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Increased Diffusivity in Superior Temporal Gyrus in Patients with Schizophrenia: A Diffusion Tensor Imaging Study

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Abstract

Background—Superior temporal gyrus (STG) volume reduction is one of the most consistent findings in schizophrenia. The goal of this study was to conduct the first diffusion tensor imaging (DTI) study to investigate altered structural integrity in STG gray and white matter in patients with chronic schizophrenia compared with healthy controls.

Methods—Magnetic resonance imaging (MRI) and DTI were acquired in 21 male patients with schizophrenia and 22 age-, handedness-, and parental social economic status-matched male comparison subjects. After manual segmentation of gray and white matter, mean diffusivity and fractional anisotropy were measured within STG. Correlational analyses were also conducted to test possible associations between DTI and clinical measures, including positive and negative symptoms of schizophrenia.

Results—Compared with controls, patients demonstrated reduced volume, bilaterally, in STG gray matter but not in white matter. For DTI measures, patients showed increased mean diffusivity, bilaterally, in STG gray matter, and in left-sided STG white matter. In addition, mean diffusivity in left-sided STG white matter showed statistically significant correlations with auditory hallucinations and attentional impairments in patients.

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Conclusions—These findings suggest a disruption of tissue integrity in STG gray and white matter in schizophrenia. In addition, increased water diffusivity in left-side STG, which was associated with auditory hallucinations and attentional impairments, suggests the possibility of a disconnection among auditory/language processing regions in schizophrenia.

Keywords

schizophrenia; superior temporal gyrus; diffusion tensor imaging; mean diffusivity; fractional anisotropy; auditory hallucination

1. Introduction

Superior temporal gyrus (STG) is a brain region that it is thought to be a substrate of both auditory and language processing (Galaburda et al., 1978), domains often impaired in schizophrenia. Indeed, converging findings suggest volume reductions in STG in schizophrenia using magnetic resonance imaging (MRI) (e.g., McCarley et al., 1999; Pearlson, 1997; Shenton et al., 2001). Of further note, thought disorder (Barta et al., 1997; Shenton et al., 1992) and auditory hallucinations (Barta et al., 1990; Gaser et al., 2004; Sumich et al., 2005), hallmark symptoms in schizophrenia, have been associated with left STG volume reduction. Such left-sided abnormalities are also observed at first episode of schizophrenia, but not at first episode of bipolar disorder (Hirayasu et al., 1998), further suggesting the possible specificity of these findings to schizophrenia. Superior temporal gyrus (STG) volume reduction is, in fact, one of the most consistent findings in schizophrenia when gray and white matter are evaluated separately (Shenton et al., 2001).

Structural abnormalities observed in MRI studies of schizophrenia have also ignited a renewed interest in post-mortem investigations. Here, numerous investigations have shown neuropathological abnormalities in schizophrenia such as reduced neuronal size, changes in neuronal or glial cell densities, aberrant clustering of neurons, fewer dendritic arborizations, and reduction of interneurons and their synaptic projections (Harrison, 1999; Harrison and Weinberger, 2005). Of note here, reduced neuropil and neuronal size, rather than a loss of neurons, has been proposed as one reason for decreased cortical volume in schizophrenia (Selemon and Goldman-Rakic, 1999). Additionally, there are a small number of studies that have investigated changes in dendritic spine density, neuronal cell volume, and axon terminal density in STG (Garey et al., 1998; Sweet et al., 2007; Sweet et al., 2003). Cytoarchitectural changes in STG, however, have not been as thoroughly investigated as MRI studies of STG, and thus while cytoarchitectural changes in STG are promising, they need to be investigating further to determine their importance with respect to the pathophysiology of schizophrenia.

Diffusion Tensor Imaging (DTI), a relatively new imaging technique, may, however, add to our understanding of STG abnormalities in schizophrenia. This method relies on the motion of water molecules to provide structural information about underlying cytoarchitectural changes, *in vivo* (e.g., Pierpaoli et al., 1996). Here, the structural environment of the brain influences water diffusion, such that the interaction of various tissue components, including cell membranes, macromolecules, myelin sheaths, and nerve fibers restrict the motion of water molecules. DTI is thus useful in evaluating the integrity of brain tissue where diffusion is anisotropic, or restricted in one direction less than in other directions (as in case of white matter, where water is restricted in directions that are parallel to the axons), as well as in tissues where diffusion is isotropic, or equally restricted in all directions (as in cerebrospinal fluid, and less so, for gray matter, where water is not restricted in mobility).

