia than control subjects. Precuneus and posterior cingulate cortex constitute important components of the posterior CMS that have yielded greater activation during self-referential processing in schizophrenia patients than controls in earlier studies as well (Blackwood et al. 2004; Holt et al. 2011). Healthy subjects have also shown involvement of precuneus in the mediation of conscious or explicit self-awareness ('autonoetic consciousness') (Lou et al. 2004) as well as self-consciousness, such as reflective self-awareness, that involves rating one's own personality traits in order to judge traits of other people (Kjaer et al. 2002; Lou et al. 2004). Thus, greater activation of posterior CMS in this study may reflect a greater focus on self-than other's perspective in decision-making, which may be a core deficit underlying difficulties in social communications in this patient population (Holt et al. 2011). Furthermore,

precuneus represents a key region in the interlinked network of the “default mode” brain areas, which is similar to the neural substrates of the resting conscious state, suggesting that self-monitoring is a core function in resting consciousness (see the online statement for further details).

Greater activation of lingual gyri and cuneus in response to self- vs. other-referential activity in schizophrenia than control subjects suggests that these patients were processing a higher level of vivid imagery in differentiating between self- and others than the controls (Cui et al. 2007). The cerebellar findings in this study are difficult to interpret, but it is possible that cerebellum has modulating effects on self-referential processing as reflected by decreased activation of cerebellum in human subjects with emotional unawareness (i.e., alexithymia) (Moriguchi et al. 2007) and increased activation of cerebellum in response to perceiving one's own actions as opposed to perceiving the actions of others (Grezes et al. 2004). Greater activation of posterior CMS in schizophrenia than controls in this study is consistent with the anterior-to-posterior shift in CMS activation first observed by Holt et al. (2011) and elaborated as a model in a recent review by Shad et al. (2011). This model is derived from extensive reviews of SA studies in healthy adults (van der Meer et al. 2010) and in patients with mood disorders (Lemogne et al. 2010). A failure to observe reduced activation of anterior CMS in schizophrenia subjects than the controls in this study could be due to small sample size and methodological differences in fMRI analyses, such as whole brain voxel-wise analysis instead of a ROI-based approach.

The contrast between self- and other-directed stimuli within the SR epoch ($SR_{Self-dir}$ vs. $SR_{Other-dir}$) yielded greater activation of inferior parietal lobule along with adjacent postcentral and supramarginal gyri in schizophrenia than control subjects. While activation of post-central gyri may represent a somatosensory processing of the stimuli, the parietal region has been associated with body image and concept of self (Torrey, 2007) and prior research has consistently reported a link between neurological lesions in this brain region and deficits of self-awareness commonly referred to as ‘anosognosia’ (Rosen, 2011). More importantly, inferior parietal lobule constitutes a network of specialized neurons known as ‘mirror neurons’ (Rizzolatti et al. 2004) that possesses the capacity to interpret the actions and gestures of others, which is vital for social interactions (Rizzolatti et al. 2004). These mirror neurons have been linked to SA in healthy subjects (Chong et al. 2008; Oberman et al. 2009). Recently, structural gray deficits in the left supramarginal gyrus were inversely correlated with social self-awareness in schizophrenia subjects (Kubota et al. 2011).

The observed group differences in this study can be explained on the basis of a *post-hoc* analysis (see online supplement) using a contrast between self- vs. other-directed stimuli that were collapsed across the cued epochs (i.e., $SR_{Self-dir} + OR_{Self-dir}$ vs. $SR_{Other-dir} + OR_{Other-dir}$). This contrast yielded greater activation (including the CMS) in the schizophrenia group than that observed in the control group, while the reverse contrast (i.e., $SR_{Other-dir} + OR_{Other-dir}$ vs. $SR_{Self-dir} + OR_{Self-dir}$) produced similar activations in both groups suggesting that only the self-directed stimuli induced greater activation in patients than the controls. It is important to note that these group differences in BOLD responses to self- vs. other-directed stimuli were observed despite no significant differences in behavioral responses to self- or other-directed stimuli between controls and schizophrenia subjects. Thus it is possible that greater activation in schizophrenia than the control subjects could reflect at least a partially successful compensatory effort to result in a similar behavioral performance as the controls. Similar compensatory hyperactivation has been observed in earlier studies using a working memory task (Kim et al. 2010; Thormodsen et al. 2011; Markov et al. 2010; Royer et al. 2009) and a procedural learning task (Zedkova et al. 2006).

The results from this study should be interpreted with caution as they are based on a small heterogeneous group of chronic schizophrenia subjects with different duration of illness and psychotropic medications. Despite observing no effects of illness duration and antipsychotic treatment on the study results, the influence of these confounders on brain changes cannot be completely ruled out based on a small sample such as used in this study. Also, using names of unknown others in this study, as opposed to using names of famous or known persons in prior studies, sacrifices control for emotional salience associated with one's own name. However, absence of group differences in activation of ventral anterior CMS as well as amygdala and insula suggests an insignificant impact of 'emotional' self on the study results. Another possible limitation of this study is using the default SPM high pass filter of 128 s for low frequency epochs may have reduced the signal from the between epoch analyses.

