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**Review Article** 

# Single episode brief psychotic disorder versus bipolar disorder: A diffusion tensor imaging and executive functions study

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A R T I C L E I N F O	A B S T R A C T
Keywords: Diffusion tensor imaging Executive functions Single episode Bipolar disorder Brief psychotic disorder	Background: Despite fast progress in neuroscientific approaches, the neurobiological continuum links psychotic spectrum, and affective disorder is obscure. White matter WM abnormalities found utilizing Diffusion Tensor Imaging (DTI) showing impaired communication in both disorders have been consistently demonstrated; how-ever, direct comparisons of findings between them are scarce. This study aims to study WM abnormalities in single episode bipolar I disorder, and single episode brief psychotic disorder related to healthy control with the association of executive function.
	<i>Methods:</i> A cross-sectional case-control study was used to assess 60 subjects divided into 20 patients with single episode bipolar I disorder, 20 individuals with single episode brief psychotic disorder (both groups of patients were in remission), and 20 healthy controls. The present study examined the superior longitudinal fasciculus (SLF), and cingulum bundle fractional anisotropy (FA) determined from DTI images symmetrically and connected these results with cognitive functions as assessed by the trail making test (TMT) and Wisconsin card sorting test (WCST).
	<ul> <li>Results: DTI data indicated that the psychotic group had a significant decrease in FA of the right SLF (p-value less than 0.001), left SLF (p-value less than 0.001), and left cingulum (p-value less than 0.001) than the bipolar I group. In terms of executive functioning, the psychotic group performed significantly worse than the bipolar I group on the TMT part B (p-value less than 0.001), the WCST (number of classifications fulfilled) (p-value less than 0.001), and perseverative errors (p-value less than 0.001).</li> <li>Conclusion: Even after clinical remission, individuals with single episode brief psychotic disorder had more pronounced white matter impairments and executive function deficiencies than individuals with single episode bipolar I disorder.</li> </ul>

#### 1. Introduction

Numerous neuroimaging studies have concentrated on distinguishing the psychotic spectrum from bipolar disorder (BD) in an attempt to identify disease-particular neuropathological pathways in both disorders (Whalley et al., 2009; Hall et al., 2010). Several studies reveal that these two disorders have a high genetic susceptibility overlap (Berrettini, 2000; Craddock et al., 2005), pharmacotherapy responses (Murray et al., 2004), deficiencies in neuropsychology (Hill et al., 2009), and epidemiological characteristics, therefore, potentially shared pathophysiology, which is recognized as kraepelin dichotomy (Kraepelin, 1919). Given this, examining the parallels, variations, and common neural pathways between these two disorders may aid in our understanding of the pathophysiological basis for psychosis's clinical continuity.

In addition to changes in gray matter and functional imaging, examining changes in the microstructure of white matter provides vital insight into the pathogenesis or course of diseases. White matter (WM) impairments revealed with DTI are commonly and consistently demonstrated in psychosis and BD (Arat et al., 2015).

The WM is abnormal in various clinical features and diseases, and their particular diagnosis is uncertain (Alnæs et al., 2018). In diagnostic nosology, psychosis and BD are currently regarded as separate classifications. However, neuropsychological, genetic, clinical proofs indicate

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that the pathophysiology and clinical aspects of psychosis are partially overlapping, with a greater symptom burden, impaired function, and a worse result in psychosis (Lagopoulos et al., 2013; Sarrazin et al., 2014). Incorporating individuals with psychosis and BD into the same analysis allows for examining shared and unique etiological pathways throughout the psychosis spectrum (Sprooten et al., 2016; Tønnesen et al., 2018).

Previous research suggested that changed connectivity has been seen frequently in both BD (Chan et al., 2010; Benedetti et al., 2011) and schizophrenia spectrum (Kunimatsu et al., 2012; Levitt et al., 2012; Mandl et al., 2013). Nevertheless, there is a dearth of literature comparing schizophrenia and BD using DTI (Fig. 1).

DTI is a magnetic resonance imaging (MRI) technique that is suitable for studying the microstructure of white matter (WM) because it gives necessary details concerning fiber integrity and direction. The preponderance of DTI studies examines WM integrity using the Fractional Anisotropy (FA) parameter (Heng et al., 2010). DTI-dependent microstructure indices of WM are highly susceptible to changes in quality performance caused by the subject motion approach (Yendiki et al., 2014).

