

Table 2 | Peak coordinates (x, y, z) and their z-values of cerebral activation by full factorial design analysis with Group effect (controls and patients).

Brain regions	BA	Coordinate			$F_{(1, 136)}$	z-value	P (FDR-corrected)
		x	y	z			
MAIN EFFECT OF GROUP (CONTROLS/SCHIZOPHRENIA)							
Controls > Patients							
L STG	41	-54	-21	3	23.20	4.47	<0.05
Patients > Controls							
L MFG	6	-26	-1	63	23.40	4.49	<0.05
R MFG	6	27	-1	61	19.50	4.10	<0.05
R SPL	7	26	-64	52	29.70	5.04	<0.05
Occipital lobe	18	8	-76	1	21.80	4.34	<0.05
R amygdala		20	-3	-21	18.40	3.99	<0.05

L, left hemisphere; R, right hemisphere; $p < 0.05$, voxel level, FDR-corrected.

A significantly positive correlation was observed ($r = 0.346$, $p < 0.05$, Figure 10). The other areas were not significantly correlated with accuracy. These findings suggest that the less the accuracy is, the less the beta value of FJT at left STG is.

DISCUSSION

To clarify cerebral function underlying the perception of voice attractiveness including greeting conversations in patients with schizophrenia, we investigated the difference of cerebral

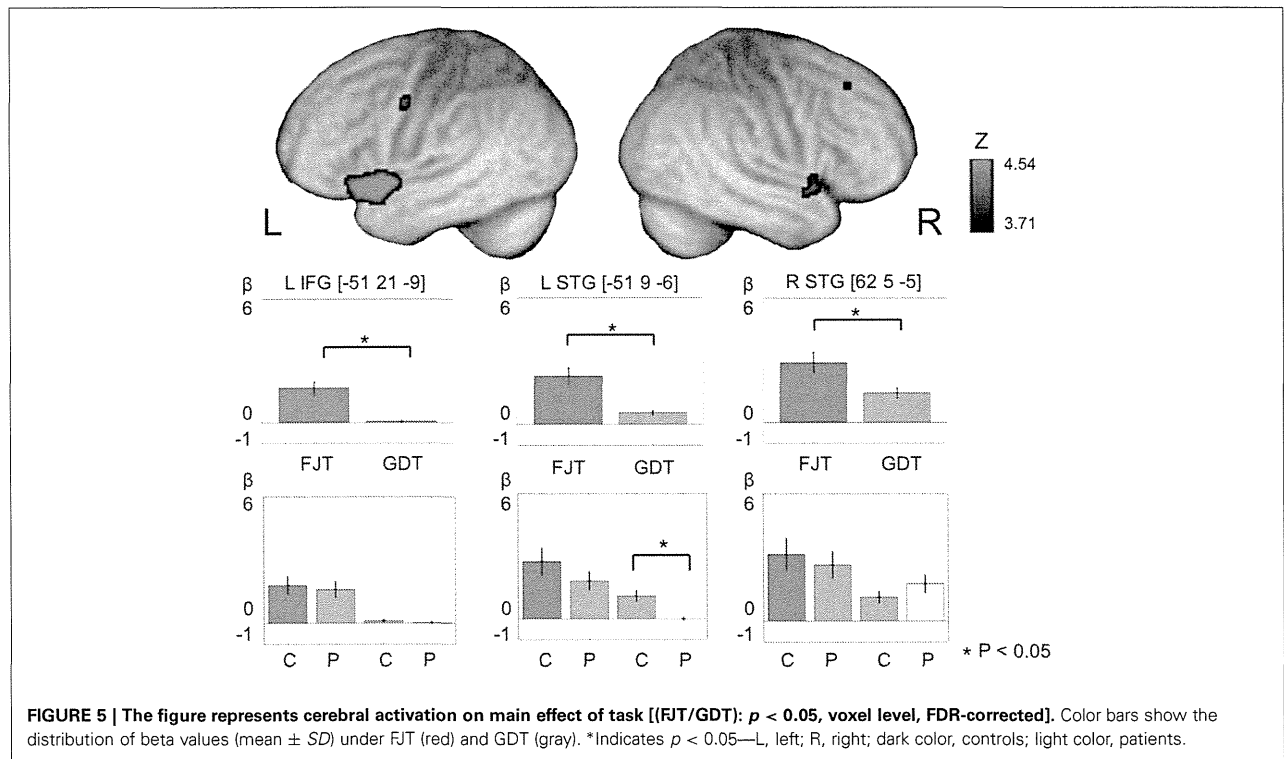


Table 3 | Peak coordinates (x, y, z) and their z-values of cerebral activation by full factorial design analysis with task effect (controls and patients).

