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Gray matter abnormalities in language processing areas and their associations with verbal ability and positive symptoms in first-episode patients with schizophrenia spectrum psychosis

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ABSTRACT

Background: Impaired verbal communication is a prominent feature in patients with schizophrenia. Verbal communication difficulties adversely affect psychosocial outcomes and worsen schizophrenia's clinical manifestation. In the present study, we aimed to investigate associations among gray matter (GM) volumes in language processing areas (LPAs), verbal ability, and positive symptoms in first-episode patients (FEPs) with schizophrenia spectrum psychosis.

Methods: We enrolled 94 FEPs and 52 healthy controls (HCs) and subjected them to structural magnetic resonance imaging. The GM volumes of the bilateral pars opercularis (POp), pars triangularis (PTr), planum temporale (PT), Heschl's gyrus (HG), insula, and fusiform gyrus (FG), were estimated and compared between the FEPs and HCs. Verbal intelligence levels and positive symptom severity were examined for correlations with the left LPA volumes.

Results: The GM volumes of the left POp, HG, and FG were significantly smaller in the FEPs than in the HCs, while the right regions showed no significant between-group difference. A multiple linear regression model revealed that larger left PT volume was associated with better verbal intelligence in FEPs. In exploratory correlation analysis, several LPAs showed significant correlations with the severity of positive symptoms in FEPs. The left FG volume had a strong inverse correlation with the severity of auditory verbal hallucinations, while the left PT volume was inversely associated with the severity of positive formal thought disorder and delusions. Moreover, the volume of the left insula was positively associated with the severity of bizarre behavior.

Conclusions: The present study suggests that GM abnormalities in the LPAs, which can be detected during the early stage of illness, may underlie impaired verbal communication and positive symptoms in patients with schizophrenia spectrum psychosis.

1. Introduction

Impaired verbal communication is a prominent feature in patients with schizophrenia; their speech is often difficult to follow as it consists of unusual content and thought associations. Difficulties of this kind tend to persist throughout the illness (Roche et al., 2015), adversely affecting social relationships and functional outcomes (Bowie and Harvey, 2008; Holshausen et al., 2014). Furthermore, less severe communication disturbances can predict the transition to full-blown psychosis in ultra-high-risk individuals (Bearden et al., 2011; DeVylder et al., 2014; Bedi et al., 2015). Decreased verbal ability in schizophrenia is thought to be neurodevelopmental in origin (Reichenberg et al., 2010; MacCabe et al., 2013), suggesting that this feature is likely to be a trait vulnerability to schizophrenia.

Multiple cortical regions across the brain interact to create a network for language processing and verbal communication. In patients with schizophrenia, the language processing areas (LPAs) in the frontal, temporal, and parietal regions of the left hemisphere (Vigneau et al., 2006) are altered, both structurally and functionally. Meta-analyses of brain structural volumes have consistently shown that shrinkage of the left superior temporal gyrus (STG) is one of the most consistent findings in patients with schizophrenia (Honea et al., 2005; Fusar-Poli et al., 2012; Shepherd et al., 2012). This region contains Heschl's gyrus (HG) and Wernicke's area, including the left planum temporale (PT), which

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are responsible for auditory speech processing and comprehension (Chang et al., 2010). The PT, which has leftward asymmetry in about two-thirds of human brains (Geschwind and Levitsky, 1968; Foundas et al., 2002), is of particular interest because patients with schizophrenia show deficits in the STG, predominantly in the left hemisphere (Barta et al., 1990; Barta et al., 1997; Kwon et al., 1999). Progressive gray matter (GM) reductions in the left STG have been also observed in patients with first-episode schizophrenia (Hirayasu et al., 2000; Kasai et al., 2003a,b; Meisenzahl et al., 2008), even before the onset of overt psychosis (Takahashi et al., 2009). Several other studies have implicated Broca's area abnormalities in the impaired verbal ability seen in schizophrenia (Wisco et al., 2007; Jung et al., 2012; Fillman et al., 2016). Broca's area is a core node of the language network with connections to the temporoparietal LPAs (Hagoort, 2014). A recent body of neuroimaging studies consistently demonstrated that formal thought disorder (FTD) in patients with schizophrenia was associated with volumetric reductions in the left inferior frontal and superior-to-middle temporal regions (Cavelti et al., 2018; Kircher et al., 2018), suggesting that deficits in multiple LPAs underlie disturbed language processing and verbal communication.