The FA in bilateral cerebellum and subsequent thalamic radiation, the corticospinal tract, and SLF were considerably lower in people with psychosis, mainly schizophrenia than in FA individuals with significant variations in their DTI schizophrenia and BD (Mamah et al., 2019).

Patients with early-onset first psychotic symptoms occurring within six months and un-medicated BD patients showed this WM affection, not just chronic schizophrenia and chronic BD patients (Lu et al., 2011). Individuals with an occurrence of psychosis and BD revealed decreased FA in the corpus callosum, cingulum, internal capsule, and occipital WM, and numerous additional WM tracts in this program for single episode psychosis (Chicago, IL, USA, 2011), where both individual groups exhibited significantly greater mean diffusivity than healthy controls.

This cognitive impairment is a minor cognitive capacity deficiency marked by a greater impairment in processing speed, memory, and executive performance. However, the degree of dysfunction varies significantly among individuals (Simonsen et al., 2011).

Memory functions were found to be more intimately connected to other critical white matter pathways, while awareness/information processing was shown to be more closely associated with composite/ total-brain FA, most notably in the frontal lobes (Wilde et al., 2011).

# 1.1. The study's aim

The objective of this paper is to make a comparison between the integrity of the superior longitudinal fasciculus and cingulum, as well as cognitive processes, in individuals with single episode psychosis and



Fig. 1. Sagittal FA color map overlaid on T1WI: Tractography of the cingulum fibers colored in yellow.

persons with single episode BD (Fig. 2).

#### 2. Subjects and methods

# 2.1. Subjects

The study enrolled 60 subjects (20 with a single manic episode (bipolar I disorder) in euthymia, 20 with first-episode psychotic disorder in recovery, and 20 healthy individuals). All men were selected from the out-patient clinic of the Institute of Psychiatry at Ain Shams University in Cairo, Egypt. The following criteria were used to determine eligibility: (a) Age ranged between 18 and 60; (b) both male and female were involved; (c) patients' diagnoses were established using the Diagnostic and Statistical Manual of Mental Disorders-Fourth Edition (DSM-IV) criteria (American Psychiatric Association, 1994) evaluated by the SCID-I (First et al., 1995); (d) bipolar individuals in euthymic phase as described by a HAM-D score of less than 7 (Hamilton, 1960) and YMRS (Young et al., 1978), which reached between six and twenty-four months following acute presentation (e) Psychotic individuals in remission as characterized by a brief psychiatric rating scale (BPRS) score equal or less than 2 which reached between second and twentyfour months following the acute presentation.

We excluded all individuals with another axis I disorder, history of alcohol or substance misuse, traumatic brain injury with unconsciousness, epilepsy, or a variety of additional neurological or health issues, such as hypertension or diabetes, and individuals with an IQ less than 80 or who had just completed a three-month course of BST (Brain Synchronizing Therapy), as those were left-handed or unable to have an MR test due to claustrophobia, metal implants, or other reasons.

All individuals who contacted the clinic between January 2020 and January 2021, and met the trial's eligibility and exclusion requirements, and submitted the informed consent form were involved in the study.

Of 20 healthy controls were chosen from the Institute of Ain Shams University employees, Egypt, similar with age, sex, the educational status with the group of individuals. They also fulfilled the exact exclusion requirements for individuals. The dearth of psychiatric diseases was evaluated utilizing the general health questionnaire (GHQ) in Arabic (Goldberg and Hillier, 1979; Ukashah, 1988).

# 2.2. Methods

The Faculty of Medicine Ain Shams University's Ethical Committee approved the study, and all participants supplied signed informed consent.

Each subject was assessed using standardized organized and/or semiorganized clinical methods to establish diagnostic and clinical features, disease progress, family history, and current and former medication: Structured Clinical Interview for Axis-I Disorders (SCID-I) (First et al.,



Fig. 2. Superior longitudinal fasciculus tractography sagittal view projected on axial FA color-coded map overlaid on T1WI.