To date, white matter investigations using DTI have been applied to schizophrenia, where both changes in integrity of large white matter regions (Buchsbaum et al., 1998; Foong et al.,

2000), as well as in small, organized white matter structures (Burns et al., 2003; Hubl et al., 2004; Kubicki et al., 2003; Wang et al., 2004) have been detected.

Gray matter has received far less attention in DTI research. One reason for this is that diffusion in gray matter is much less anisotropic than in white matter, thus standard techniques used to analyze the principal direction of diffusion, or the degree of anisotropy, become less meaningful. However, very recent investigations demonstrate the utility of DTI for the analysis of gray matter regions in schizophrenia as well in multiple sclerosis and in other conditions (Kalus et al., 2005; Munoz Maniega et al., 2004; Oreja-Guevara et al., 2005). Moreover, measures such as diffusivity, a measure of diffusion in all directions, may be more meaningful in gray matter than measures of anisotropy, such as fractional anisotropy, since the latter is abetter indicator of anisotropic diffusion, which is an excellent measure of white matter integrity.

The current study investigates possible alterations in the structural integrity of STG gray and white matter in schizophrenia using quantitative analyses of the diffusion tensor, using both fractional anisotropy (FA), a measure of anisotropic diffusion, or the magnitude of the diffusion ascribed to FA, while mean diffusivity measures the average diffusion of water within tissues, in all directions. Thus altered tissue integrity may be reflected by either decreased FA or increased mean diffusivity. Accordingly, we will test the hypothesis that mean diffusivity is increased and fractional anisotropy is decreased in STG gray and white matter in schizophrenia. Additionally, correlations between DTI and clinical measures, including positive and negative symptoms, as well as demographic variables such as duration of illness, will be investigated in an exploratory manner, although we predict that auditory/language processing measures, particularly auditory hallucinations and formal thought disorder, will be associated with STG abnormalities."

2. Methods and Materials

2.1 Subjects

Twenty-one male patients with chronic schizophrenia were recruited from the Veteran's Administration (VA) Boston Healthcare System, Brockton, MA. In addition, 22 normal male subjects, group-matched to patients on age, handedness, and parental socioeconomic status, were recruited from the community. We note that while there was some overlap in the patients and controls between this study and two previous diffusion studies of uncinate fasciculus (UF; Kubicki et al., 2002) and cingulum bundle (CB; Kubicki et al., 2003), we decided not to include UF and CB data for comparison in the current study, since these earlier studies used slightly different methods of analysis and our main focus in the current study was on STG.

Inclusion criteria are described in a previous study (Hirayasu et al., 1998). Briefly, all subjects were right-handed, between 18-55 years, with no history of neurological illness, electroconvulsant therapy, and no substance dependence history over the last 5 years. Diagnoses were based on the Structured Clinical Interview for DSM-IV-TR (SCID) (First MB, 2001), in conjunction with a review of hospital course, and the patients' medical records. All of the patients had longer than 2 years of illness duration. The current study population overlaps with two previous studies, in that 33 and 34 patients in the current study were participants in two previous studies of uncinate fasciculus and cingulum bundle, respectively (Kubicki et al., 2002; Kubicki et al., 2003). The study was approved by the local IRB (VA Boston Healthcare System, Harvard Medical School and Partners Healthcare System), and subjects provided written informed consent prior to study participation.

2.2 Clinical and Cognitive Measurements

Socioeconomic status (SES) of subjects and of their parents was assessed using the Hollingshead two-factor index (Hollingshead, 1965). Handedness was evaluated using a modified Edinburgh inventory (Oldfield, 1971). Intelligence was measured using the Wechsler Adult Intelligence Scale (WAIS-III). The Scale for the Assessment of Positive Symptoms (SAPS) and the Scale for the Assessment of Negative Symptoms (SANS) were used to evaluate positive and negative symptoms in schizophrenia (Andreasen, 1984).

