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이학석사 학위논문

**Association of cingulum and  
superior longitudinal fasciculus  
with theory of mind  
in first-episode psychosis**

초발 정신증 환자군의 마음 이론 능력 손상과  
띠다발과 위세로다발과의 연관성 연구

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# Abstract

Deficit in *Theory of Mind* (ToM), the ability to infer others' mental state, is considered as a core feature of schizophrenia (SCZ) evident since the prodromal stage of psychosis. Previous functional magnetic resonance imaging (fMRI) studies have suggested that abnormal activities among the regions comprising the mentalizing network are related to the observed ToM deficits. However, the structural connectivity underlying the functional network of ToM in SCZ remain unclear. To investigate the relation between white matter integrity and ToM deficits, diffusion tensor imaging (DTI) data of 35 patients with first-episode psychosis (FEP) and 29 matched healthy controls (HC) were analyzed via tract-based spatial statistics (TBSS). The acquired fractional anisotropy (FA) values of the two regions of interest (ROI) - cingulum and superior longitudinal fasciculus (SLF) - and ToM task scores of FEP went through correlation analysis and compared with that of HC. A positive correlation was found between the integrity of the left cingulum and ToM strange story score in patients with FEP. Also, the integrity of the left SLF was positively correlated with ToM strange story score in FEP. These results suggest the crucial roles of the cingulum and SLF in ToM deficits of SCZ. Our study is the first to demonstrate white

matter connectivity underlying mentalizing network, as well as its relation to the behavioral outcome of social cognition in the early phase of SCZ.

**Keywords:** Theory of mind, Schizophrenia, First-episode psychosis, Diffusion tensor imaging (DTI), Tract-based spatial statistics, Cingulum, Superior longitudinal fasciculus

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# 1. Introduction

Schizophrenia (SCZ) is one of the most disabling psychiatric disorder, that affects 0.3 to 0.7% of the global population (Mathers et al., 2008; Saha et al., 2005; DSM-5). It is well known for a wide range of positive and negative symptoms including delusion, hallucination, disorganized thinking, avolition, affecting, and etc (DSM-5). Other than its symptoms, SCZ is characterized as impairments in social cognition closely associated with the patients' functional disabilities of daily life, such as loss of social connection, long-term unemployment, and poverty (Fett et al., 2011; Green et al., 2012; Mathers et al. 2008; Murray et al., 1997). Along with the early age of onset and chronicity, the social and functional disabilities make SCZ a leading burden of psychiatric disorder despite its low prevalence (Green et al., 2015; Chong et al. 2016; DSM-5;). While the management of clinical symptoms of SCZ have been dramatically improved by antipsychotics treatment and the related studies, social cognition and daily social lives of the patients changed little over the decades.

Social cognition refers to the various cognitive processes underlying social interactions, including perception and interpretation of social cues, storage and retrieval of social memory, and response regulations (Frith, 2006; Green et al., 2008; Cotter et al. 2018). Among many aspects of social

cognition, the theory of mind (ToM) is one of the most complex sub-domain reflecting the mentalizing capacity to infer others' thoughts, intentions, beliefs, and emotions. ToM impairment is more significant in SCZ than those in other psychiatric disorders, and it is strongly associated with symptoms, neurocognition, and daily functions (Bora et al., 2009; Cotter et al., 2018; Fett et al., 2011; Champagne-Lavau et al., 2012; Roncone et al., 2002). Moreover, deficient ToM has a trait-like characteristic, which precedes the illness onset and persists across the disease progression, even after remission (Fett et al., 2011). The deficit also has been reported as a possible predictor distinguishing the converters from non-converters in samples at high risk for developing psychosis (Green et al. 2018; Kim et al., 2011). All together, these observations suggest the significance of ToM in understanding the pathophysiology of SCZ.