Another key region for language processing is the left fusiform gyrus (FG), which processes visual forms of language, such as words (Cohen et al., 2000). The FG is mainly known as a center of face-specific processing, but it may also perform visual language processing lateralized to the left hemisphere (Caspers et al., 2014). Recent neuroimaging studies have demonstrated that the left FG is interconnected with other LPAs in the frontal and temporoparietal regions that support semantic language processing (Ardila et al., 2015; Walenski et al., 2019). Reduced GM volume in the left FG has been observed in first-episode patients (FEPs) with schizophrenia (Lee et al., 2002), as well as in those with chronic schizophrenia (Onitsuka et al., 2003), suggesting that the relevant neural processes function poorly in these patients. In addition to structural abnormalities, the LPAs also show a lack of functional coupling that has also been implicated in the aberrant language processing seen in schizophrenia (Griego et al., 2008; Szycik et al., 2009). Therefore, to elucidate the associations between verbal communication and its neural correlates, the various LPAs must be considered together.

Certain brain regions related to impaired language processing in patients with schizophrenia have also been associated with positive symptoms other than FTD, particularly auditory verbal hallucinations (AVHs). Previous studies have reported that structural abnormalities in the STG, including those in the HG and PT, are significantly associated with AVH severity and delusional behaviors in patients with first-episode psychosis (Kasai et al., 2003b; Sumich et al., 2005). A meta-analysis of voxel-based morphometry studies showed that AVH severity was associated with decreased GM volume in the left STG (including the HG) in patients with schizophrenia (Modinos et al., 2013). Moreover, another meta-analysis identified a significant inverse correlation between AVH severity and GM volume in the left insula (Palaniyappan et al., 2012). Functional neuroimaging studies further implied that the frontotemporal LPA is involved in AVHs by measuring brain activity in patients experiencing AVHs (Jardri et al., 2011; Zmigrod et al., 2016). Therefore, as impaired language processing and underlying brain alterations are the main characteristics present during the early phase of illness, the associations between verbal ability and positive symptoms must be determined in all LPA regions in patients with schizophrenia.

The present study aimed to investigate the associations among GM volume in the LPAs, verbal ability, and positive symptoms in FEPs with schizophrenia spectrum psychosis. We hypothesized that (1) GM volumes in the LPAs are smaller in FEPs than in healthy controls (HCs) and that (2) GM volumes in LPAs, particularly in the STG, are associated with verbal intelligence levels and positive symptoms in FEPs.

2. Materials and methods

2.1. Participants

We recruited 94 participants diagnosed with first-episode schizophrenia spectrum psychosis from among those receiving treatment in either an inpatient or outpatient setting at the Department of Psychiatry, CHA Bundang Medical Center (Seongnam, Republic of Korea) between February 2014 and July 2017. The FEPs were diagnosed using the DSM-IV-TR criteria for psychotic disorders, as determined using the Structured Clinical Interview for DSM-IV-TR Axis I Disorders (First et al., 2002); 71 of the patients had schizophrenia, nine had schizophreniform disorder, seven had a brief psychotic disorder, and seven had schizoaffective disorder. All FEPs were in their first psychotic episode and had an illness duration of < 5 years (Breitborde et al., 2009). In addition, 52 HCs were recruited from the local community using online and print advertisements. Only individuals with no personal or first-relative family history of psychiatric disorders were included as HCs. Study participants were excluded if they had a current or past history of substance-related problems, neurological diseases, intellectual disability (IQ < 70), or head trauma with loss of consciousness. Left-handed individuals were also excluded according to the Edinburgh Handedness Inventory (Oldfield, 1971).

All study procedures were reviewed and approved by the Institutional Review Board of CHA Bundang Medical Center, in accordance with the latest version of the Declaration of Helsinki and principles of Good Clinical Practice. All study participants, or one parent if they were <18 years old, provided written informed consent following a thorough explanation of the study procedures.