2.3 MRI Acquisition and Data Processing

2.3.1 Acquisition of structural MRI and segmentation—MR images were acquired using a 1.5-T GE scanner (GE Medical Systems, Milwaukee). The acquisition protocol included two MRI pulse sequences. The first resulted in contiguous spoiled gradient-recalled acquisition (SPGR) with the following parameters; TR=35 ms, TE=5 ms, FA 45 degree, FOV 24 cm^2, NEX=1.0, matrix=256×256 (192 phase-encoding steps). The voxel dimensions were 0.9375×0.9375×1.5mm. The second acquisition sequence produced an axial series of contiguous double-echo (proton density and T2-weighted) images (TR=3000 ms, TE=30 ms and 80 ms, 24 cm^2 field of view, interleaved acquisitions with 3.0mm slice thickness). The voxel dimensions were 0.9375×0.9375×3.0mm. This latter pulse sequence was used to measure the volume of total intracranial contents (ICC).

Gray and white matter of STG were segmented manually by one rater (T.Y.) who was blind to the diagnosis. Established procedures were used based on our previous report (Hirayasu et al., 2000). After delineating gray matter, the boundary of STG white matter was delineated by connecting a straight line between two open ends of the ROI of gray matter (See Figure 1). Three raters, blind to diagnosis, independently created the ROI on five subjects to test the inter-rater reliability (intraclass correlation coefficients for left and right STG were 0.988 and 0.987 for gray matter, 0.996 and 0.999 for white matter).

2.3.2 Diffusion Tensor Imaging—DTI data were acquired using line scan diffusion imaging (LSDI), a protocol implemented on conventional MR scanners (Maier et al., 1998). MR diffusion scans were performed on a 1.5 T GE scanner, which permits maximum gradient amplitudes of 40 mT/m. Coronal LSDI scans were acquired perpendicular to both the AC–PC line and interhemispheric fissure. For each line, six images with high (1000 sec/mm^2) diffusion-weighting along six non-collinear directions and two images with low (5 sec/mm^2) diffusion-weighting were collected. The following scan parameters were used: FOV 220×165mm^2; scan matrix 128×128 (image matrix 256×256); slice thickness 4mm; interslice distance 1mm; receiver bandwidth ± 4kHz; TE=64ms; effective TR=2592ms; scan time 60sec/slice. Mean diffusivity (Dm), and Fractional Anisotropy (FA) were calculated.

To calculate the mean regional Dm and FA in STG, ROI maps of the STG were transformed in the DTI space. For each subject, this transformation was estimated by registering the SPGR images to the B0 maps of the DTI using a mutual information rigid body coregistration algorithm (Wells et al., 1996). ROI maps of STG were then realigned and resampled to the B0 maps by applying the corresponding transformation matrix. To test the reliability of this coregistration method, measurements of Dm and FA in STG were repeated three times in five cases. The intraclass correlation coefficients were 0.984 (right gray matter), 0.988 (left gray matter), 0.999 (right white matter), 0.993 (left white matter) for Dm, and 0.947 (right gray matter), 0.998 (left gray matter), 0.990 (right white matter), 0.953 (left white matter) for FA.

Motion-related artifact maps (Maier et al., 1998) were also constructed and the number of lines missing in the raw LSDI data due to subjects' motion within the segmented ROI of STG was

calculated. There was no significant difference in the number of lines between groups. Nonetheless, all voxels within the missing lines were removed for further analyses.

2.4 Statistics

Two sample t-tests were used to compare demographic characteristics and WAIS-III IQ between groups. Repeated measures two-way ANOVA, with group as a between-subject factor and hemisphere (right, left) as a within-subject factor, was used to test for group differences in mean gray and white matter volumes, mean Dm, and mean FA in STG.