Despite a significant group difference in education, education was not used as a covariate in the imaging analysis because education is expected to be generally lower in this patient population reflecting lower cognitive function as an inherent characteristic of this group. Thus, inclusion of education as a covariate would violate the analysis of covariance assumption of expected random distribution at the population level across groups because group membership would be confounded with the education covariate (Miller and Chapman, 2001). Nevertheless regression analysis for each group separately and then combined revealed no significant correlation between self-directed activation and education.

Bearing these limitations in mind, the present study provides preliminary support for the hypothetical model of self-awareness deficits in schizophrenia, which will enhance our understanding of the neurobiology of self-awareness in schizophrenia.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Figure 1.

Self-Awareness Task: Presentation of stimuli under two conditions (i.e., self and other). The epochs at the top were followed by self-and other-referential statements with neutral and negative trait adjectives. Self-referential statements used patients' proper names, while other-referential statements used neutral names predetermined to be unrelated or unknown to the patients.

Figure 2. Brain regions, where schizophrenia subjects showed significantly higher BOLD activation in response to the self-vs. other-related stimuli within the self-referential condition compared to normal controls. The activations are overlaid in color on axial slices of the MNI single-subject template brain. The number below each slice indicates slice location (mm) of MNI z coordinate. Scale on color bar represents t values.

Table 1

Demographic and Clinical Characteristics of the Study Groups

	Normal Controls (n=15)	Schizophrenia Patients (n=17)
Age in years (SD) (range)	44.3 ± 9.6 (24-57)	40.0 ± 10.3 (22-57)
Gender (Males/Females)	8/7	14/3
Mean Education in Years	14.7 ± 1.7 (12-18)	13.2 ± 1.9 (9-18)
^a Premorbid Verbal IQ (range)	102 ± 11.0 (79-117)	98 ± 11.4 (79-118)
PANSS Total (range)		64.76 ± 14.67 (43-100)
PANSS Positive Subscale (range)		17.1 ± 4.6 (7-26)
PANSS Negative Subscale (range)		15.0 ± 3.7 (10-22)
PANSS General Psychopathology Subscale (range)		32.7 ± 8.0 (24-52)
Duration of Illness (years)		17.88 ± 5.63
Chlorpromazine Equivalent Dose		346.3 ± 234.0

There were no significant differences between the control and schizophrenia groups for the demographic measures, except education ($t = 2.33$; $df = 30$; $p = .03$).

PANSS. Positive and Negative Syndrome Scale (Kay et al 1987).

^a Measured with the Wechsler Test for Adult Reading (WTAR; Wechsler, 2001).

Table 2

The behavioral responses (yes or no) to the self- versus other-directed sentence stimuli in self-referential (SR) vs. other-referential (OR) conditions in the normal controls and schizophrenia subjects.

Normal Controls (n=15)				
	SR _{self-directed}	SR _{other-directed}	OR _{self-directed}	OR _{other-directed}
Mean response (SD)	0.72 (0.28)	0.89 (0.21)	0.74 (0.26)	0.89 (0.19)
Schizophrenia (n=17)				
	SR _{self}	SR _{other}	OR _{self}	OR _{other}
Mean Response (SD)	0.60 (0.27)	0.82 (0.25)	0.71 (0.31)	0.81 (0.27)

Table 3

Comparison of activation between controls (n=15) and schizophrenia patients (n=17). Within each significant cluster, the relative maximal voxel t value and its approximate anatomical location within 3 mm is listed. CI = confidence interval; [x, y, z] = Montreal Neurological Institute (MNI) standard space coordinates (mm); negative x = left hemisphere. L = left; R = right; g = gyrus; BOLD = blood oxygen level dependent effect; WB = whole brain. Smoothness of residual field (Full Width at Half Maximum "FWHM") = [11.8 11.9 12.2] mm. Voxel size = [3.0 3.0 3.0] mm. Search volume = 37,404 voxels = 517.9 resolution elements (resels). df = degrees of freedom. NS = no significant activation.

Comparison	Two-tailed FWE-corrected cluster p	Number of voxels in cluster	Difference in activation between groups at maximal voxel in cluster (% of WB BOLD) $\pm 90\%$ CI	Maximal voxel t value in cluster [29 df]	MNI coordinates of maximal voxel in cluster [x, y, z]	Location of maximal voxel in cluster
<i>A. During self-directed sentence-stimuli vs. other-directed sentence-stimuli within the self-referential (SR) cue epoch (i.e., "are they talking about you?")</i>						
Schizophrenia > Controls	< 0.05	210	1.39 $\pm$ 0.65	3.98	-36, -12, 39	L postcentral gyrus
Controls > Schizophrenia	NS					
<i>B. During self-directed sentence-stimuli in the self-referential (SR) cue epoch (i.e., "are they talking about you?") vs. other-directed sentence-stimuli in the other-referential (OR) cue epoch (i.e., "are they talking about someone else?")</i>						
Schizophrenia > Controls	< 0.024	216	1.35 $\pm$ 0.87	3.18	9, -45, 0	R lingual gyrus
Controls > Schizophrenia	NS					