Over the last few decades, the neural correlates of ToM have been mainly investigated using the functional magnetic resonance (fMRI) approach (Kronbichler et al., 2017; Wang et al., 2018). Extensive literature in healthy subjects has suggested the mentalizing network, including medial prefrontal cortex (mPFC), temporoparietal junction (TPJ), and precuneus/posterior cingulate cortex (PCC), is activated during the performance of various ToM tasks, irrespective to the task modalities (Carrington and Bailey 2009; Green et al., 2015; Wang et al., 2018; Schurz

et al., 2014; Mar 2011). In SCZ, the aberrant activities of mPFC, TPJ, and precuneus/PCC within the mentalizing network were related to the ToM deficits (Lee et al., 2011; de Achaval et al., 2012; Das et al., 2012; Eack et al., 2013; Dodell-Feder et al., 2014).

However, fMRI studies could not be sufficient to reveal the neural mechanisms of ToM deficits, because they only show neural activation without providing information about the underlying structure. Indeed, the white matter structures mediating social cognition have been largely disregarded despite their critical roles in communication among distal cortical areas (Wang et al., 2018). Especially in SCZ, only few studies have attempted to investigate the relation between the white matter and the social cognition, such as in face perception (Zhao et al., 2017), emotion attributions (Miyata et al., 2010), empathy (Fujino et al. 2014), and social relationships (Saito et al., 2018). Structural abnormalities that may cause disrupted neural activations and ToM impairment in SCZ still remain unclear. To specify the vulnerable white matter tracts related to ToM deficits in SCZ, in depth investigation of structural connectivity of the mentalizing network is necessary.

To explore the white matter neural correlates of ToM deficit in SCZ, diffusion tensor imaging (DTI) data of the first-episode psychosis (FEP) and healthy controls (HC) were analyzed via tract based spatial statistics

(TBSS). Based on the previous fMRI researches on SCZ and DTI literature of healthy individuals and other diseases, the cingulum connecting the mPFC and precuneus/PCC and superior longitudinal fasciculus (SLF) passing through the PFC and TPJ were selected as the regions of interest (ROI) (Wang et al. 2018; Jalbrzikowski et al., 2014; Levin et al., 2011; Yordanova et al., 2017). ToM abilities of the participants were assessed via two verbal ToM tasks; false belief task and strange story task (Wimmer and Perner, 1983; Wimmer and Perner, 1985; Happé et al., 1994; Happé et al., 1999).

The aim of this study was to investigate the association of ToM deficit and the two white matter tracts, cingulum and SLF. In respect to the ToM performance, it is hypothesized that the patients with FEP would have decreased ToM abilities than those of HCs. Also in the light of previous findings, impaired ToM abilities of the patients were hypothesized to be related with the FA reduction of cingulum and SLF.

## 2. Methods

### *2.1 Participants*

Thirty-five patients with FEP and 29 HC participated in the study. Age, sex, and handedness were matched between the groups. All participants were part of a prospective cohort study recruited from the psychosis clinic at Seoul National University Hospital. Past and current psychotic symptoms of the patients were evaluated using Positive and Negative Syndrome Scale (PANSS) (Kay et al., 1987) and Structured Clinical Interview for DSM-IV Axis I disorders was administered. The inclusion criteria for FEP were aged between 15 and 37 with a brief psychotic disorder, schizophreniform disorder, schizophrenia or schizoaffective disorder. The duration of illness of all FEP was less than a year. Individuals were excluded from HC if they had past or current SCID-I Non-patient Edition (SCID-NP) axis I diagnose, and any first- to third-degree biological relatives with a psychiatric disorder. The exclusion criteria for both groups were substance abuse, medical illness that could cause psychiatric symptoms, intellectual disability (intelligence quotient [IQ] < 70), neurological disorders or previous head injury. The study procedures were explained in detail to all participants and provided with written informed consent. This study has been approved by the Institutional Review

Board of Seoul National University Hospital.

## ***2.2 Behavioral measures***

ToM was assessed with the short form of two verbal ToM tasks, the false belief and strange story tasks. A set of control, physical stories was presented to the subjects as well. All tasks were translated into Korean by psychiatrists and clinical psychologists, taking cultural backgrounds into accounts (Chung et al. 2008). The false belief task consisted of the first order (Wimmer and Perner, 1983) and the second order (Perner and Wimmer, 1985) tasks. The first order task was used to evaluate whether the subject recognizes a character's false belief about reality. The second order task questions character's understanding of the other character's mental state. Each task is comprised of a short vignette with a picture and two questions; one for comprehension test and the other to assess the subjects' capacity to infer the character's thoughts (justification question). The maximum total score of false belief task was 12 points.