Brain regions	BA	Coordinate			$F_{(1, 136)}$	z-value	P (FDR-corrected)
		x	y	z			
MAIN EFFECT OF TASKS (FJT/GDT)							
L PrCG	6	-50	-4	42	18.50	4.00	<0.05
R MFG	8	27	27	43	16.00	3.70	<0.05
L IFG	47	-51	21	-9	23.90	4.54	<0.05
R insula	13	38	5	-3	19.70	4.13	<0.05
L STG	22	-59	9	-2	30.80	5.13	<0.05
R STG	22	62	5	-5	19.00	4.05	<0.05
L Claustrum		-36	-10	-2	22.20	4.39	<0.05
L cerebellum		-12	-43	-21	20.20	4.13	<0.05

L, left hemisphere; R, right hemisphere; $p < 0.05$, voxel level, FDR-corrected.

activation between control subjects and schizophrenia patients while they were judging favorability or gender of vocalizations. In our present experiment, the left IFG-STG was activated in the processing of favorability judgment in both controls and schizophrenia patients. Although cerebral activation in the left STG was reduced in schizophrenia, cerebral activation in the right MFG, right IPL, and right amygdala was increased. Further, by correlation analysis between psychiatric symptom and cerebral activation of favorability, we confirmed that positive and negative symptoms in schizophrenia are closely related to cerebral dysfunction in the left STG and right MFG-IPL (Figure 9).

FRONTOTEMPORAL FUNCTION TO AUDITORY ATTRACTIVENESS AND ITS DYSFUNCTION IN SCHIZOPHRENIA

Our results by full factorial design also exhibited main effect of experimental Task (FJT/GDT) in the left STG and left IFG (Figure 5, Table 3). Recent auditory fMRI studies demonstrated that the cerebral function of STS is important to grasp auditory social cues (Saarela and Hari, 2008; Scharpf et al., 2010). Further, a recent fMRI study concerning auditory attractiveness demonstrated the importance of the functional connection between STG and IFG (Bestelmeyer et al., 2012). In accord with these findings, our results showed left STG-IFG activation in the recognition of auditory attractiveness including social communications.

