

Original Article

Reduced white matter integrity associated with cognitive deficits in patients with drug-naive first-episode schizophrenia revealed by diffusion tensor imaging

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Abstract: Patients with schizophrenia have shown widespread white matter microstructural abnormalities and cognitive deficits, but the definitive relationship between white matter and cognitive performance remains unclear. In this study, we investigated the possible associations between white matter integrity and cognitive deficits in drug-naive first-episode schizophrenia (dn-FES) using diffusion tensor imaging (DTI). A total of 96 participants, including 46 dn-FES patients and 50 healthy individuals, underwent 3.0 T magnetic resonance diffusion-weighted imaging and cognitive assessments using the Chinese version of the Measurement and Treatment Research to Improve Cognition in Schizophrenia (MATRICS) Consensus Cognitive Battery (MCCB). Group differences were tested using tract-based spatial statistics (TBSS). Compared with the control group, the dn-FES group exhibited reduced white matter integrity, as indexed using fractional anisotropy (FA) metrics, in the right-hemispheric cluster comprising the posterior thalamic radiation, posterior corona radiata, superior longitudinal fasciculus, retrolenticular part of the internal capsule, tapetum, splenium of the corpus callosum, sagittal stratum, and inferior longitudinal fasciculus. We found that social cognitive deficit is significantly correlated with reduced FA in these white matter regions, except the sagittal stratum and inferior longitudinal fasciculus. Furthermore, we found that speed of processing is positively correlated with reduced FA in the right superior longitudinal fasciculus of dn-FES patients. In summary, white matter deficits were validated in dn-FES patients and could be associated with speed of processing and social cognition, providing clues about a neural basis of schizophrenia and a potential biomarker for clinical studies.

Keywords: Diffusion tensor imaging, fractional anisotropy, first episode schizophrenia, cognition, MATRICS consensus cognitive battery

Introduction

Schizophrenia is a complex, serious, and disabling mental disorder characterized by a broad array of symptoms including positive symptoms, negative symptoms, and cognitive deficits. The disconnection hypothesis recognizes schizophrenia as a disconnection illness caused by white matter tracts between multiple brain areas [1-5]. The white matter microstructure can be quantitatively assessed by diffusion tensor imaging (DTI) in vivo [6]. Currently, the most widely applied scalar measure is fractional anisotropy (FA) [7, 8]. Recently, the field has largely focused on cerebral white matter connections in patients with schizophrenia [9-

11]. These studies have revealed lower FA in the corpus callosum, thalamic radiation, corona radiata, longitudinal fasciculi, and other areas, as well as higher FA in the arcuate fasciculus [12, 13] and caudate [14]. However, consensual white matter alterations have not yet been identified due to the heterogeneity in the anatomical scope of FA reduction reported across studies [15-18]. Sources of heterogeneity among these studies may be attributed to variations in medications, duration of illness, study samples, and other variable factors [19].

Cognitive deficits are a core symptom of schizophrenia [20, 21] and have a substantial influence on patients' psychosocial life. Assessed

using the MATRICS Consensus Cognitive Battery (MCCB) [22], cognitive deficits have emerged as important targets of treatment-oriented research. Cumulative evidence has shown that patients with schizophrenia experience cognitive decline from before to after illness onset [23]. Recently, several studies have shown that white matter abnormalities are linked to cognitive performance [24-27]. However, these studies had small sample sizes or included only male patients, and their results were unclear. Further, only a limited number of studies have investigated the association between FA values and cognitive performance with all seven cognitive domains of the MCCB in the drug-naïve patients with first-episode schizophrenia. Recently, one study [25] used whole-brain tract-based spatial statistics (TBSS) [28] and the MCCB to reveal that mean FA values in the left superior longitudinal fasciculus show positive correlations with working memory and visual learning. However, the study found no significant correlation between FA alteration and the other cognitive domains: attention, speed of processing, verbal learning, reasoning/problem solving, and social cognition.

In the present study, we used the MCCB to assess cognition and TBSS to investigate white matter integrity in drug-naïve first-episode schizophrenia (dn-FES) patients in order to address the variations in medications and minimize illness chronicity. Following the disconnection hypothesis [2], we expected widespread subtle white matter abnormalities characterized by lower FA in dn-FES patients than in healthy participants. In addition, we explored correlations between FA values and both cognitive performance and the five-factor model of the Positive and Negative Syndrome Scale (PANSS) [29]. We hypothesized that aberrant white matter fiber integrity is associated with levels of cognitive performance and clinical psychotic symptoms in patients with schizophrenia.