2.2. Assessments

The verbal subtests of the Korean Wechsler Adult Intelligence Scale (K-WAIS; Yeom et al., 1992) were administered to 67 FEPs after their acute exacerbation had stabilized. Trained clinical psychologists performed the verbal subtests (information, comprehension, arithmetic, digit span, similarities, and vocabulary) using standard administration and scoring procedures. The severity of the clinical symptoms at baseline was assessed in all FEPs by experienced psychiatrists using the Scale for the Assessment of Negative Symptoms (SANS; Andreasen, 1984a), the Scale for the Assessment of Positive Symptoms (SAPS; Andreasen, 1984b), and the Clinical Global Impression Severity of Illness Scale (CGI-S; Haro et al., 2003).

2.3. Neuroimaging data acquisition and analysis

All study participants underwent brain magnetic resonance imaging (MRI) on a 3.0-Tesla GE Signa HDxt scanner (GE Healthcare, Milwaukee, WI, USA). High-resolution structural images were acquired using a three-dimensional, T1-weighted, fast-spoiled, gradient-recalled echo sequence (repetition time = 6.3 ms; echo time = 2.1 ms; flip angle = 12°; field of view = 256 mm; matrix = 256 × 256; voxel size = 1 × 1 × 1 mm^3). Structural MRI data were analyzed using FreeSurfer (version 5.3; http://surfer.nmr.mgh.harvard.edu) with standard image processing steps, including volumetric segmentation, cortical surface reconstruction (Fischl et al., 1999a,b, 2002; Fischl and Dale, 2000), and estimated total intracranial volume (ICV) (Buckner et al., 2004). The post-processing outputs of each study participant were examined visually by experienced researchers (S.H.L. and A.L.) to ensure processing accuracy and image quality. The Desikan–Killiany (Desikan et al., 2006) and Destrieux (Fischl et al., 2004; Destrieux et al., 2010) cortical atlases, implemented in FreeSurfer, were used to label the cerebral cortex. The following regions of interest (ROIs) were selected from both the left and right hemispheres, as described by Greve et al. (2013): (1) pars opercularis (POp) of the inferior frontal gyrus; (2) pars triangularis (PTr) of the inferior frontal gyrus; (3)

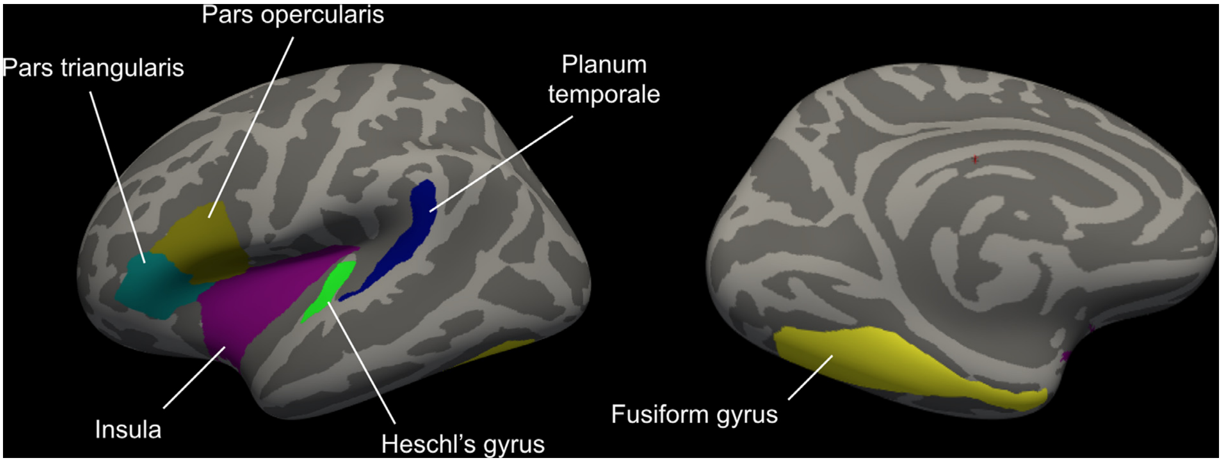

Fig. 1. Regions of interest in the language processing areas of the left hemisphere. The same areas from the right hemisphere were also included in the analysis.