For correlation analyses between DTI measures and other measures, the presence of a normal distribution for each variable was first tested using both a Kolmogorov-Smirnov test and a Shapiro-Wilk test. Pearson's r was used as a correlation measure if the variable passed both tests, otherwise Spearman's rho was used. For correlation analyses between DTI and clinical measures, the sum of each item score of symptom types on the SAPS (Hallucinations, Delusions, Bizarre Behavior, and Positive Formal Thought Disorder) was used. For SAPS-Hallucinations score, we extracted three items (Auditory Hallucinations, Voices Commenting, and Voices Conversing) to create an additional score, SAPS-Auditory Hallucinations. As with the SAPS, the sum of each item score of symptom types on the SANS (Affective Flattening or Blunting, Alogia, Avolition-Apathy, Anhedonia-Asociality, Attention) was used for correlation analyses.

3 Results

3.1 Demographic data

There were no significant differences in age, handedness, or parental SES between groups. Patients diagnosed with schizophrenia showed lower SES, education level, and total IQ than controls. Mean age at onset and mean duration of illness were 21.5 years (SD; 4.40) and 17.9 years (SD; 9.05), respectively (see Table 1). All patients were receiving antipsychotic medication: 5 were taking typical antipsychotics, 15 atypical, and 1 both. Mean dose in chlorpromazine equivalence was 418.2 mg/d (SD; 307.9).

3.2 Relative volume of gray and white matter of STG

Relative STG gray matter volume in patients was decreased compared with normal controls, where a repeated measures two-way ANOVA showed a statistically significant main effect for group (F=6.801, df=1,41, p=0.013). Further post-hoc contrasts using Bonferroni correction (2-tailed) revealed significant differences in STG gray matter volume between groups for both left (F=6.362, df=1, p=0.016) and right (F=4.962, df=1, p=0.031) hemispheres. For relative STG white matter volume, there was no main effect of group observed (F=0.049, df=1,41, p=0.827) (see Table 2).

3.3 DTI Measures

Descriptive statistics for the DTI measures and results of the repeated-measures two-way ANOVA are summarized in Table 3. For STG gray matter, Dm was increased in patients compared with controls (F=12.447, df=1,41, p=0.001). There was no differences between groups for FA (F=1.407, df=1,41, p=0.242). Further post-hoc contrasts using Bonferroni correction (2-tailed) revealed significant differences in gray matter Dm between groups for left (F=7.772, df=1, p=0.008) and right (F=16.527, df=1, p<0.001) hemispheres. When group comparisons were repeated after controlling for possible confounding effects of volume, group differences in Dm for STG gray matter were still significant for left (F=4.073, df=1, p=0.050) and right (F=12.130, df=1, p=0.001) hemispheres. In addition, correlational analyses between

D*m* and relative volumes of STG gray matter showed no significance for either right or left hemisphere in either patients or controls.

For STG white matter, there was no main effect for group, for either D*m* (F=2.214, df=1,41, p=0.144) or FA (F=1.963, df=1,41, p=0.169). However, a significant group-by-hemisphere interaction was observed for D*m* (F=5.119, df=1,41, p=0.029). In post-hoc contrasts using Bonferonni correction (2-tailed), D*m* for left STG white matter was increased in patients compared to controls (F=4.789, df=1, p=0.034), while right hemisphere showed no significant difference (F=0.566, df=1, p=0.456). Group differences in D*m* for left STG white matter remained significant (F=4.783, df=1, p=0.035) after controlling for volume; there was no significant correlation between D*m* and relative volume for STG white matter.

3.4 Correlation Analyses between DTI measures and Clinical Measures

Duration of illness was positively correlated with D*m* for left and right STG gray matter (left, rho=0.728, p<0.001; right, rho=0.590, p<0.008). Furthermore, using partial correlation coefficients adjusted for age, these findings remained significant for left (r=0.549, p=0.015) and right (r=0.466, p=0.045) STG gray matter. Neither age at onset nor intelligence score were correlated with any of the DTI measures. In correlation analyses between DTI measures and SAPS scores, a positive correlation was observed between D*m* in left STG white matter and SAPS-Auditory Hallucination score (rho=0.465, p=0.039). Further analyses for each sub-item showed that D*m* in left STG white matter was positively correlated with "Voices Commenting" score (rho=0.542, p=0.017) and "Voices Conversing" score (rho=0.635, p=0.004; see Figure 2). Using Bonferonni correction for the 8 correlations, with statistical significance at p<0.0063, the "Voices Conversing" score remained statistically significant. In correlation analyses between DTI measures and SANS scores, increased D*m* in the left STG white matter was positively associated with high score of SANS-Attention score (rho=0.547, p=0.010). In further analyses for sub-items, Dm in left STG white matter was positively correlated with "Social Inattentiveness" score (rho=0.495, p=0.031) and "Global Rating of Attention" score (rho=0.519, p=0.019). None of the SANS score remained significant after Bonferonni correction for multiple correlations.