Materials and methods

Participants

Fifty-five never-medicated Chinese patients were recruited from the inpatient department or outpatient clinic of the Affiliated Brain Hospital of Nanjing Medical University, Jiangsu,

China, from September 2015 to December 2019 (**Table 1**). They were diagnosed using the Diagnostic and Statistical Manual of Mental Disorders (DSM)-5 patient edition and determined to meet the criteria for schizophrenia according to two senior psychiatrists. Inclusion criteria for patients were as follows: Han ethnicity, right-handedness, age between 16 and 45, first episode illness, duration of untreated psychosis ≤ 24 months, and IQ greater than 70. Exclusion criteria included any diagnosis of physical or neurological illness, pregnancy, head injury, substance dependence, or contraindications for magnetic resonance imaging (MRI) scanning. Fifty-five healthy participants (control group) were recruited from the local area and matched with patients by age and gender (**Table 1**). Inclusion criteria for healthy participants were as follows: Han ethnicity, right-handedness, age between 16 and 45, no personal or family history of psychiatric or other inherited illness. Exclusion criteria were the same for healthy controls as those for the patients. After quality control procedures, 9 patients and 5 healthy participants were excluded, so the final analysis included 46 patients and 50 health participants.

The study was approved by the Medical Research Ethics Committee of the Affiliated Brain Hospital of Nanjing Medical University. All patients and healthy participants provided written informed consent before study participation. For those younger than 18, consent was provided by their parent or guardian.

Psychopathological assessment in patients

At both time points, psychiatric symptoms were assessed using the PANSS [30]. The five-factor model [31] was used, dividing the PANSS in the positive factor, negative factor, excited factor, disorganized factor, and depressed factor.

Intelligence quotient and cognitive assessment

The intelligence quotient (IQ) was estimated using the Chinese version of the Wechsler Adult Intelligence Scale-Revised, which includes the common sense, similarity, and picture completion tests, and block design subtests. Cognition was assessed with the Chinese version of the MCCB [32]. The MCCB provided the overall composite score and seven domains including speed of processing, attention/vigi-

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Table 1. Demographic, cognitive and clinical characteristics of all subjects

	dn-FES (n = 46)	HC (n = 50)	statistic	
	Mean ± S.D.	Mean ± S.D.	t/t'/X ²	p
Age (years)	24.20 ± 7.85	26.06 ± 7.40	t = -1.198	0.234
Gender (male/female)	32/14	26/24	X ² = 3.09	0.079
Handedness (right/left)	46/0	50/0		
Years of education	12.35 ± 2.51	14.5 ± 3.12	t = -3.703	0.000
DUP (months)	9.67 ± 7.14	NA		
WAIS (IQ)	102.76 ± 11.96	115.22 ± 8.70	t = -5.868	0.000
MCCB T-scores				
Speed of processing	35.63 ± 12.09	51.12 ± 8.62	t' = -7.171	0.000
Attention/vigilance	36.91 ± 10.13	46.24 ± 6.21	t' = -5.386	0.000
Working memory	33.17 ± 10.64	44.32 ± 6.67	t' = -6.087	0.000
Verbal learning	36.02 ± 11.15	45.24 ± 10.61	t = -4.150	0.000
Visual learning	40.33 ± 12.89	49.78 ± 8.44	t' = -4.212	0.000
Reasoning/problem solving	44.65 ± 11.69	52.52 ± 7.32	t' = -3.914	0.000
Social cognition	32.50 ± 9.71	37.90 ± 9.28	t = -2.785	0.006
MCCB overall composite	28.93 ± 13.06	44.72 ± 7.94	t' = -7.081	0.000
PANSS subscale score				
Positive factor	16.20 ± 2.87	NA		
Negative factor	18.04 ± 2.98	NA		
Excited factor	10.57 ± 2.18	NA		
Depressed factor	7.46 ± 2.04	NA		
Disorganized factor	8.13 ± 2.21	NA		

Abbreviations: dn-FES: drug-naïve first-episode schizophrenia; HC: healthy control; DUP: duration of untreated psychosis; WAIS: Wechsler Adult Intelligence Scale; IQ: intelligence quotient; MCCB: the MATRICS Consensus Cognitive Battery; PANSS: Positive and Negative Syndrome Scale; NA: not applicable.

lance, working memory, verbal learning, visual learning, reasoning/problem solving, and social cognition [33]. The seven cognitive domain T-scores were corrected by age, gender, and years of education in the software and were matched with the MCCB.