The strange story task (Happé et al., 1994) consisted of 8 vignettes, each accompanied by a picture and two questions; one for comprehension test and the other to measure subjects' cognitive capacity to infer the character's mental state and emotion in complex and naturalistic situations. The task included two examples for each 4 types of stories; double bluff, white lie, persuasion, and misunderstanding. The maximum score of the

story task was 26.

The physical story task comprised of 8 vignettes that do not involve mental states. Each vignette was followed by a comprehension question and a justification question, asking physical causes of the situation (Happé et al., 1999). The maximum score of the physical story was 24.

### ***2.3 Image Acquisition and DTI preprocessing***

All participants underwent Magnetic resonance imaging scanning on a 3T scanner (MAGNETOM Trio Tim Syngo MR B17, 12 channel head coil, Siemens, Erlangen, Germany) at Seoul National University Hospital. Diffusion tensor images were acquired via echo-planar imaging with the following parameter: TR 11400 ms, TE 88 ms, matrix  $128 \times 128$ , FOV 240 mm and a voxel size of  $1.9 \times 1.9 \times 3.5$ . Diffusion-sensitizing gradient echo encoding was applied in 64 directions using a diffusion-weighting factor  $b$  of  $1000 \text{ s/mm}^2$ . One volume was acquired with  $b$  factor of  $0 \text{ s/mm}^2$  (without gradient).

The diffusion images were preprocessed via three steps with the FSL software package (version 5.0.10; <https://fsl.fmrib.ox.ac.uk/fsl/fslwiki/>). First, the eddy-current correction was applied to correct distortions and subject movements. Then the skull was removed by the brain extraction tool (BET). After BET process, raw brain images went through visual inspection and one healthy control was excluded because the dorsal surface of the brain

was not covered in the MRI. As the final step, DTIFIT was applied to fit the diffusion tensor model and individual FA values were obtained.

#### ***2.4 Region of interest (ROI)***

To test the structural connectivity among the mentalizing network, two white matter tracts were selected as the regions of interest (ROI). The tracts were the left and right cingulum, which pass PFC and precuneus, and left and right SLF, which pass MPFC and TPJ. The ROI masks were obtained from Johns Hopkins University ICBM-DTI-81 white-matter labels atlas (Mori et al., 2005; Wakana et al., 2007; Hua et al., 2008) (**Figure 1**).

#### ***2.5 DTI processing***

Voxel-wise statistical analysis was performed using Tract-based spatial statistics (TBSS) in FSL (Smith 2006, Smith et al. 2004). First, brain mask was generated as a preprocessing step. Then, all subjects' FA images were aligned into 1mm X 1mm X 1mm Montreal Neurological Institute (MNI) 152 Space via FMRIB's Nonlinear Image Registration Tool (FNIRT). The aligned images were all merged into a single 4D image file and the mean FA image was created. A 4D image of FA skeleton was generated from the mean FA with a threshold of 0.2.

Voxel-wise significant differences between the FEP and HC were investigated using randomise tool in TBSS. Before the process, age, sex,

and handedness were demeaned and fed into the design matrix and contrast file as covariates. The randomise was carried out with 5,000 permutation and threshold-free cluster enhancement (TFCE). Left and right cingulum and SLF masks were used as ROI masks. The threshold for significance was  $p < 0.05$ .

## ***2.6 Statistical analysis***

Age, sex, and handedness of the final set of subjects were tested to see whether the variables matched between the groups. The normality of the ToM task scores (e.g. false belief, strange story, and physical story) was verified and the scores were compared between the groups via Mann-Whitney test.

To explore the correlation between ToM task results and white matter integrity of ROIs, individual mean FA of each ROI was acquired from 3D individual skeleton image. The individual images were obtained by splitting the 4D skeleton image, which was created from TBSS analysis. Each mean FA of cingulum and SLF for both left and right went through correlation with the false belief, strange story, and physical story scores. All statistical analyses were performed via SPSS, version 25 (IBM, Armonk, N.Y.).