1995), Hamilton Depression Scale for the diagnosis of a single manic episode with psychotic symptoms and a first brief psychotic episode, as well as to rule out other concomitant psychiatric disorders; Hamilton Depression Scale (HAM-D) (Hamilton, 1960), and Young Mania Rating Scale (YMRS) (Young et al., 1978) to make sure that remission in candidates diagnosed bipolar I disorder, and the brief psychiatric rating scale (BSRS) to make sure that remission in individuals undergone a brief psychotic episode.

Additionally, a fully qualified clinical psychologist administered an intelligence quotient experiment utilizing the Wechsler adult intelligence measure (Wechsler, 1991) to weed out instances of mental illness. The Wisconsin card sorting test (WCST) was one of the cognitive processes assessed, as it allowed the researchers to measure the relevant "frontal" lobe functions (e.g., structured exploring, crisis management, directing action toward a purpose using contextual feedback, shifting cognitive sets, and controlling impulsive response) (Heaton, 1981). The trail-making tests A and B (Reitan, 1958) were utilized to assess the eyetracking organization, planning, attention, established changing, and cognitive flexibility.

# 2.3. Neuroimaging evaluation: DTI protocol and imaging acquisition

All patients and healthy controls were evaluated in a brief acquisition period, and fast processing was critical for determining the clinical viability of a particular approach. We employed echo-planar imaging (EPI), single-shot spin-echo, and contemporary imaging approaches to obtain motion-free and higher signal-to-noise ratio (SNR) DTI. As per the section numbers introduced to the standard MR imaging examinations, the entire imaging duration for DTI and Fiber tracking (FT) was 7–9 min.

A 1.ST scanner (Achiva Philips) was used to examine all subjects. The signal strength was detected using an S-channel head coil. DTI was regarded as a one-shot diffusion-weighted spin-echo EPI sequence (TR/TE, 8000/68.7 ms; concurrent imaging [array special sensitivity encoding technique] with accelerating factor 2; matrix,  $80 \times 78$ ; field of view, 22 cm; section thickness, 2 mm; 50 continuous sections).

Data from the DTI were investigated and processed offline; we integrated data from the DTI into the software application, which allowed us to conduct seed investigation in the targeted region. Based on the proposed anatomical regions, regions of interest (ROIs) were defined. Tractography was done to isolate the suspected tracts by tracking multiple ROIs (right and left superior longitudinal fasciculus and right and left cingulum). For both categories, pathway-dependent spatial statistics were utilized to measure fractional anisotropy (FA) as a sign of white matter integrity.

#### 2.4. Statistical analysis

SPSS (Statistical Package for the Social Sciences) version 25 was used to code and interpret the data.

In quantitative data, the minimum, maximum, median, mean, and standard deviation were used to summarize the data, while in categorical variables, the frequency (count) and relative frequency (%) were used to summarize the data.

Quantitative variables were compared, implying the non-parametric Kruskal-Wallis and Mann-Whitney analyses.

To contrast categorical data, the Chi-square (c2) strategy was applied. When the projected frequency is less than 5, an accurate alternate test was used. p-Values less than 0.05 were considered statistically significant.

# 3. Results

When it came to socio-demographic data, there have been no statistically significant differences among groups based on age, gender, or level of education (Table 1).

There was a substantial difference in marital status between the

Table 1

Comparison between	a groups according	to socio-demographic data
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Socio- demographic data	Bipolar I group (n = 20)	Psychotic group (n = 20)	Healthy controls $(n = 20)$	Test	p-Value
Age (years)					
Mean $\pm$ SD	$\begin{array}{c} 23.30 \pm \\ 4.33 \end{array}$	$25.05 \pm 5.51$	$\begin{array}{c} \textbf{26.10} \pm \\ \textbf{4.36} \end{array}$	F = 1.761	0.181
Range	17-a35	18-a37	20-a38		
Sex					
Female	8 (40.0%)	5 (25.0%)	8 (40.0%)	$x^2 =$	0.517
Male	12 (60.0%)	15 (75.0%)	12 (60.0%)	1.319	
Marital					
Divorced	1 (5.0%)	1 (5.0%)	3 (15.0%)	$x^2 =$	<0.001**
Married	4 (20.0%)	3 (15.0%)	14 (70.0%)	21.407	
Single	15 (75.0%)	16 (80.0%)	3 (15.0%)		
Occupation					
Employed	6 (30.0%)	5 (25.0%)	15 (75.0%)	$x^2 = 15.593$	0.004*
Unemployed	14 (70.0%)	15 (75.0%)	5 (25.0%)		
Years of education	1				
Mean $\pm$ SD	12.15 $\pm$	11.85 $\pm$	12.80 $\pm$	F =	0.290
	1.98	1.69	2.09	1.266	
Range	10-a15	10-a15	10-a15		

Using: one way analysis of variance; t-independent sample t-test; x<sup>2</sup>: Chi-square test.

p-Value > 0.05 NS; \*p-value < 0.05 S; \*\*p-value < 0.001 HS.