MRI acquisition

All participants were asked to remain motionless and keep their eyes closed during scanning in a 3.0 T Siemens Verio magnetic resonance imaging scanner (Erlangen, Germany). Diffusion-weighted volumes were acquired using a pulsed gradient, echo planar imaging sequence: repetition time/echo time, 7900/97 ms; field of view, 23 × 23 cm²; matrix size, 122 × 122; voxel size, 1.9 × 1.9 × 2.3 mm³; slice thickness, 2.3 mm; 55 axial slices, no gap. Sixty-four diffusion weighted images (b-value = 1000 s/mm²) and one image with b = 0 (b0 image) were acquired. The total time of the diffusion tensor imaging sequence was approximately 9 minutes.

Data processing

The imaging data was processed using TBSS analysis in FMRIB Software Library 5.0.9 (FSL, <http://www.fmrib.ox.ac.uk/fsl>) [28]. First, the DICOM files were transformed into compressed NIFTI format using dcm2nii in FSL. Next, it was corrected for eddy currents and head motion using the linear image registration tool (FLIRT v6.0) in FSL [34]. Then, the b0 image was skull stripped using the brain extraction tool (BET v2.1), and a brain mask was acquired. Finally, the FA images were generated through reconstruct diffusion tensors using FMRIB's diffusion toolbox (FDT 3.0) in FSL. All above processing steps were the preprocessing stages.

For the next step, each FA image was aligned to 1 × 1 × 1 mm FMRIB58_FA standard space using FMRIB's nonlinear image registration tool (FNIRT). The mean FA image and the mean FA skeleton were then created by averaging all the registered FA images. Next, the threshold was set at 0.2 to remove peripheral brain

areas, followed by creation of a 4D file of all skeletonized images and a mean FA skeleton mask. Finally, all FA skeletonized images and the mean FA skeleton mask were inputted into voxel-wise statistical analyses.

Data analysis

Demographic, IQ, and cognitive characteristics were compared between patients and healthy participants using the chi-square and independent sample *t*-tests in the Statistical Package for the Social Sciences version (SPSS v.25.0). If the variance was not homogeneous, the *t'*-tests were used. The significant differences of FA data between the patient and control groups were detected by voxel-wise statistical analysis using randomize v2.9 in FSL. In the final statistical model, nonparametric permutation-based tests were applied with 5000 permutations, using age, gender, and years of education as covariates. The threshold for statistical significance was set at $P < 0.05$ with threshold-free cluster enhancement [35] and family-wise error correction for multiple comparisons using the null distribution of the maximal voxel-wise test statistic. The Johns Hopkins University (JHU) International Consortium for Brain Mapping DTI-81 white matter labels [36] were used to assign the white matter tract name with significant group differences; if the voxels did not match the labels, the JHU white matter tractography atlas was used to localize [28]. The mean FA value was extracted within each cluster mask with significant group differences. Pearson correlation analysis was used to further explore the correlation between the mean FA value of each cluster and both cognitive performance and clinical psychotic symptoms in the SPSS software.

Results

Demographic, cognitive, and clinical characteristics

No significant group differences in age, gender, and handedness were found between patients with schizophrenia and healthy participants. However, years of education was lower in the patient group than in the control group. The cognitive domain T-scores are shown in **Table 1**. The dn-FES group had significantly lower scores in all seven cognitive domains than the control group. This was particularly true in two

domains: speed of processing and working memory; the least impaired domain was social cognition (**Table 1; Figure 1**).

Group differences in FA values

As shown in **Figure 2**, the patient group showed significantly lower FA than the control group, distributed over the posterior thalamic radiation, posterior corona radiata, superior longitudinal fasciculus, retrolenticular part of the internal capsule, tapetum, and splenium of corpus callosum of the right hemisphere (Cluster 6, **Table 2**). In addition, the dn-FES group exhibited lower FA in the right sagittal stratum (Cluster 5, **Table 2**), right superior longitudinal fasciculus (Cluster 4, **Table 2**), and right inferior longitudinal fasciculus (Cluster 3, **Table 2**). Lower FA values were also observed in splenium of corpus callosum, the posterior thalamic radiation, the posterior corona radiata (Cluster 2, **Table 2**) and the superior longitudinal fasciculus (Cluster 1, **Table 2**) of the right hemisphere. No significant cluster of FA was higher in patients than in healthy participants.