In correlation analyses between DTI measures in STG and chlorpromazine equivalent antipsychotics dose, increased D*m* was associated with a higher dose of antipsychotics use in left (r=0.502, p=0.028), but not in right gray matter (r=0.377, p=0.111). Neither D*m* in STG white matter nor FA in STG gray or white matter showed a significant correlation with antipsychotics dose.

4. Discussion

The most novel and intriguing findings of this study are the detection of increased D*m*, bilaterally, in STG *gray matter*, and increased D*m* in *left* STG *white matter*, in patients with schizophrenia, compared with healthy controls. In addition, mean diffusivity in left STG white matter showed significant correlations with auditory hallucinations, most particularly "voices conversing", in schizophrenia. This is the first study, to the best of our knowledge, to use DTI to investigate STG gray and white matter in patients with schizophrenia, a brain region that has figured prominently in volume studies of schizophrenia (see review in Shenton et al., 2001).

Diffusion Anisotropy in Gray Matter

In general, diffusion anisotropy in *gray matter* is much lower than in white matter because the cell membranes comprising neuronal processes are not orientated along a preferential direction. Therefore trace, or mean diffusivity, may be a more appropriate and sensitive indicator of gray

matter integrity than an anisotropy index such as fractional anisotropy. This is also why we included a measure of mean diffusivity (Dm) in this study, and it is also likely the main reason for the significant finding for Dm group differences, but the lack of significant FA group differences in STG gray matter in our study.

Since increased diffusivity in gray matter is likely largely the effect of increased unoccupied intercellular space, and since this increase is not due to a change in neuronal cell density, increased diffusivity in STG gray matter, while speculative, might be the result of reduced cortical neuropil, which includes axonal, dendritic, and glial processes (branchings) embedding neuronal cell bodies.

Changes in Neuropil in the Temporal Region

Of note here, although most investigations have generally focused on prefrontal regions, there are several studies that suggest changes in neuropil in the temporal region. One study reports reduced dendritic spine density in the temporal region, including BA 22 (Garey et al., 1998). There is also a series of investigations that report decreased pyramidal cell somal volume in BA41 and BA42, which the authors suggest likely the result of a reduction in dendritic arborization and hence reduced neuropil volume of dendrites and associated synaptic structures (Sweet et al., 2004; Sweet et al., 2003). Furthermore, Sweet and co-investigators have recently reported more direct evidence of reduced neuropil in their study, where the density of axon terminal was lower in patients with schizophrenia than in control subjects (Sweet et al., 2007).

Gray Matter and White Matter Volume in Schizophrenia

We also replicated previous findings of STG gray matter volume reduction in patients with schizophrenia. It is notable that there was no significant correlation between volumes and Dm in STG gray matter. In addition, group differences in Dm in STG gray matter was still significant after controlling for volume.

In contrast to STG gray matter, we failed to find differences in STG white matter volume between patients and control groups. This finding is consistent with at least one study in the literature which evaluated the volume of both STG gray and white matter and reported no volume differences in STG white matter (Hajek et al., 1997). We did, nonetheless, observe an increase of Dm in left STG white matter in patients with schizophrenia. This is of particular note because while white matter abnormalities have been demonstrated by decreases in anisotropy indices in major white matter tracts such as internal capsule, corpus callosum (Buchsbaum et al., 1998; Foong et al., 2000), and in small, organized white matter structures such as uncinate fasciculus, arcuate fasciculus or cingulum bundle (Burns et al., 2003; Hubl et al., 2004; Kubicki et al., 2003; Wang et al., 2004), abnormalities in STG *white matter* have not been specifically investigated. Our finding of increased diffusivity in left STG white matter could reflect loss of organization in white matter fiber tracts such as loss of myelin, axonal fibers, and/or increased extracellular space in this region. Moreover, Dm in STG white matter might be a more appropriate measure than an anisotropy index such as FA because this region is composed of multiple directional nerve fibers, and numerous fiber-crossings exist within this anatomically complicated white matter region.