## 3. Results

### 3.1 Demographic data

The subjects and demographic data are presented in **Table 1**. There were no significant differences in sex ratio, age, handedness, IQ, and education year between the FEP and HC.

### 3.2 Theory of mind task scores

Mann-Whitney test revealed significant group differences in all three task scores (**Table 2**). FEP exhibited significantly poorer performance compared to HC in false belief task ( $z = -3.506, p < 0.001$ ), strange story task ( $z = -4.049, p < 0.001$ ), and physical story task ( $z = -2.826, p = 0.005$ ). The ToM task results are presented in **Figure 2**.

### 3.3 TBSS data and correlations

TBSS analysis showed no significant voxel-wise difference in any of the ROI regions between FEP and HC. To explore the relation between ToM and the white matter integrity, correlational analyses were performed. The results, presented in **Figure 3**, showed a significant positive correlation between the FA value of left cingulum and strange story task score in FEP ( $r = 0.35, p = 0.039$ ). Moreover, a significant positive correlation was observed

between the FA value of left SLF and the score of strange story task ( $r = 0.374, p = 0.027$ ) in FEP. No correlation was found between the FA values and false belief score or physical story scores in FEP. In the HC group, a correlation between the FA values of the left cingulum and physical story task was observed ( $r = 0.386 p = 0.042$ ). There was no significant correlation among the FA values and ToM tasks in HC.

## 4. Discussion

The present study was designed to explore the structural basis of theory of mind (ToM) deficits in schizophrenia (SCZ). To the best of our knowledge, this is the first attempt to demonstrate the relation between the white matter integrity and ToM in first-episode of psychosis (FEP). The behavioral result showed impaired ToM abilities of patients with FEP. The ToM task results then correlated with the integrities of cingulum and SLF, obtained via tract-based spatial statistics (TBSS). In FEP, the correlation analysis revealed the positive association between the integrities of left ROIs and ToM deficits. These results underscore crucial roles of the left cingulum and left SLF as the structural basis of impaired ToM abilities of FEP.

### *ToM abilities of FEP*

ToM task results were consistent with the previous researches that showed decreased ToM performance in FEP (Frith & Corcoran, 1996; Sprong et al., 2007; Bora et al., 2009; Bora et al., 2013; Song et al., 2015). In this study, two verbal ToM tasks - false belief task and strange story task - were conducted. The false belief task is the most heavily researched ToM task that is used to assess the participants' ability to understand others mental states, such as thoughts and intentions. The strange story task, which

was invented to measure higher order ToM, is employed to evaluate the ability to infer not only the thoughts or intentions but also the emotions of others in naturalistic and complex situations (Happé et al., 1994). In the false belief task, the FEP patients scored significantly lower than the healthy controls, suggesting that the patients have impaired ability to recognize others' mental states. Similar to the false belief result, the strange story score of FEP were also significantly lower than that of HC, suggesting the difficulties in inferring other's mental states and emotions in FEP. As previous meta-analyses have suggested, these ToM impairments may be related to the functional outcome of the patients and could be able to predict prognosis (Fett et al., 2011; Champagne-Lavau et al., 2012).

### ***White matter integrities and ToM abilities***

The two ROIs - cingulum and SLF - were selected based on the atlas-listed white matter tracts that are reported to connect the nodes of the mentalizing network; the mPFC, TPJ, and precuneus/PCC. Our results suggest that the integrities of these white matter ROIs are positively correlated with the strange story task performance in FEP. This finding is in the line with the recent DTI studies in healthy participants and other patient groups that reported ToM abilities in association with the integrities of cingulum and SLF (Wiesmann et al., 2017; Jalbrzikowski et al., 2014; Levin et al., 2011; Yordanova et al., 2017).