Correlation of FA values with cognitive domain scores and the PANSS subscale score

We calculated mean FA values within the clusters with significant group differences in FA. In the patient group, mean FA values within Cluster 6 (**Figure 3B**)-which consisted of the right posterior thalamic radiation, right posterior corona radiata, right superior longitudinal fasciculus, right retrolenticular part of the internal capsule, right tapetum, and splenium of the corpus callosum-were positively correlated with social cognition scores ($r = 0.309$, $P = 0.037$) (**Figure 3A**). In addition, mean FA values in Cluster 1 (**Figures 4B and 5B**), which consisted of the right superior longitudinal fasciculus, showed positive correlations with social cognition scores ($r = 0.355$, $p = 0.015$) and speed of processing ($r = 0.352$, $P = 0.016$) (**Figures 4A, 5A**). No significant correlations were found between FA values and the PANSS subscale score in the patient group. In addition, correlation analyses revealed there were no significant associations between the mean FA values and cognitive domain scores in the control group.

Discussion

In the present study, we used both a TBSS approach and the MCCB to explore the cogni-

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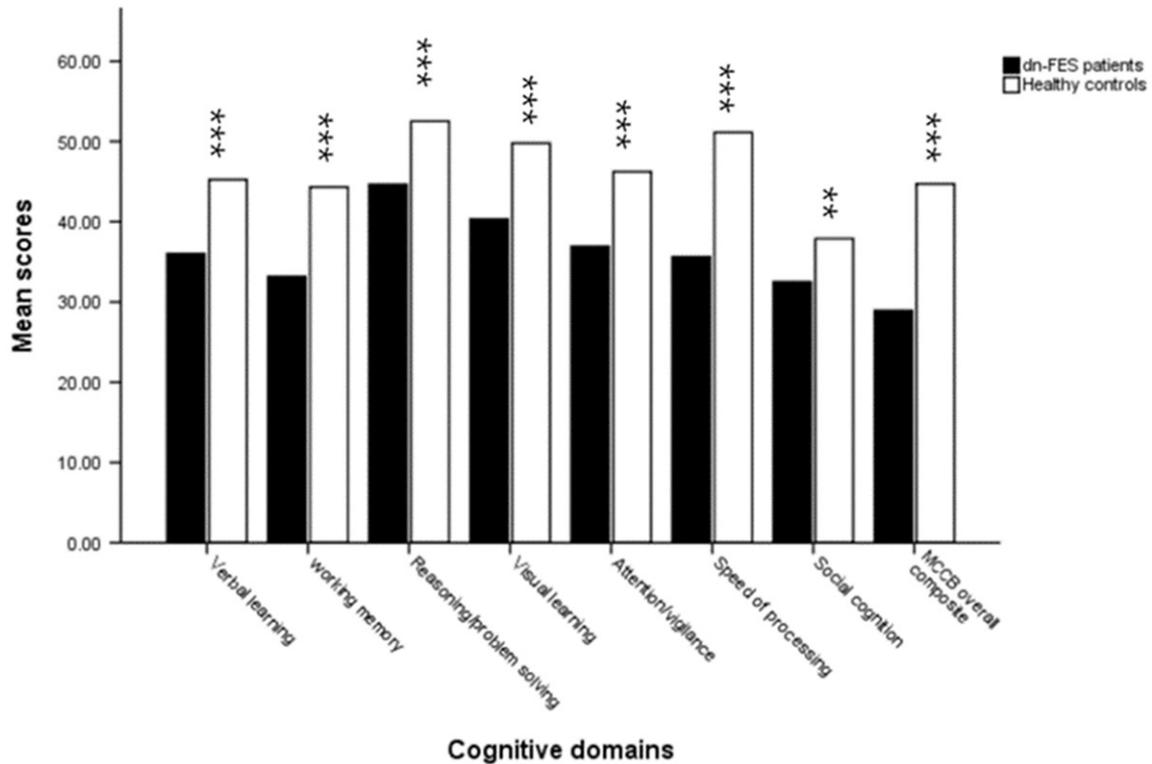


Figure 1. Seven cognitive domain scores in dn-FES patient group and healthy control group. Compared to healthy control group, the dn-FES patient group had significantly lower scores in all seven cognitive domains, particularly in two domains: speed of processing and working memory, while the least impairment domain was social cognition. ** $P < 0.01$ compared with healthy controls at the same cognitive domain. *** $P < 0.001$ compared with healthy controls at the same cognitive domain.