Correlations between Dm in STG White Matter and Clinical and Cognitive Abnormalities

In correlation analyses, Dm in STG white matter, on the left, showed an association with auditory hallucinations. This finding is consistent with evidence for altered STG being associated with auditory hallucination in structural MRI (Barta et al., 1990; Gaser et al., 2004; Sumich et al., 2005), functional MRI (Dierks et al., 1999; Lennox et al., 2000), and electrophysiological studies (Youn et al., 2003). In addition, attentional impairment was

positively correlated with increased diffusivity in left STG white matter. Although this finding is consistent with the previous observation of decreased white matter volume in left temporal regions in patients with prominent negative symptoms (Sigmundsson et al., 2001), it is still not clear whether left STG white matter abnormalities are associated with negative symptoms because there are several studies using PET (Potkin et al., 2002; Thoma et al., 2005), that have shown correlations between negative symptoms and functional impairment in the right temporal lobe. Of further note, D*m* in STG gray matter showed a positive correlation with duration of illness, suggesting a possible progressive deterioration of STG tissue integrity. This is consistent with the finding of progressive volume reduction of STG in patients with schizophrenia (Kasai et al., 2003). Importantly, however, this can only be addressed by conducting a longitudinal study to provide direct evidence for progressive cytoarchitectural changes in schizophrenia.

Possible Limitations of the Study

Several methodological issues in this study need to be mentioned. First, because our study focused on males, generalizations can not be made to females as they have not been evaluated separately. Second, STG is not a unitary structure but is composed of several functionally distinctive subdivisions characterized by different cytoarchitectonic features (Sweet et al., 2005). A further study using higher resolution DTI data will be required for subregional analyses. Finally, all patients were medicated with antipsychotics, which might affect DTI measures. However, correlational analyses between DTI measures and dose of antipsychotics showed inconsistent results in that only D*m* in left STG gray matter showed a statistically significant correlation. There is a study by our group which reports no significant correlations between FA and medication (Kubicki et al., 2002), and another study which reports a positive correlation between FA and antipsychotic medication (Minami et al., 2003). Of further note, a recent study reported no difference in axon terminal density between haloperidol-treated and control monkeys (Sweet et al., 2007). Thus while our mean diffusivity finding for left STG gray matter is not likely attributable to antipsychotic medication, possible confounds with medication need to be considered.

Conclusions

In conclusion, our findings of increased diffusivity in STG gray and white matter provide evidence for alteration of structural integrity in this brain region in schizophrenia. Moreover, the finding of increased diffusivity in STG gray matter, while speculative, may reflect a reduction of neuropil in gray matter (e.g., similar reductions in neuropil in prefrontal cortex have been reported (Selemon and Goldman-Rakic, 1999)). Importantly, and less speculative with respect to our findings, significant correlations between mean diffusivity and auditory hallucination and attentional impairment in left STG white matter suggest the possibility of a disconnection among auditory/language processing regions in schizophrenia.