There were no statistically significant differences between the bipolar group and the psychotic group as regards family history and duration of illness.

control and illness groups, with 70% of the control group being married and the majority of the psychotic and bipolar group being single with a p-value less than 0.001. Also, most of the psychotic group (15 (75.0%)), and bipolar group (14 (70.0%)) were unemployed (p-value = 0.004) (Table 1).

In terms of family history and disease duration, there were nonsignificant differences between the bipolar and psychotic groups (Table 2). Table 3 shows the comparison of DTI results between groups.

In comparison to the control group, we observed statistically significantly greater FA of the right SLF (p-value less than 0.001), left SLF (p-value = 0.001), right cingulum (p-value = 0.001), and left cingulum (p-value = 0.001) in the control group than in the psychotic and bipolar groups. While the comparison of psychotic and bipolar groups revealed statistically significantly lower FA of right SLF (p = 0.001), left SLF (p = 0.001), and left cingulum (p = 0.001) in the psychotic group. The bipolar group revealed statistically significantly lower FA of right SLF (p = 0.001), left SLF (p = 0.001), and left cingulum (p = 0.001) in the psychotic group.

#### Table 2

Comparison between psychotic and bipolar groups according to the duration of illness and family history.

	Bipolar I group (n = 20)	Psychotic group (n = 20)	Test	p- Value
FH				
Negative	11 (55.0%)	11 (55.0%)	$x^2 =$	1.000
Positive	9 (45.0%)	9 (45.0%)	0.000	
Duration of i	llness (months)			
Mean $\pm$	$13.65\pm6.48$	$11.85\pm5.45$	t = 0.903	0.348
SD				
Range	6–24	6–24		

Using: one way analysis of variance; t-independent sample t-test;  $\mathbf{x}^2$ : Chi-square test.

p-Value > 0.05 NS; statistically significance statistically significance \*=p<0.05; high statistical significance = \*\*p=<0.001.

#### Table 3

Comparison between groups as regards DTI findings.

DTI findings Fractional anisotropy (FA)	Bipolar I group (n = 20)	Psychotic group (n $= 20$ )	Healthy controls ( $n = 20$ )	ANOVA	p-Value
Right superior longitudinal fasciculus Mean $\pm$ SD Range	0.452 ± 0.043 0.400-0.533	$\begin{array}{c} 0.393 \pm 0.018^a \\ 0.361  0.425 \end{array}$	$\begin{array}{l} 0.524\pm 0.037^{ab}\\ 0.4710.612\end{array}$	72.298	<0.001**
Left superior longitudinal fasciculus Mean $\pm$ SD Range	$\begin{array}{c} 0.461 \pm 0.052 \\ 0.329  0.548 \end{array}$	$\begin{array}{l} 0.374\pm 0.016^{a} \\ 0.3380.404 \end{array}$	$\begin{array}{l} 0.511 \pm 0.029^{ab} \\ 0.463  0.575 \end{array}$	76.527	<0.001**
<i>Right cingulum</i> Mean ± SD Range	$\begin{array}{c} 0.474 \pm 0.039 \\ 0.412 0.561 \end{array}$	$\begin{array}{c} 0.442 \pm 0.020 \\ 0.386 0.471 \end{array}$	$\begin{array}{l} 0.512 \pm 0.041^{ab} \\ 0.436 0.613 \end{array}$	20.528	<0.001**
<i>Left cingulum</i> Mean ± SD Range	$\begin{array}{c} 0.457 \pm 0.046 \\ 0.413  0.571 \end{array}$	$\begin{array}{l} 0.486 \pm 0.025^a \\ 0.416 {-} 0.530 \end{array}$	$\begin{array}{l} 0.555 \pm 0.047^{ab} \\ 0.466 {-} 0.621 \end{array}$	31.269	<0.001**

F-one way analysis of variance; statistically significance \*=p<0.05; high statistical significance =\*\*p=<0.001.