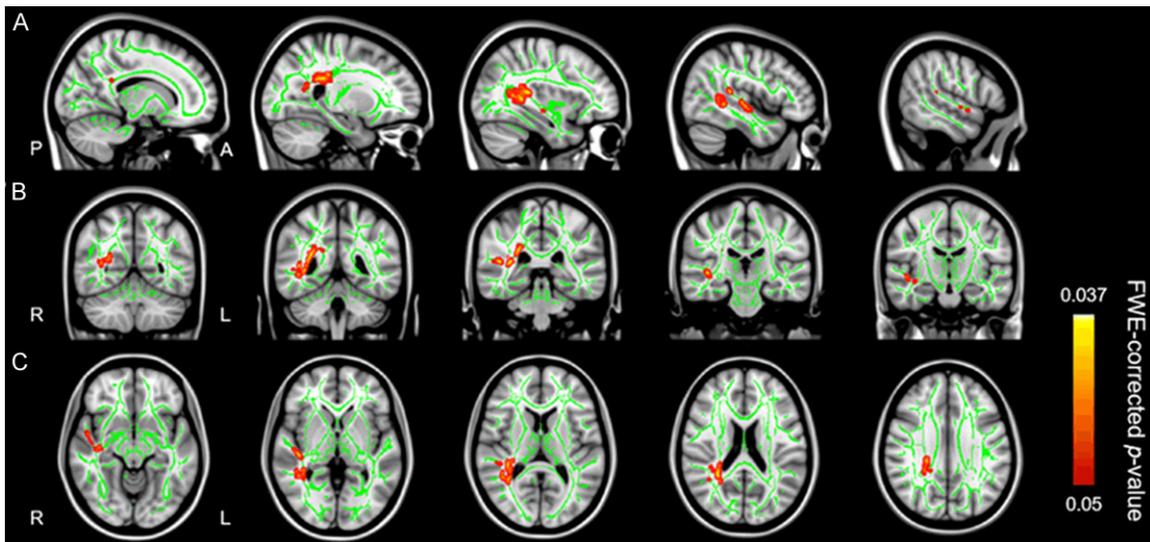


Figure 2. TBSS results in dn-FES patient group and healthy control group. The patient group showed significantly lower FA than the control group, distributed over the posterior thalamic radiation, posterior corona radiata, superior longitudinal fasciculus, retrolenticular part of the internal capsule, tapetum, sagittal stratum, the inferior longitudinal fasciculus and splenium of corpus callosum of the right hemisphere. No significant cluster of FA was higher in patients than in healthy participants. The green color shows the mean FA skeleton, the color scale red to yellow which expand by `tbss_fill` indicates significant FA reduction. Results are overlaid on (A) (sagittal slice, $X = 15, 25, 35, 45, 55$), (B) (coronal slice, $Y = -55, -45, -35, -25, -15$) and (C) (axial slices, $Z = -10, 0, 10, 20, 30$) from the Montreal Neurological Institute standard brain at a permutation-based threshold of $P < 0.05$ (FEW-corrected).

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Table 2. FA differences between 46 dn-FES patients and 50 healthy controls

Cluster Index	Cluster voxels	p	MNI coordinates of peak voxel			Side	Anatomical region
			X	Y	Z		
6	852	0.037	32	-48	17	Right	Posterior thalamic radiation Posterior corona radiata Superior longitudinal fasciculus Retrolenticular part of internal capsule Tapetum Splenium of corpus callosum
5	236	0.046	42	-23	-3	Right	Sagittal stratum
4	54	0.046	46	-35	14	Right	Superior longitudinal fasciculus
3	45	0.048	52	-2	-9	Right	inferior longitudinal fasciculus
2	44	0.049	28	-59	14	Right	Splenium of corpus callosum Posterior thalamic radiation Posterior corona radiata
1	37	0.049	43	-43	4	Right	Superior longitudinal fasciculus

Abbreviation: MNI: Montreal Neurological Institute. Notes: No regions of increased FA were found in patients vs control participants.