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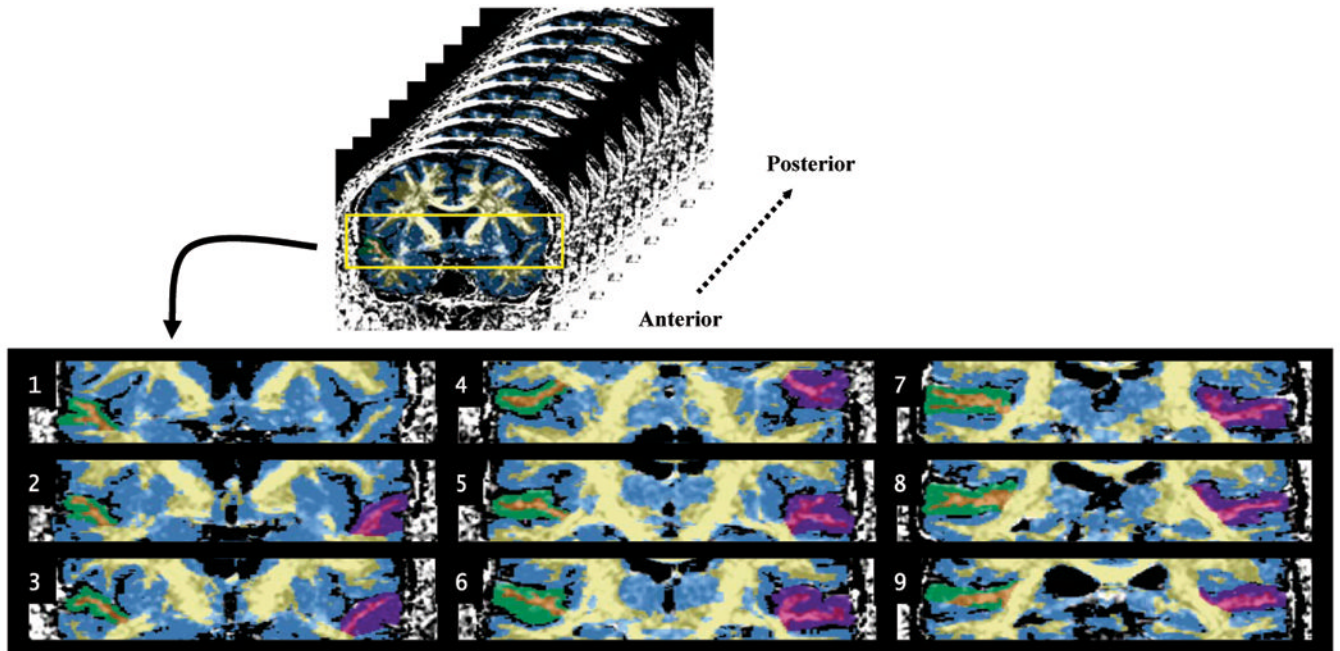
Figure 1.
ROI maps of superior temporal gyrus superimposed on fractional anisotropy maps in one normal comparison subject. The most anterior part of superior temporal gyrus begins at slice 1 and ends at slice 9. Fractional anisotropy in each voxel was calculated and scaled from 0 to 1. Segmented regions of interest are shown in different colors (right gray: green, right white: brown, left gray: purple, left white: pink). Note also the result of whole brain segmentation by expectation-maximization algorithm (gray matter: blue, white matter: light yellow).
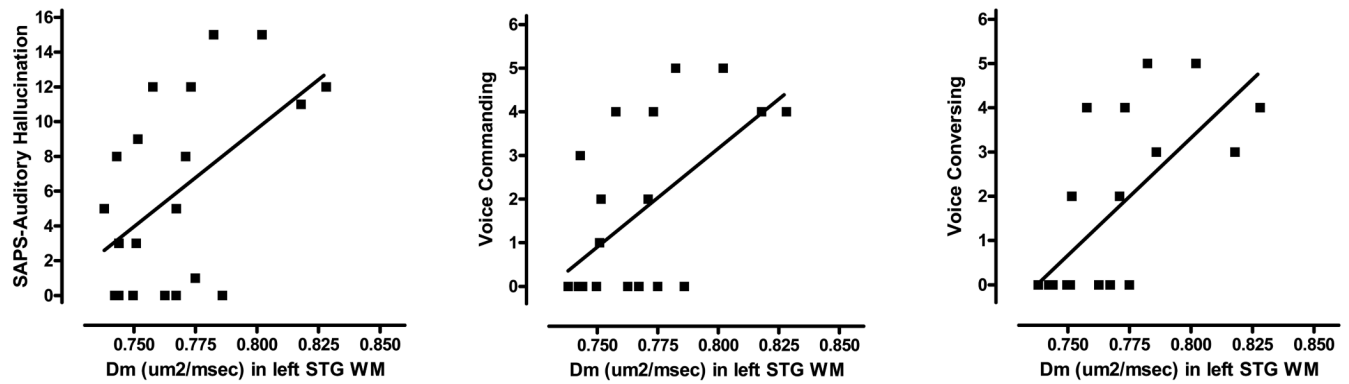
Figure 2.
Scatter plots for correlations between attention scores on SANS and mean diffusivity of left STG white matter in patients with schizophrenia (n=21): (a) SANS-Attention (rho=0.547, p=0.010); (b) "Social Inattentiveness" score (rho=0.495, p=0.031); (c) "Global Rating of Attention" (rho=0.519, p=0.019).