The cingulum is an association fiber that starts from the mPFC and passes through PCC and precuneus. More precisely, a probabilistic tractography study has revealed 62.59% of dorsomedial prefrontal cortex (dmPFC)-PCC and 92.01% of ventromedial prefrontal cortex (vmPFC)-PCC fibers overlap with the cingulum (Wang et al., 2018). The tract is known to be involved in attention, memory, and emotional processing (Catani and Thiebaut de Schotten, 2008; Catani et al., 2013) and has been postulated as a major white matter tract comprising the mentalizing network (Yordanova et al., 2017). In SCZ, decreased FA of cingulum has been reported in both chronic patients and FEP (Kubicki et al., 2003; Sun et al., 2003; Wang et al., 2004; Federspiel et al., 2006; Lee et al., 2013) and linked to both positive and negative symptoms and decreased neurocognition (Fujiwara et al., 2007; Whitford et al., 2014).

The SLF is a large association fiber bundle that connects the parietal, occipital and temporal lobes with the frontal cortex (Schmahmann et al., 2008; Kamali et al., 2014). The SLF is a core structure subserving attention, memory, language, and emotions (Mesulam 1998; Petrides and Pandya, 2002). According to a probabilistic tractography study, 45% of fibers between dmPFC and TPJ overlap with SLF (Wang et al., 2018). Similar to the cingulum, abnormalities in SLF have been observed in SCZ (Buchsbaum et al., 2006; Knochel et al., 2012) and also in association with the symptoms and neurocognition (Karlsgodt et al., 2008; Szeszko et al.,

2018). Along with our results, the abovementioned observations provide converging evidence of the cingulum and SLF as key structures underlying the symptoms and both social and non-social cognitions of SCZ.

This study has several intriguing findings. First, among the two ToM tasks, only strange story task score was correlated with the white matter integrities in FEP. According to previous studies, complex and higher order ToM continues to mature until adulthood (O'Hare et al., 2009; Kaland et al., 2008; Stanford et al., 2011). Furthermore, several imaging studies have demonstrated the neural activations and brain structures related to higher order ToM change over adolescence in accordance with age (Wang et al., 2006; Moriguchi et al., 2007; Blakemore, 2008). These evidence suggest that the correlation between strange story score and white matters found in this study may reflect abnormal developmental trajectory of the higher order ToM and related white matter structures in SCZ. These findings corroborate the neurodevelopmental hypothesis of SCZ (Owen et al. 2011) and could offer an insight into the pathophysiology of SCZ, especially focusing on the prodromal and early phase of the illness.

Second, another interesting result is that only the left ROIs (e.g. cingulum and SLF) were correlated with the decreased ToM task score in FEP. This finding matches with the studies of children with traumatic brain injury and patients with surgical resection for diffuse low-grade glioma that

reported associations between the left cingulum and ToM abilities (Levin et al., 2011; Herbet et al., 2015a). Together, these observations suggest that the key white matter structures underlying ToM deficits in FEP may be lateralized to the left hemisphere. However, there were several studies indicating the bilateral or right cingulum contributions to ToM abilities (Yordanova et al., 2017; Herbet et al., 2014). Such inconsistency is also evident in the findings of SLF. According to DTI researches in healthy individuals and other clinical disorders, the right SLF is associated with ToM ability (Cabinio et al., 2015; Kana et al., 2014; Herbet et al., 2014; Herbet et al., 2015b). By contrast, some studies have reported that the bilateral SLF subserves ToM (Jalbrzkowski et al., 2014; Wiesmann et al., 2017). Despite the mixed findings, it has been proposed that the right SLF may play a crucial role in ToM abilities while the left contributes mainly to the language processing (Herbet et al., 2014; Nageh et al., 2012). This argument is contrary to our findings, which showed the relation of left SLF and ToM ability in FEP. There are several possible explanations for this discrepancy. First, the ‘right social brain’ argument was developed based on the studies reported the relation among right hemisphere and social cognition using other subject groups, such as healthy participants and brain damaged patients (Saxe and Wexler, 2005; Winner et al., 1998). However, multiple fMRI studies in SCZ and FEP reported bilateral abnormalities of ToM networks (Beauchamp 2015; Brune et al., 2008; Lee et al., 2011).

Additionally, the results of this study showed no correlation between the left SLF and the score of physical story task score, which assessed non-social verbal ability. This observation suggests that the left SLF may contribute to the ToM impairment of FEP in separation with the language process.