PT; (4) HG; (5) insula; (6) FG (Fig. 1). The GM volumes of the total cortex, as well as the ROIs on both sides, were extracted from each study participant and then adjusted for ICV to account for individual differences in head size (Buckner et al., 2004).

2.4. Statistical analysis

To compare demographic and clinical characteristics between FEPs and HCs, independent *t*-tests were used for continuous variables, while chi-squared tests were used for categorical variables. The GM volumes of the ROIs on both sides were compared using multivariate analysis of covariance (MANCOVA), with demographic differences acting as covariates. Multiple linear regression analysis was then performed, with the level of verbal intelligence as a dependent variable and the GM volumes of the ROIs as independent variables in FEPs. The explanatory variables were selected using a stepwise selection procedure. The association between verbal intelligence and the severity of positive symptoms was examined in the same way. Exploratory correlation analysis was performed to assess the associations between the GM volumes of the ROIs and the verbal subtest scores for severity of positive symptoms. All statistical procedures were performed using the Statistical Package for the Social Sciences, version 24 (IBM Corp., Armonk, New York). All p-values were presented uncorrected for multiple testing, unless otherwise indicated.

3. Results

3.1. Demographic and clinical characteristics of study participants

The demographic and clinical profiles of all study participants are shown in Table 1. Although neither sex nor total intracranial volume differed significantly between the FEPs and HCs, the FEPs were significantly younger and less educated than the HCs. The ICV was not associated with age or years of education in either group. In addition, neither chlorpromazine equivalent dose of antipsychotic medication nor duration of illness were correlated with ICV, GM volumes of the total cortex and ROIs, verbal intelligence, or severity of clinical symptoms in FEPs.

3.2. Comparison of GM volumes in the LPAs between FEPs and HCs

Table 2 presents ICV-adjusted GM volumes of the total cortex and bilateral ROIs in FEPs and HCs. After controlling for demographic differences (age and years of education), there was no significant difference in the total cortex volume between FEPs and HCs. For the bilateral ROIs, a significant between-group effect was found on the left ($F = 2.85$, $p = 0.012$), but not on the right ($F = 1.75$, $p = 0.114$). Specifically, the GM volumes in the POp, HG, and FG out of the six LPAs from the left hemisphere were smaller in the FEPs than in the HCs. The between-group results remained the same when only participants with schizophrenia were compared to HCs.

3.3. Associations of GM volumes in the LPAs with verbal intelligence and positive symptoms

The level of verbal intelligence in FEPs was correlated with age ($r = 0.315$; $p = 0.009$) and years of education ($r = 0.465$; $p < 0.001$), so these variables were controlled for as covariates in the subsequent analysis. Among the six LPAs, the GM volume in the left PT was positively associated with verbal intelligence (variance inflation factor = 1.19–2.20; Table 3) in both HCs and FEPs. The left PT volume was correlated with each verbal intelligence subtest, showing less than medium effect size ($r = 0.143$–0.216; for detailed results, see Supplementary Table). Although the level of verbal intelligence was not associated with the severity of any positive symptoms in the regression model, the severity scores for positive FTD and bizarre behavior were inversely correlated with performance in the information, vocabulary, and comprehension subtests, with medium-to-large effect sizes ($r = -0.283$ to -0.410; for detailed results, see Supplementary Table).

To examine the relationships between the GM volumes in the left LPAs and positive symptoms, an exploratory correlation analysis was performed (Table 4). The subscales of hallucinations from the SAPS were examined separately for AVHs (auditory hallucinations, voices commenting, and voices conversing) and other hallucinations (somatic or tactile hallucinations, olfactory hallucinations, and visual hallucinations). The AVH scores showed a significant inverse correlation with left FG volume, even after Bonferroni's correction for multiple comparisons was applied (Bonferroni-corrected $p = 0.010$). The left PT volume was inversely associated with the severity of positive FTD and delusions, whereas the left insular volume was positively associated with bizarre behavior scores.