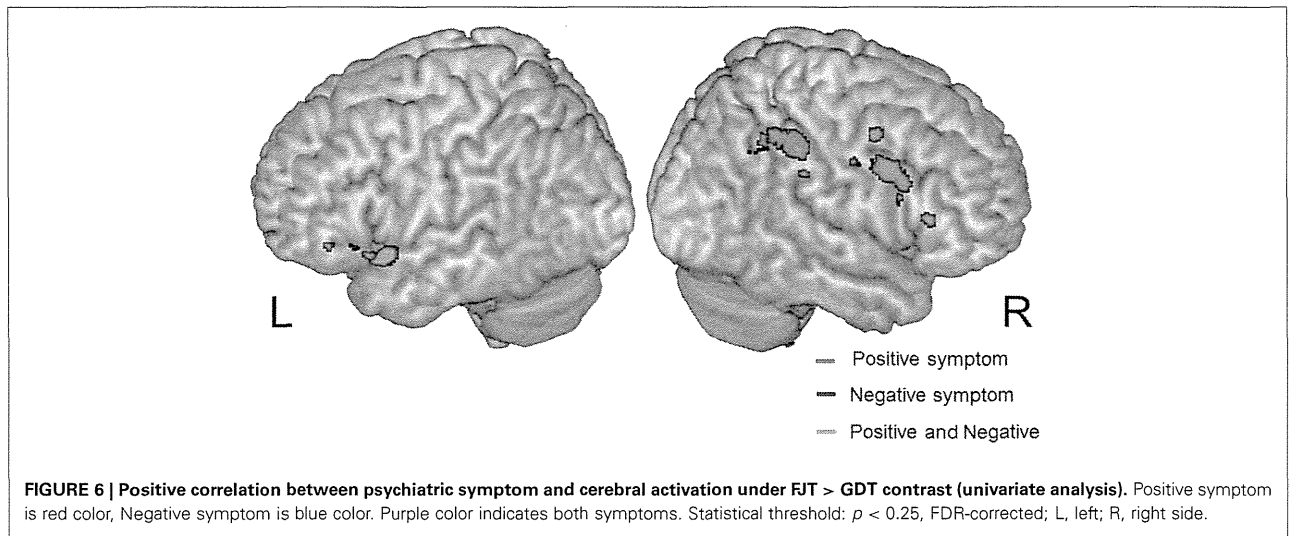
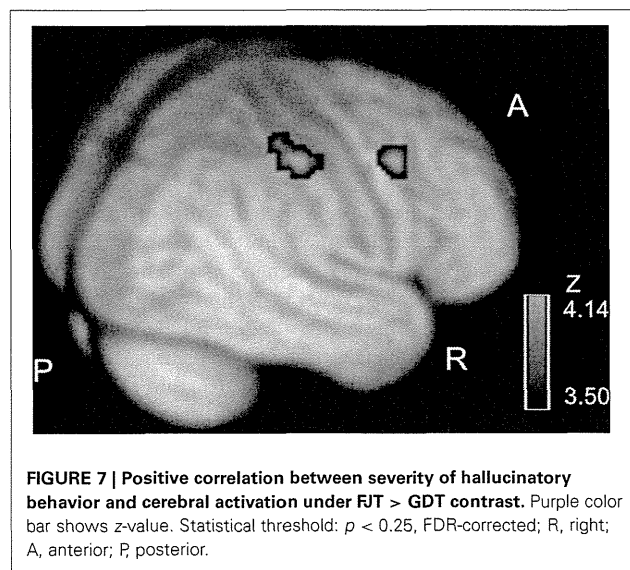


Table 4 | Positive correlation between PANSS and cerebral activation under FJT minus GDT, $p < 0.0001$ uncorrected ($p < 0.25$, FDR-corrected), R, right hemisphere.

Brain regions	BA	Coordinate			z-value	P (uncorrected)	P (FDR-corrected)
		x	y	z			
L SFG	6	-6	9	55	3.73	<0.0001	<0.25
R SFG	6	9	8	60	4.04	<0.0001	<0.25
R MFG	9	51	6	36	3.77	<0.0001	<0.25
L STG	38	-50	12	-8	3.72	<0.0001	<0.25
R IPL	40	40	-43	49	4.16	<0.0001	<0.25