The inconsistency between the previous literature and our current results may not be solely due to the limitations of our study designs. Instead, it could support Crows' lateralization hypotheses of SCZ (Crow, 1989a). Numerous studies have indicated reduced or altered asymmetry in both brain functional connectivity and structures in SCZ patients (Mitchell and Crow, 2005; Rebolso et al., 2014), and such alterations are also found in FEP (Crow et al. 1989a; James et al., 1999). The abnormality in brain asymmetry and functional outcomes are related to the developmental problem and the laterality changes in accordance with age (Crow et al., 1989b). Therefore, factors such as the age of onset are closely related to the abnormal brain asymmetry (Aso et al., 1995). Along with the variance of ToM task modalities and heterogeneity among FEP groups, the altered or reduced brain asymmetry may have affected differently to the results. Since this is the first attempt to investigate the specific white matter structure underlying ToM deficit in SCZ, future studies are necessary to provide reliable evidence on the structural basis of ToM impairment.

Contrary to our basic assumption, no significant differences in FA values between FEP and HC were found in this study. Previous findings have been mixed in regards to the white matter changes in FEP groups. Several DTI studies have found the arcuate fasciculus, SLF, and cingulum to be intact in FEP (Peters et al., 2008; Kawashima et al., 2009; Luck et al., 2011), while others have reported white matter alterations in SLF and cingulum (Federspiel et al., 2006; Szeszko et al., 2008). Such inconsistencies may reflect the heterogeneity of the study subjects. Symptoms, medications, age of onset, treatment intervention, and other factors may affect differently on white matters changes. To elucidate the structural abnormalities of FEP, it would be beneficial to control the covariates or divide the group into subtypes in future studies.

### ***Limitations***

Several limitations must be taken into consideration in interpreting the present results. First, the FEP patients were on antipsychotics at the time of scanning and ToM measurements. Though the effects of antipsychotics are relatively small in FEP compared to chronic SCZ, medication can still cause changes in brain structure (Ho et al., 2011). Second, if the abnormal structure of FEP were located in small sub-regions within the cingulum or SLF or even in other white matters, the ROI based TBSS approach would not be able to detect it. Cingulum and SLF are widely distributed fibers connecting various distal

brain regions, and by averaging the FA values across the whole ROI can risk of losing some valuable information. To address these issues and to elucidate the precise fiber tracts related to impaired ToM in FEP, a probabilistic tractography analysis would be necessary.

### ***Conclusion***

Our study was the first to demonstrate the associations between FA values of the two white matters, cingulum and SLF and ToM ability in FEP patients. White matter study using DTI methods extends our insight into the neural basis of ToM and suggests left cingulum and SLF as vulnerable structures underlying the impairment of ToM in SCZ.

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**Table 1.** Demographics of the subjects

Variables	FEP (n = 35)	HC (n = 28)	Statistical Differences	
			$\chi^2, F$ or $t$	$p$
Age (years)	23.40 ± 5.76	21.68 ± 3.48	-0.612	0.543
Sex (male/female)	16/19	15/13	0.384	0.535
Handedness (right/left) <sup>†</sup>	30/5	26/2	0.804	0.370
IQ	98.11 ± 13.94	100.50 ± 10.63	0.748	0.458
Education (year)	13.26 ± 2.02	13.79 ± 1.89	-1.187	0.235
Parental SES score	2.71 ± 0.86	2.79 ± 0.63	4.28	0.233
PANSS total	68.54 ± 12.00			
PANSS positive	16.23 ± 4.61			
PANSS negative	17.63 ± 4.64			
PANSS general	34.69 ± 6.80			

Data given as mean ± S.D.