4. Discussion

In the present study, GM volumes in the left POp, left HG, and left FG were smaller in the FEPs than in the HCs. The verbal intelligence of the FEPs was positively correlated with GM volume in the left PT. This region was associated with the severity of positive FTD and delusions in FEPs. Furthermore, GM volumes in the left FG and left insula were associated with AVH severity and bizarre behavior, respectively. Our findings suggest that structural abnormalities in the brain regions involved in language processing may play a substantial role in

Table 1
Demographic and clinical characteristics of study participants.

	FEPs (*n* = 94)	HCs (*n* = 52)	Statistics	*p*
Sex				
Male, *n* (%)	35 (37.2)	25 (48.1)	χ^2 = 1.27	0.202
Female, *n* (%)	59 (62.8)	27 (51.9)		
Age (years), mean ± SD	33.1 ± 11.0	38.7 ± 10.3	*t* = −3.05	0.003
Education (years), mean ± SD	12.9 ± 2.8	17.1 ± 2.0	*t* = −9.62	< 0.001
Duration of illness (months), mean ± SD	21.8 ± 36.3			
Intracranial volume (ml), mean ± SD	1479.1 ± 149.3	1517.3 ± 135.8	*t* = −1.53	0.129
Antipsychotic medications (mg/day)[a], mean ± SD	520.6 ± 249.5			
SANS (composite score), mean ± SD	51.1 ± 21.7			
Affective flattening	14.9 ± 7.6			
Alogia	9.8 ± 5.0			
Avolition-apathy	8.1 ± 3.8			
Anhedonia-asociality	12.6 ± 5.2			
Inattentiveness	5.7 ± 2.4			
SAPS (composite score), mean ± SD	61.6 ± 19.3			
Hallucinations	12.4 ± 5.3			
Delusions	22.9 ± 8.1			
Bizarre behavior	9.1 ± 4.3			
Positive formal thought disorder	17.2 ± 7.3			
CGI-S, mean ± SD	4.8 ± 1.0			
Verbal intelligence, mean ± SD	96.8 ± 17.1			
Information	9.9 ± 3.1			
Digit span	9.1 ± 3.2			
Vocabulary	10.0 ± 3.0			
Arithmetic	8.6 ± 3.2			
Comprehension	9.8 ± 3.5			
Similarities	10.4 ± 3.2			

[a] Chlorpromazine equivalent doses were calculated according to Gardner et al. (2010).
FEPs, first-episode patients; HCs, healthy controls; SD, standard deviation; SANS, Scale for the Assessment of Negative Symptoms; SAPS, Scale for the Assessment of Positive Symptoms; CGI-S, Clinical Global Impression Severity of Illness.

impairments to verbal communication and the development of positive symptoms in patients with schizophrenia spectrum psychosis.

The smaller GM volumes in the left POp, left HG, and left FG observed in the FEPs corroborate previous reports showing decreased GM volumes in Broca's area (Jung et al., 2012; Fillman et al., 2016), the left STG (Hirayasu et al., 2000; Kasai et al., 2003a,b), and the left FG (Lee et al., 2002; Onitsuka et al., 2003) in patients with schizophrenia. This finding likely did not result from an overall reduction in brain volume, since the ICV-adjusted GM volumes of the total cortex did not differ significantly between FEPs and HCs in the present study. Furthermore, the ROIs in the right hemisphere showed no significant difference between the groups, indicating that the LPA abnormalities have left lateralization. The GM volumes of the total cortex and ROIs were not associated with antipsychotic medication dose or duration of illness in the FEPs. Previous studies have suggested that the total brain volumes of patients with schizophrenia do not differ from those of HCs (Harrison et al., 2003; Steen et al., 2006). Although the present study focused on selected brain regions involved in language processing, the three regions exhibiting lower GM volumes in the FEPs than in the HCs overlapped consistently with the risk-associated brain regions found in individuals at high risk for psychosis (Sun et al., 2009; Smieskova et al., 2013; Bois et al., 2015). Therefore, our findings may partly support the hypothesis that abnormalities in specific brain regions, rather than global changes, are more relevant to the pathogenesis of schizophrenia

Table 2
Comparison between FEPs and HCs in terms of gray matter volumes in the regions of interest in both hemispheres.[a]