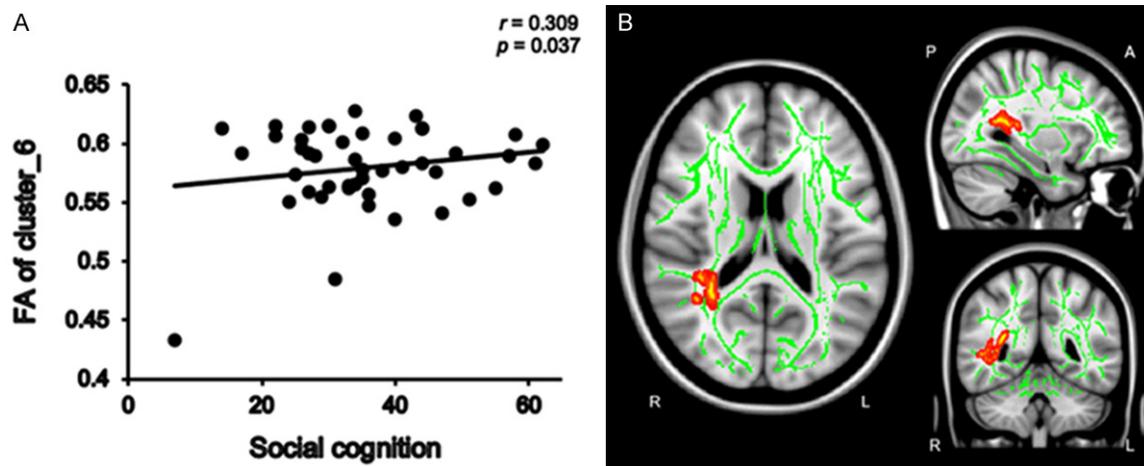


Figure 3. The positive correlation between social cognition and mean FA values within cluster 6 in dn-FES patient group. Mean FA values within Cluster 6 were positively correlated with social cognition scores ($r = 0.309$, $P = 0.037$) in the patient group (A). The green color shows the mean FA skeleton, the color scale red to yellow which expand by *tbss_fill* indicates cluster 6 (B), which consisted of the right posterior thalamic radiation, right posterior corona radiata, right superior longitudinal fasciculus, right retrolenticular part of the internal capsule, right tapetum, and splenium of the corpus callosum.

tive changes and the whole-brain white matter integrity alteration in dn-FES patients. We found that patients had significantly more cognitive deficits and lower FA than healthy participants. Furthermore, we identified significant correlations between cognitive domain scores and FA values in regions showing reduced white matter integrity in patients. Our findings revealed that social cognitive score is positively correlated with FA values in the posterior tha-

lamic radiation, posterior corona radiata, superior longitudinal fasciculus, retrolenticular part of the internal capsule, tapetum of the right hemisphere, and splenium of the corpus callosum. The aberrant white matter integrity of right superior longitudinal fasciculus may be a potential neural basis of cognitive impairment in schizophrenia as evidenced by significant associations between its FA values and processing speed in our sample. However, no sig-

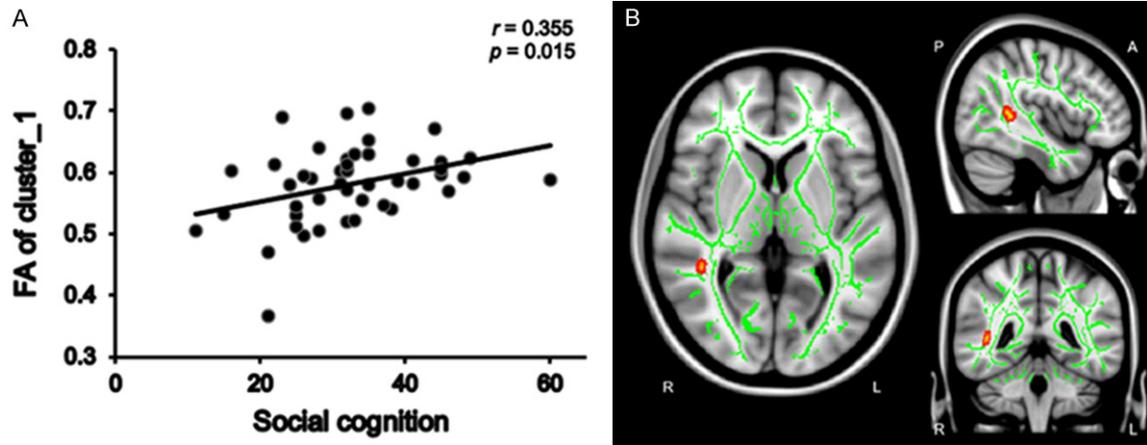


Figure 4. The positive correlation between social cognition and mean FA values within cluster 1 in dn-FES patient group. The mean FA values within cluster 1 were positively correlated with social cognition ($r = 0.355$, $P = 0.015$) in the patient group (A). The green color shows the mean FA skeleton, the color scale red to yellow which expand by *tbss_fill* indicates the right superior longitudinal fasciculus of cluster 1 (B).