Post HOC test: a: significant difference with Bipolar I group; b: significant difference with Psychotic group.

Comparison between groups as regards executive functions.

0.001) in the psychotic group. There is no statistically significant difference between the two groups regarding the right cingulum.

## 3.1. Comparison between groups as regards executive functions

Comparing the psychotic and bipolar groups to the control group revealed statistically significant impairments in TMT part B (p-value = 0.001), category finished subtest of WCST (p-value lower than 0.001), and perseverative errors subtest of WCST (p-value lower than 0.001). While, the comparison between psychotic and bipolar groups showed statistically significant deficits in the psychotic group than the bipolar group as regards TMT part B (p-value  $\leq$  0.001), WCST (category completed, and perseverative errors with p-value less than 0.001). There were no statistically significant differences between groups in the trailmaking test part A and the Wisconsin card sorting test conceptual level subtest. The correlations between DTI findings and executive functions.

We found no significant correlation between DTI findings and executive functions in each group of patients individually. In contrast, as one group (both psychotic and bipolar groups), there were statistically significant negative correlations between FA of left superior longitudinal fasciculus and trail making test B (p-value 0.007). Moreover, perseverative errors (p-value 0.012) positively correlated with category completed (p-value 0.020). Also, FA of right superior longitudinal fasciculus negatively correlated with trail-making test B (p-value 0.02).

#### 4. Discussion

A rising number of research have focused on the association between psychotic spectrum and affective disorders especially BD, as both have a high severity of genetic homology in terms of chances of danger (Lichtenstein et al., 2009; International Schizophrenia Consortium et al., 2009), neuropsychological deficiency (Hill et al., 2009; Kumar et al., 2015), actions to pharmacologic medication (Murray et al., 2004; Maier et al., 2006), and epidemiological characteristics, potentially indicating to a shared pathogenic mechanism and contradicting the kraepelinian dichotomy (Craddock and Owen, 2005). The two disorders remain among the biggest causes of disability in the world.

The underlying neurobiological continuity connecting the two psychotic diseases is unknown, resulting in poor therapeutic and predictive relevance. Further research into the underlying neurobiology of these illnesses would be beneficial (Frangou, 2014).

Diffusion tensor imaging (DTI) permits the analysis of microstructural changes in the shape and direction of WM pathways in this context by generating corresponding diffusion indices. The fractional anisotropy (FA) of a voxel indicates how much one direction dominates over the others (Pierpaoli and Basser, 1996; Beaulieu, 2002). Although a few studies, such as Kumar et al. (2015) and Lu et al. (2011), have attempted to compare these two conditions, the consistency and replicability of findings concerning white matter abnormalities in the two psychotic disorders remain uncertain.

Despite the similarity in WM changes between BD and psychosis, these two psychiatric disorders have received little attention in terms of brain diffusion. Additionally, SCZ and BD have been categorized as disconnection disorders (Friston, 1998, Pettersson-Yeo et al., 2011; Vai et al., 2014).

It is crucial to study individuals throughout the "integrating years" between the single episode and the onset of the persistent disorder in order to improve consequences and determine when interventions would be most helpful (Kathryn et al., 2020).

The focus of this research was to broaden the knowledge of the frequent microstructural alterations associated with psychotic disorder and BD type I by analyzing the SLF and cingulum bundle following a single episode and linking them with executive function. We performed a DTI study on 20 individuals with a single manic episode BD I, 20 individuals with the first psychotic episode, and 20 healthy controls. All individuals were in remission.

Superior longitudinal fasciculus (SLF) is an associative tract implicated in our study; it joins the frontal lobe to the parieto-temporal regions and required for the establishment of a multimodal neural network required for the basic cascades of memory, language, attention, and emotion (Petrides and Pandya, 2002). The prefrontal cortex is connected to the limbic portions of the temporal lobe associated with memory and cognitive control (Mori and Aggarwal, 2014).

In the bilateral superior longitudinal fasciculi and bilateral cingulum bundles, individuals with one psychotic episode demonstrated substantial white matter destruction compared to the control group (Table 1). These observations support the hypothesis that WM abnormalities manifest at the onset of schizophrenia's clinical presentation (Yao et al., 2013; Samartzis et al., 2014).