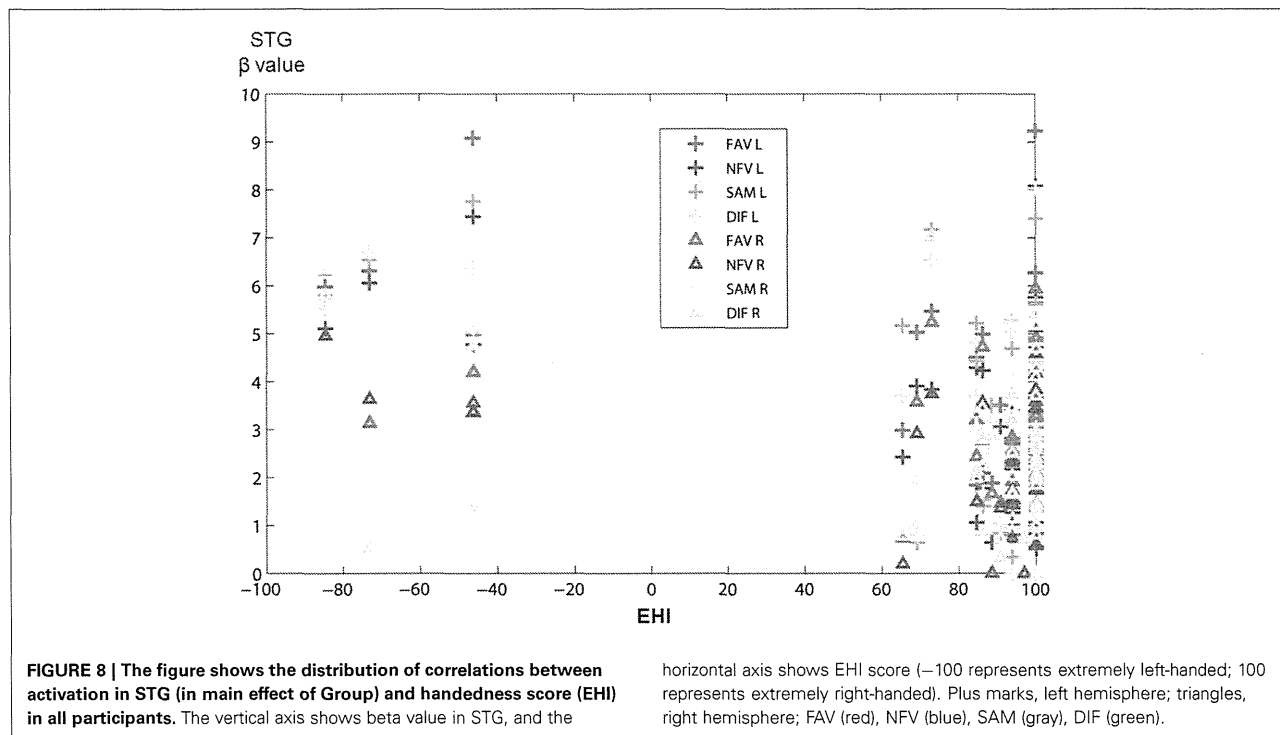
Before the experiment, we hypothesized that left STG-IFG activation by auditory attractiveness could be impaired in schizophrenia. Predictably, cerebral activation in schizophrenia patients was greater in the bilateral prefrontal regions in

comparison with control subjects (Figure 5). A recent study indicated that brain activity in the left prefrontal regions reflected the overall perceived attractiveness of the voices (Bestelmeyer et al., 2012). Further, another fMRI study indicated that the left ventrolateral prefrontal cortex, bilateral dorsal IFG, and medial frontal cortex are activated when the subjects judged whether pairs of human individuals were friends or enemies (Farrow et al., 2011). These reports indicate that prefrontal regions are associated with the judgment of favorability and friendliness. In our present study, hyper-frontality and hypo-temporality in schizophrenia patients could designate the dysfunction of left STG-IFG when they judged favorability.

In our study, cerebral activation to favorability judgment was reduced in the left STG, while it was increased in the MFG, amygdala, TPJ, and occipital lobe in the right hemisphere. A recent fMRI study suggested that paradoxical brain activation in schizophrenia patients with auditory hallucination may be caused by both reduced activation due to impaired brain function in auditory processing and increased activation due to disturbance of attention bias toward internally generated information (Jardri et al., 2011; Kompus et al., 2011). In accordance with this recent study, less activation in schizophrenia could represent impairment of favorability judgment in auditory processing, whereas greater activation in schizophrenia may reflect disturbance of attention bias toward

Table 5 | Positive correlation between the severity of hallucinatory behavior and cerebral activation under FJT minus GDT, $p < 0.0001$ uncorrected ($p < 0.25$, FDR-corrected), R, right hemisphere.

Brain regions	BA	Coordinate			z-value	P (uncorrected)	P (FDR-corrected)
		x	y	z			
CORRELATION OF HALLUCINATORY BEHAVIOR							
R PsCG	2	48	-19	30	4.55	<0.0001	<0.25
R PrCG	6	46	-16	30	4.10	<0.0001	<0.25
R MFG	9	48	8	42	3.72	<0.0001	<0.25
R IPL	40	45	-33	46	4.14	<0.0001	<0.25



internally generated information by the appearance of auditory hallucination.