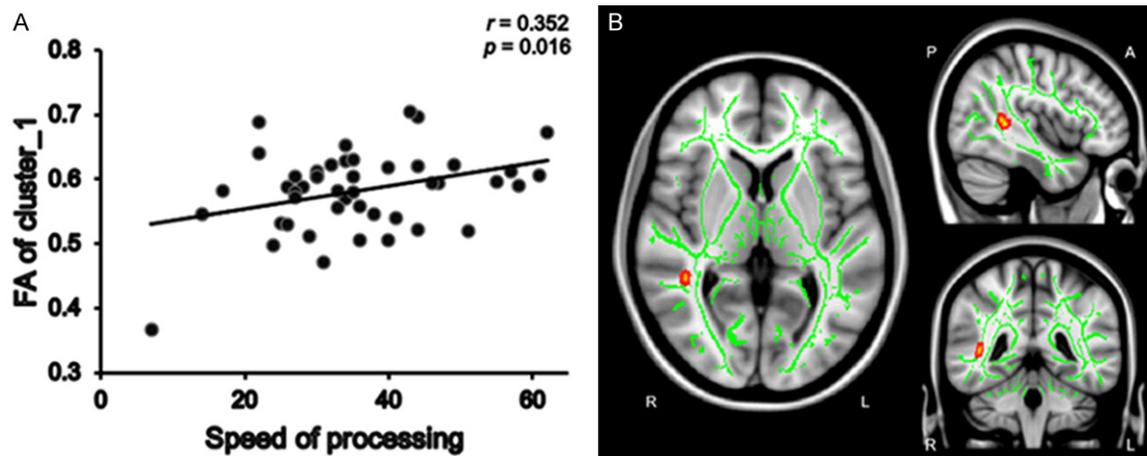


Figure 5. The positive correlation between speed of processing and mean FA values within cluster 1 in dn-FES patient group. The mean FA values within cluster 1 were positively correlated with speed of processing ($r = 0.352$, $P = 0.016$) in patient group (A). The green color shows the mean FA skeleton, the color scale red to yellow which expand by *tbss_fill* indicates the right superior longitudinal fasciculus of cluster 1 (B).

nificant correlations were found between FA values and the PANSS subscale score in patients with schizophrenia in our study.

Cognitive deficits have been identified as a core feature of schizophrenia [21, 37]. A meta-analysis found that schizophrenia has cognitive impairments, including speed of processing, working memory, verbal learning, reasoning/problem solving, visual learning, attention/vigilance, and social cognition, particularly in speed of processing and attention/vigilance [33]. Our study used the same instrument to demonstrate that dn-FES patients show severe and widespread cognitive deficits in all domains, particularly in speed of processing

and working memory, with the least impairment shown in social cognition. However, we found that working memory, not attention/vigilance, was significantly lower in patients than in healthy participants. Similar to our study, one study found that cognitive deficits are present at the onset of schizophrenia but that the speed of processing and executive functions remain stable after ten years [38]. These concordant results may support that a subgroup of patients with schizophrenia would benefit from cognitive remediation.

Patients showed a significantly lower FA in the posterior thalamic radiation, posterior corona radiata, superior longitudinal fasciculus, retro-

lenticular part of the internal capsule, tapetum, sagittal stratum, and inferior longitudinal fasciculus of the right hemisphere, as well as the splenium of the corpus callosum. The results were largely consistent with previous DTI studies [9, 15, 39, 40]. These findings support the disconnection hypothesis as the primary pathophysiology of schizophrenia, indicating disrupted white matter integrity between these brain areas are present even at the onset of schizophrenia. One study [15] evaluated DTI data from 1963 patients with schizophrenia and 2359 healthy participants and found that FA is lower globally across the whole-brain white matter skeleton; specifically, the anterior corona radiata, body, and genu of the corpus callosum showed the greatest effects. However, in our results, we found reduced FA across the posterior corona radiata and a portion of the splenium of the corpus callosum. To date, the most consistent research findings in the schizophrenia have included aberrant interhemispheric connectivity [15, 41], and this was also demonstrated in our study. Notably, white matter changes are almost always observed in the right hemisphere; for example, one study also found more extensive disruption in the right hemisphere [42]. Although it is difficult to interpret, these results may suggest that a pathological disruption of white matter integrity in the right hemisphere is typical for first-episode schizophrenia.