Table 1

Demographic characteristics for patients with chronic schizophrenia (SZ) and normal comparison (NC) subjects

	SZ (n=21)	NC (n=22)	Two sample t-test (2-tailed)		
			t	df	p
Age (yr)	**40.3 ± 8.61** (41)	40.4 ± 9.00 (41)	0.011	41	0.991
Socioeconomic status (SES) [*]	4.05 ± 1.24 (5)	2.35 ± 1.09 (2)	-4.639[++]	41	**<0.001**
Parental SES [*]	2.63 ± 1.21 (3)	2.91 ± 1.37 (2)	0.680	41	0.501
Education (yr)	12.3 ± 1.91 (12)	15.4 ± 1.84 (16)	5.207[++]	41	**<0.001**
Handedness	0.78 ± 0.24 (0.87)	0.82 ± 0.16 (0.87)	0.648	41	0.520
WAIS-III IQ	89.5 ± 11.02 (90)	110.6 ± 14.17 (109)	5.115[++]	41	**<0.001**
Duration of illness	17.85 ± 9.04 (21)	-	-	-	
Age at onset	21.48 ± 4.40 (21)	-	-	-	

Mean ± S.D (Median)

[++] p<0.01

[*] Higher numbers represent lower SES.

WAIS-III IQ, Intelligence Quotient by the third edition of the Wechsler Adult Intelligence Scale

Table 2

Superior temporal gyrus relative gray and white matter volumes in patients with schizophrenia and normal comparison subjects

RV (%) of superior temporal gyrus[*]	SZ subjects (n=21)		NC subjects (n=22)		main effect of group		group × hemisphere	
	Mean	SD	Mean	SD	F(1,41)	P	F(1,41)	P
Gray matter								
Right	0.644	0.075	0.696	0.077	6.801[+]	0.013	0.070	0.793
Left	0.575	0.079	0.632	0.069				
White matter								
Right	0.337	0.046	0.337	0.047	0.049	0.827	0.094	0.761
Left	0.306	0.029	0.302	0.042				

Repeated measures two-way ANOVA with group as a between-subject factor and hemisphere (right, left) as a within-subject factor.

[*] Relative volume (RV) = [absolute volume] / [volume of intracranial contents] × 100

[+] $p<0.05$

Table 3

DTI measurements in superior temporal gyrus in patients with chronic schizophrenia and normal comparison subjects

DTI measures	SZ subjects (n=21)		NC subjects (n=22)		main effect of group		group × hemisphere	
	Mean	SD	Mean	SD	$F_{(1,41)}$	p	$F_{(1,41)}$	P
Gray matter								
Dm (μm^2/msec)								
Right	0.886	0.042	0.841	0.030	12.447[++]	0.001	0.113	0.738
Left	0.909	0.064	0.859	0.051				
FA								
Right	0.232	0.016	0.240	0.028	1.407	0.242	0.054	0.818
Left	0.228	0.016	0.235	0.025				
White matter								
Dm (μm^2/msec)								
Right	0.750	0.028	0.744	0.026	2.214	0.144	5.119[+]	0.029
Left	0.767	0.025	0.751	0.023				
FA								
Right	0.351	0.029	0.357	0.028	1.963	0.169	1.405	0.243
Left	0.336	0.027	0.351	0.025				

Repeated measures two-way ANOVA with group as a between-subject factor and hemisphere (right, left) as a within-subject factor.

[+] p<0.05,

[++] p<0.01