<sup>†</sup>Classified using Annett Hand Preference Questionnaire

FEP: first-episode psychosis; HC: healthy control; SES: socioeconomic status; PANSS:

Positive and Negative Syndrome Scale

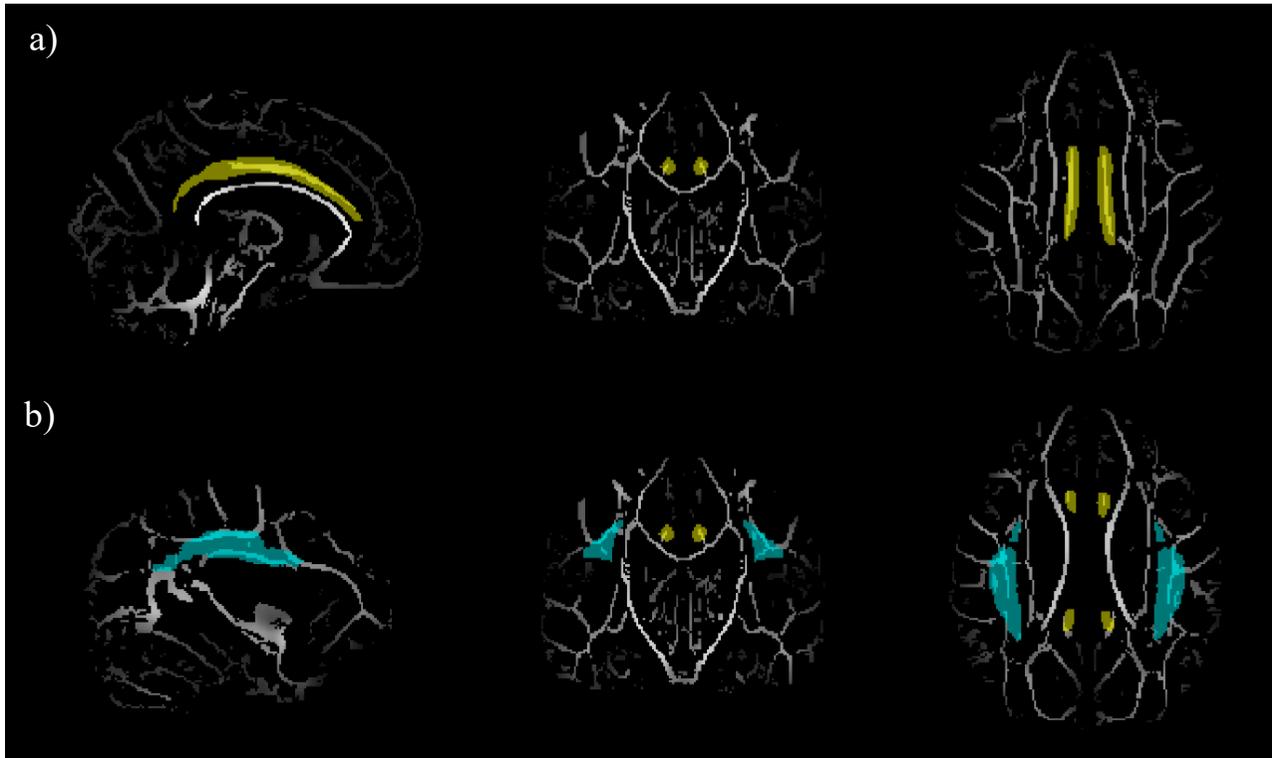
**Table 2.** Theory of mind task results

Variables	FEP (n=35)	HC (n=28)	Statistical Differences	
			<i>Z</i>	<i>p</i>
False belief task	7.54±2.24	9.68±2.21	-3.506	.000
Strange story task	20.06±2.84	22.75±1.65	-4.049	.000
Physical story task	17.89±2.55	20±2.46	-2.826	.005

Data given as mean ± S.D.

FEP: first-episode psychosis, HC: healthy control.

**Figure 1.** Region of Interest (ROI) masks obtained from Johns Hopkins University ICBM-DTI-81 white-matter labels atlas overlaying on white matter skeleton. a) Cingulum (Yellow). b) Superior longitudinal fasciculus (blue).