Increasingly, studies have shown cognitive deficits are associated with white matter integrity, suggesting that disruption of white matter integrity leads to cognitive dysfunction [25, 27, 43, 44]. One study found that deficits in working memory and visual learning are correlated with lower FA in the left longitudinal fasciculus [25]. However, we found that deficits in speed of processing is correlated with reduced FA value in the right superior longitudinal fasciculus. The precise functions of the superior longitudinal fasciculus are not fully understood. The superior longitudinal fasciculus is a major associative connection between the superior parietal, angular gyrus, and temporal and ipsilateral frontal lobes [45]. Recent findings [25, 43] have indicated that the superior longitudinal fasciculus mediates the transmission of neurotransmitters, such as glutamate, the most common excitatory neurotransmitter [46], and may explain the lower speed of processing in

schizophrenia patients. In addition, a new finding demonstrated that the interaction between glucose and FA in the longitudinal fasciculus is associated with the Trail Making Test Part A, which is part of speed of processing [47]. The relationship between the reduced FA in the longitudinal fasciculus and speed of processing may provide a biomarker for clinical studies of schizophrenia.

We also found that deficits in social cognition are associated with lower FA values in the posterior thalamic radiation, posterior corona radiata, superior longitudinal fasciculus, retrolenticular part of the internal capsule, and tapetum of the right hemisphere, as well as the splenium of the corpus callosum. The correlation between social cognition impairment and white matter integrity is similar to the findings of a previous study [48]. In addition, another recent study found that social cognition impairment is related to white matter disarray of the splenium, corpus callosum, forceps major, and inferior longitudinal fasciculus [9]. These fiber tracts could be partially included in the revised face perception circuitry, which is composed of the temporo-occipital regions and the frontal-limbic system [49]. Furthermore, Andreasen demonstrated the connection between the thalamus and the frontal cortex plays a vital role in social cognition in schizophrenia [50, 51]. Therefore, it is plausible that the posterior thalamic radiation, posterior corona radiata, and superior longitudinal fasciculus (including the connection between the temporo-occipital region, frontal cortex, and thalamus) may be associated with social function in patients with schizophrenia. Another study [52] reported that motor dexterity is related to FA in the left frontal lobe, including the forceps minor, inferior fronto-occipital fasciculus, and anterior thalamic radiation. In addition, executive function impairment was associated with reduced FA values in the left and right anterior thalamic radiation, forceps minor, inferior fronto-occipital fasciculus, and left superior and inferior longitudinal fasciculus. However, we failed to find significant correlation between the aberrant white matter integrity and attention/vigilance, verbal learning, visual learning, reasoning, and problem solving or working memory in patients and controls. This may be because FA can be affected by multiple pathological processes, potentially leading to negative results.

Recently, some cross-sectional studies examining the relationship between the integrity of white matter and clinical variables in schizophrenia have had inconsistent findings. One study reported that negative symptoms are negatively correlated with FA values in the forceps major, left superior longitudinal fasciculus, anterior thalamic radiation, and inferior fronto-occipital fasciculus [25]. Nevertheless, other studies reported that positive symptoms are negatively correlated with FA values in the left superior longitudinal fasciculus [53] but positively correlated with FA values in the left fronto-occipital fasciculus and left inferior longitudinal fasciculus [54]. Interestingly, a recent study reported that PANSS positive factor was negatively associated with reduced FA in the left inferior fronto-occipital fasciculus, inferior longitudinal fasciculus, and forceps major; moreover, PANSS negative factor was negatively related to FA in the left inferior longitudinal fasciculus [9]. Nevertheless, some studies failed to find correlations between the FA value with clinical symptoms [43, 55-57]. We also failed to detect the correlation between reduced FA and positive factor, negative factor, excited factor, disorganized factor, or depressed factor in dn-FES patients. This may be because our study was of short duration and included dn-FES patients with mild to moderate symptoms and small variances in PANSS scores, potentially leading to negative results in correlational analyses between FA and the severity of clinical symptoms. In addition, the size of the sample and the heterogeneity of the patients' characteristics may have also led to discrepancies.

Our study has some limitations. First, the years of education were not matched in the patient and control groups. However, the MCCB subtest scores were corrected by years of education so that the variable could be compared at the same level. Second, the cross-sectional study design had a limited capacity to demonstrate direct causal relationship between white matter deficits and cognitive deficits in patients with schizophrenia. Third, the size of the sample was relatively small. Ultimately, a longitudinal study with a larger sample size is warranted to reveal the relationship between white matter deficits and cognitive deficits in schizophrenia.

In conclusion, this study showed not only robust and widespread white matter changes

across multiple regions but also cognitive deficits across all domains in patients with first-episode schizophrenia. In addition, our study suggests a correlational relationship exists between specific brain structures and cognitive deficits in schizophrenia, providing clues about the neural basis of the disease and a potential biomarker for clinical studies.

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Disclosure of conflict of interest

None.

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