Volume (mm^3)	FEPs (*n* = 94)	HCs (*n* = 52)	*F*	*p*	ES[d]
Total cortex	485756 ± 32302	491653 ± 26841	1.25	0.265	0.009
Left[b]					
Pars opercularis	4501 ± 626	4717 ± 766	5.16	0.025	0.035
Pars triangularis	3789 ± 541	3827 ± 633	0.55	0.458	0.004
Insula	6885 ± 588	6811 ± 555	0.06	0.801	0.0004
Heschl's gyrus	1017 ± 252	1090 ± 248	6.39	0.013	0.043
Planum temporale	1828 ± 401	1858 ± 356	0.39	0.535	0.003
Fusiform gyrus	9918 ± 1372	10754 ± 1549	9.34	0.003	0.062
Right[c]					
Pars opercularis	3984 ± 605	4164 ± 715			
Pars triangularis	4386 ± 656	4536 ± 666			
Insula	7058 ± 696	7075 ± 604			
Heschl's gyrus	836 ± 172	860 ± 176			
Planum temporale	1595 ± 226	1626 ± 300			
Fusiform gyrus	9515 ± 1189	10017 ± 1294			

[a] Mean values are presented with standard deviations.
[b] There was a significant between-group effect (F = 2.85, p = 0.012, ES = 0.111).
[c] No significant between-group difference was found (F = 1.75, p = 0.114, ES = 0.071).
[d] ESs were calculated using partial eta squared (η_p^2).
FEPs, first-episode patients; HCs, healthy controls; ES, effect size.

Table 3
Hierarchical multiple linear regression analysis of verbal intelligence and gray matter volume in the left language processing areas of FEPs (n = 67).[a,b]

Explanatory variables	B	SE	95% CI for B	t	p
Age	0.472	0.164	0.143 to 0.800	2.87	0.006
Education years	2.611	0.612	1.389 to 3.834	4.27	< 0.001
Left planum temporale volume	0.010	0.004	0.001 to 0.019	2.28	0.026

[a] Age and education years were entered as covariates in the first step, followed by GM volume in the six left LPAs in the second step with a stepwise selection procedure.
[b] Adjusted R^2 of the final model = 0.31, F = 11.07, $p < 0.001$.
FEPs, first-episode patients.

spectrum psychosis.

The verbal intelligence of the FEPs was significantly associated with the GM volume of the left PT. The left PT volume itself did not differ significantly between the FEPs and HCs, but its association with verbal ability corroborated previous investigations showing that the size of the left PT, rather than anatomical asymmetry or hand dominance, can account for inter-individual functional variability in language comprehension (Tzourio et al., 1998; Josse et al., 2003). The left PT, which contains part of Wernicke's area, is essential to higher-order auditory processing and speech perception (Griffiths and Warren, 2002). Moreover, increasing evidence indicates that the PT, including Wernicke's area, is crucial for phonological retrieval and thus for communicative speech production (Indefrey, 2011; Pillay et al., 2014). Aberrations in this function causes paraphasia, which leads to errors in the phoneme sequence and disrupts the semantic sense of speech (Binder, 2017). In this context, the inverse association found between the left PT volume and severity of positive FTD in the present study was unsurprising.

Although verbal intelligence was not associated with positive FTD, performance in several subtests that require verbal comprehension (information, vocabulary, comprehension, and similarities; Allen et al., 1998) showed inverse correlation with the severity of positive FTD and bizarre behavior. This finding backs up a previous report showing that lower verbal intelligence was associated with disorganized language and behavior (O'Leary et al., 2000). However, found no association between verbal subtests and delusion severity, which was inversely correlated with left PT volume. Because the present study had a cross-sectional design, we could not differentiate causality in these intertwining relationships. Future research should more clearly elucidate this aspect. Despite this limitation, the correlations among the LPAs, verbal intelligence, and positive symptoms may suggest that impaired verbal ability and underlying brain abnormalities contribute to the development of positive symptoms.