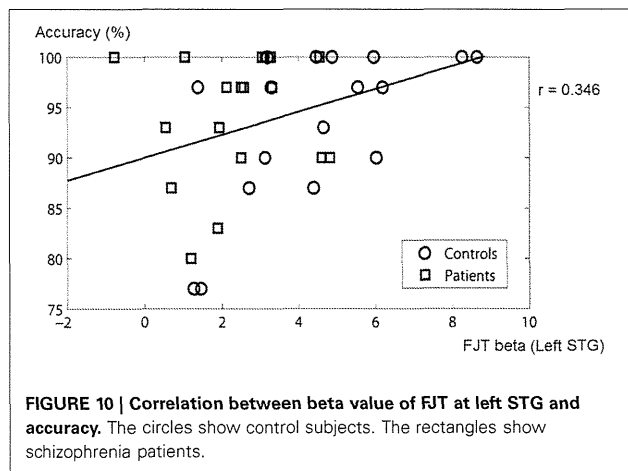
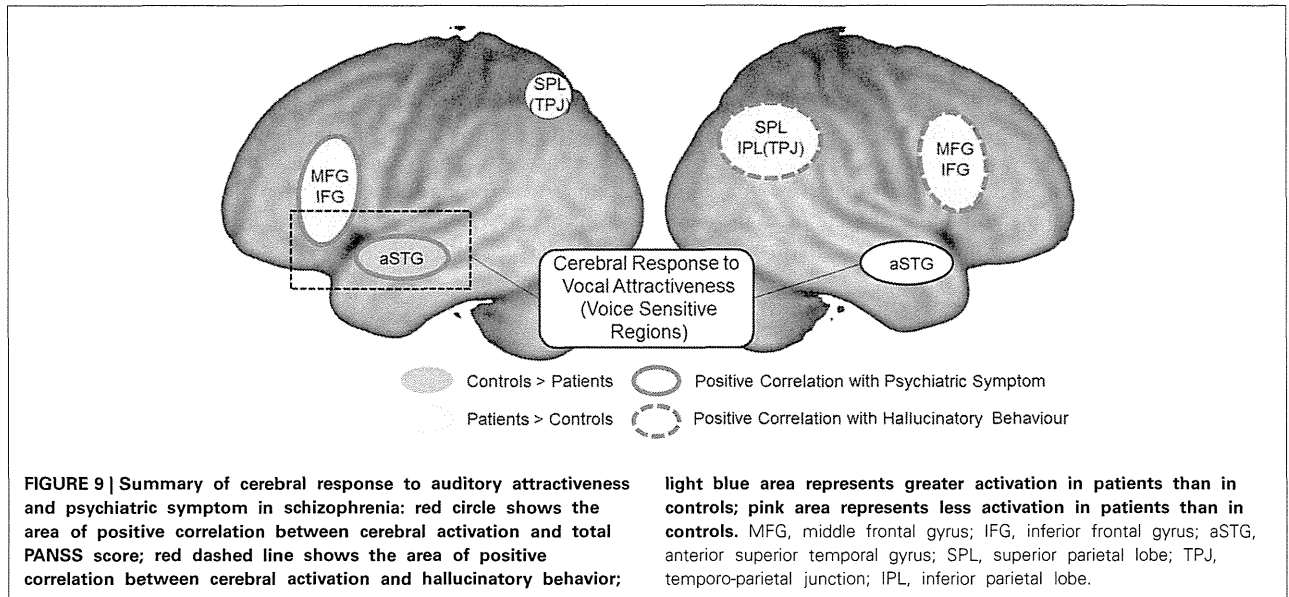
CEREBRAL LATERALITY TO AUDITORY ATTRACTIVENESS IN SCHIZOPHRENIA