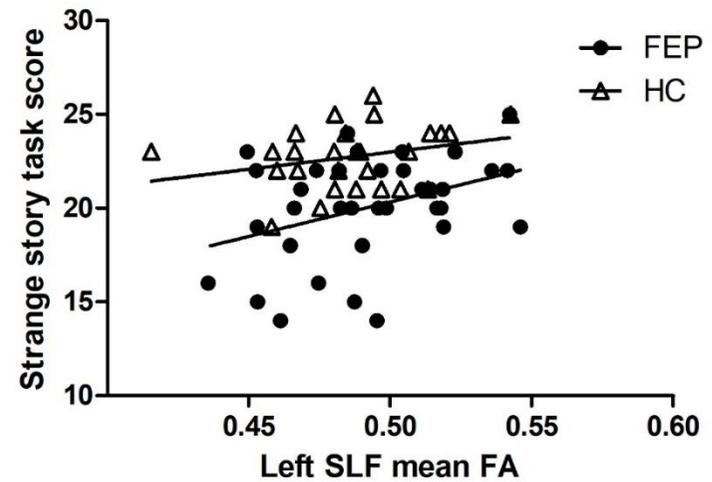
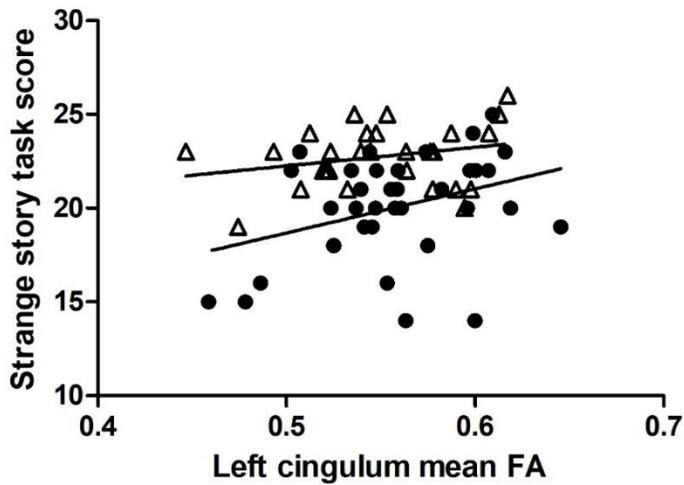




**Figure 3.** The correlations between mean FA values and strange story task score. a) Left cingulum mean FA and strange story score.

FEP:  $r = 0.350$ ;  $p = 0.039$ . HC: no correlation. b) Left superior longitudinal fasciculus (SLF) mean FA and strange story

score. FEP:  $r = 0.374$ ;  $p = 0.027$ . HC: no correlation. FEP: first-episode psychosis; HC: healthy control.



## 초록

다른 사람들의 정신 상태를 추론하는 능력인 ‘마음 이론’의 손상은 조현병 환자의 핵심적 특징이며 이는 증상 발병 이전 단계인 전구기부터 꾸준히 관찰되는 것으로 알려져 있다. 이전의 기능적 자기공명영상 연구를 통해 mentalizing network에 해당하는 영역들의 활동 이상이 마음 이론 능력 손상에 관련 있는 것으로 보고 되었으나 마음 이론 능력을 담당하는 기능적 네트워크의 기저가 되는 백질 구조의 역할은 아직 조현병 환자군에서 밝혀진 바가 없다.

조현병 환자의 마음 이론 능력에 관련된 뇌 백질 구조를 연구하기 위하여, 초발 정신증 환자 35명과 정상 대조군 29명의 확산텐서영상을 tract based spatial statistics (TBSS) 방법으로 분석하고 두가지 관심영역, 즉 띠다발과 위세로다발의 FA 값과 마음 이론 과제 점수와의 상관 관계를 살펴보았다.

그 결과 초발 정신증 환자의 왼쪽 띠다발과 마음 이론 과제 중 strange story의 점수가 유의한 양의 상관 관계를 보이는 것이 관찰되었다. 또한 초발 정신증 환자의 왼쪽 위세로다발도 strange story 점수와 유의한 양의 상관관계를 가지는 것으로 나타났다.

본 연구를 통해 조현병 환자의 마음 이론 능력 손상에 띠다발과 위세로다발이 주요한 역할을 하는 것이 증명되었다. 본 연구는 초발 정신증 환자군에서 백질 구조의 완전성과 마음 이론 손상의 관련을 밝힌

첫번째 시도이며 향후 연구에서 사회인지의 손상을 백질을 통해 살펴보는 접근이 필요하다는 증거를 제공한다.