Although the left PT was the only region that showed a significant association with verbal intelligence, our exploratory correlation analysis revealed that other LPAs showed several significant correlations with the severity of positive symptoms in FEPs. In particular, there was a strong association between left FG volume and AVH severity: FEPs with smaller left FG volume experienced more severe AVHs. Although the left FG was previously regarded as modality-specific to visual stimuli, more recent studies have observed activation of the left FG under verbal listening conditions (Dehaene et al., 2002; Crottaz-Herbette et al., 2004). Furthermore, recent evidence implied that the left FG is engaged in general semantic retrieval as a multimodal association region adjacent to the hippocampus (Noppeney and Price, 2003; Binder et al., 2009). Our finding of an inverse association between left FG volume and AVH severity is consistent with previous investigations showing that aberrant semantic top-down processing affects the experience of AVHs (Vercammen and Aleman, 2010; Daalman et al., 2012). Although we cannot interpret our results to determine the left FG's exact role in verbal intelligence and positive symptoms, our findings may suggest that the left FG is substantially involved in semantic processing related to the experience of AVHs. Future investigations are warranted to further elucidate the associations among brain regions, verbal ability, and positive symptoms in patients with schizophrenia spectrum psychosis.

The present study had a number of limitations that must be considered during interpretation of the results. First, only some FEPs and no HCs were assessed for verbal intelligence. Although a relatively large sample size of study participants were enrolled and underwent MRI scan, further investigations with more comprehensive assessments are recommended. Second, all FEPs involved in this study were taking antipsychotic medications at the time of the MRI scan. Since antipsychotic medications may reduce brain volume (Moncrieff and Leo, 2010), future investigations involving drug-naïve patients are required to exclude this confounding effect. Third, because the study had a cross-sectional design, the causal chain of the structural changes in the brain cannot be determined. Although brain structural abnormalities were investigated in FEPs during the early phase of illness, longitudinal follow-up studies are required to elucidate the neural correlates of schizophrenia development.

In conclusion, the present study demonstrated that the GM volumes of the LPAs, particularly the left POp, left HG, and left FG, were smaller in FEPs than in HCs. Impaired verbal ability was associated with smaller GM volume in the left PT, which was also associated with more severe positive FTD. In addition, the left FG volume showed a strong inverse association with AVH severity, although there was no significant volumetric difference between FEPs and HCs in this regard. The findings of the present study suggest that GM abnormalities in the LPAs, which can be detected during the early stage of the illness, may underlie impaired verbal communication and positive symptoms in patients with schizophrenia spectrum psychosis. Our findings may provide some clues for understanding the neural underpinnings of schizophrenia spectrum psychosis.

Table 4
Correlations between gray matter volume in the left language processing areas of FEPs and positive symptoms (n = 67)

	Left POp	Left PTr	Left insula	Left HG	Left PT	Left FG
Positive symptoms						
Auditory verbal hallucinations	r = −0.228	r = 0.074	r = −0.134	r = −0.136	r = 0.110	**r = −0.433**
	p = 0.067	p = 0.555	p = 0.289	p = 0.281	p = 0.384	**p < 0.001**
Other hallucinations	r = 0.065	r = 0.167	r = 0.106	r = 0.061	r = 0.011	r = −0.077
	p = 0.605	p = 0.183	p = 0.401	p = 0.627	p = 0.931	p = 0.540
Delusions	r = 0.116	r = 0.236	r = 0.200	r = −0.125	**r = −0.255**	r = 0.005
	p = 0.359	p = 0.058	p = 0.110	p = 0.321	**p = 0.041**	p = 0.969
Bizarre behavior	r = 0.004	r = 0.245	**r = 0.265**	r = −0.093	r = −0.023	r = 0.098
	p = 0.972	p = 0.050	**p = 0.033**	p = 0.461	p = 0.856	p = 0.439
Positive formal thought disorder	r = −0.107	r = 0.146	r = 0.129	r = −0.018	**r = −0.373**	r = 0.094
	p = 0.396	p = 0.246	p = 0.306	p = 0.885	**p = 0.002**	p = 0.458

FEPs, first-episode patients; POp, pars opercularis; PTr, pars triangularis; HG, Heschl's gyrus; PT, planum temporale; FG, fusiform gyrus.

Declaration of Competing Interest

None.

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Supplementary materials

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