Interestingly, our results in schizophrenia patients exhibited enhanced right-lateralization to auditory attractiveness mainly in MFG and IPL (Figure 4). Previous fMRI studies concerning language processing have demonstrated that schizophrenia patients show either reduced left hemispheric activation (Kiehl and Liddle, 2001; Kircher et al., 2001; Koeda et al., 2006) or reversed language dominance (Woodruff et al., 1997; Menon et al., 2001; Ngan et al., 2003; Bleich-Cohen et al., 2009). Conversely, previous fMRI studies concerning non-linguistic processing in schizophrenia indicated reduced right hemispheric activation (Koeda et al., 2006), reversed right-lateralized activation (Mitchell et al., 2004), or enhanced right-lateralized activation (Bach et al., 2009). In accordance with the latter report, our

results showed greater right prefrontal and inferior parietal activation during favorability judgment in schizophrenia (Figure 4). In the analysis by full factorial design, main effect of Group (controls/patients) revealed greater activation of schizophrenia in the right hemisphere compared with controls (Figure 4). This result also indicates enhanced right hemispheric activation by auditory attractiveness in schizophrenia. It could be speculated that these strong right hemispheric activations compensate the dysfunction of left STG-IFG related to auditory attractiveness (Figure 4).

PSYCHIATRIC SYMPTOMS AND AUDITORY ATTRACTIVENESS IN SCHIZOPHRENIA

Our results revealed a positive correlation between psychiatric symptom (total PANSS score, positive and negative symptom) and cerebral activation under FJT vs. GDT contrast at left STG-IFG and right prefrontal and superior/inferior parietal cortex (Figure 6 and Table 4). In both positive and negative symptoms,



almost the same regions were correlated with cerebral activation for auditory attractiveness. Left STG-IFG activation was observed in the favorability judgment (Figure 5). These findings could be considered to reflect the dysfunction of the left STG-IFG region in the recognition of auditory attractiveness. Crucially, cerebral activation in the right prefrontal and superior/inferior parietal region was positively correlated with the severity of auditory hallucination (Figure 7, Table 5). These areas also demonstrated greater activation under FJT vs. GDT contrast in schizophrenia (Figure 5, Table 3). These findings indicate that greater activation to the favorability judgment in schizophrenia is related to severity of auditory hallucinations. Previous studies indicate that the right MFG/IFG-IPL region is closely related to self-referential processing (Fossati et al., 2003; Canessa et al., 2005; Uddin et al., 2005). Especially, one study demonstrated that right fronto-parietal regions as well as left prefrontal and parietal regions were activated when subjects understood the context related to social

communications when two persons exchange goods, i.e., if you give me one, I will give you the other (Canessa et al., 2005). Further, another study exhibited that right dorsal IFG was activated in the processing of social alliance (friendliness) (Farrow et al., 2011). These previous findings support that the right MFG/IFG-IPL region associates with the recognition of social communications such as judgment of favorability. These activations could be attributed to representing the dysfunction of the fronto-parietal region in the processing of social communications by auditory hallucinations.

Recent fMRI studies investigated cerebral function when the subjects mentalize the other person's thoughts and behavior. These reports indicate that the role of the temporal-parietal junction is closely associated with comprehending the mental states of others (Siegal and Varley, 2002; Finger et al., 2006; Shamay-Tsoory et al., 2006; David et al., 2008). A recent study investigated cerebral activation in the processing of self-other distinction. This study demonstrated that the increase in cerebral activation in the right IPL correlated positively with the strength of psychiatric symptoms in schizophrenia (Jardri et al., 2011). Further, recent studies of schizophrenia reported that functional connectivity in the fronto-temporal network was decreased when the subjects comprehended the behavior of the other person (Das et al., 2012), or when the subjects listening to the other person's speech compared it with self-generated speech (Mechelli et al., 2007). Findings of greater right prefrontal-parietal activation (Figure 4) in schizophrenia may reflect brain activation due to comprehending other person's mental states through auditory hallucination as well as dysfunction of the fronto-temporal region in perception of vocal attractiveness.

In summary, when cerebral function in auditory attractiveness including social conversations was investigated, cerebral activation was revealed in the left STG and left IFG. Particularly, in schizophrenia, less activation was observed at the left STG

compared with control subjects. In addition, greater activation in schizophrenia was confirmed in the right fronto-parietal region. Further, cerebral response in this region was correlated with the severity of auditory hallucinations. These findings suggest that dysfunction in the left fronto-temporal regions is related to the ability to appropriately assess the attractiveness of vocal communications in schizophrenia. The right fronto-parietal region could offset cerebral dysfunction to auditory attractiveness including social communications.

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