Likewise, to our findings, it was observed that psychotic disorders spectrum people originally had much lower FA of SLF than healthy controls during the disease and even after the start of the first psychotic event (Melicher et al., 2015; Reid et al., 2016; Vitolo et al., 2017; Mamah et al., 2019), and cingulate bundle (Camchong et al., 2011). Nevertheless, there has been considerable variation in the studied locations, with some studies revealing no substantial anomalies (Peters et al., 2010; Mulert et al., 2012; Wheeler and Voineskos, 2014).

Thus, our results indicate that WM deficits may be an initial stage endophenotype of the disease (Liu et al., 2014).

In addition, in those with a single manic episode vs. the control group, we detected significant white matter abnormalities in the cingulum and superior longitudinal fascicles (Table 1). The findings of Barnea-Goraly et al. (2009), Chan et al. (2010), and Lin et al. (2011) corroborate research results of lowered FA in the cingulum bundle bilaterally. In their study, Wise et al. (2016) reported FA reduction in the left cingulum and right superior longitudinal fasciculus (Table 4).

Additionally, voxel-based studies consistently discovered that bipolar patients had decreased FA across a variety of broad pathway classifications: linkages between the frontal lobe and the limbic system including the cingulum bundle and long-distance linkages between correlation cortices, including the superior longitudinal fasciculus (Brambilla et al., 2001; Heng et al., 2010; Nortje et al., 2013). Nevertheless, Teixeira et al. (2014), Sprooten et al. (2016), Ji et al. (2017), and Mamah et al. (2019), discovered no decrease in FA of SLF in the bipolar population.

Otherwise, a limited number of studies have demonstrated that persons with bipolar disorder have a larger white matter of FA, implying that specific white matter pathways may have a higher degree of directionality in some people (Versace et al., 2008; Mahon et al., 2009).

Numerous investigations concurred with our findings and revealed FA loss in left posterior cingulum fibers in both patient groups, which is critical for neurocognitive abilities, including planning, memory, and attention (Kantarci et al., 2011; Delano-Wood et al., 2012), and this tract's diminished integrity may contribute to the reported deterioration of executive functioning in both psychotic groups (Barch et al., 2003; Xu et al., 2012). Thus, those mentioned above diminished structural integrity may represent a shared mechanism underlying psychological instability in both disorders.

Regarding the comparison between the psychotic and bipolar groups, the study discovered statistically low significant differences in the FA of the right and left superior longitudinal fasciculus and left cingulum between psychotic and bipolar groups. However, no statistically significant difference was observed in the FA of the right cingulum between the two groups.

Our consequences corroborated previous research indicating that schizophrenia has a higher rate of white matter abnormalities than BD

#### Table 4

	Comparison	between	groups	as regards	executive	functions.
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Executive functions	Bipolar I group (n = 20)	Psychotic group (n = 20)	Healthy controls $(n = 20)$	ANOVA	p-Value
Trail making test	Α				
Mean $\pm$ SD	63.35 $\pm$	58.35 $\pm$	52.25 $\pm$	1.337	0.271
	16.45	30.58	13.42		
Range	40–90	20-150	30-85		
Trail making test	В				
Mean $\pm$ SD	135.00 $\pm$	196.65 $\pm$	110.75 $\pm$	13.979	<0.001**
	46.03	72.20 <sup>a</sup>	32.98 <sup>ab</sup>		
Range	65–250	74–300	60–200		
Wisconsin card so	orting test (WC	ST)			
Categories		- /			
Mean + SD	5 20 ±	4 00 +	6.00 +	15 781	<0.001**
Media ± 0D	1.24	1.52 <sup>a</sup>	0.00 <sup>ab</sup>	10.701	<0.001
Range	2–6	2–6	6–6		
Conceptual					
level					
$\text{Mean} \pm \text{SD}$	66.25 $\pm$	$60.35~\pm$	66.45 $\pm$	1.303	0.280
	15.79	16.77	4.71		
Range	26-88	32-80	60–72		
Preservative					
errors					
$\text{Mean} \pm \text{SD}$	11.50 $\pm$	$\textbf{27.15} \pm$	$8.85 \pm$	14.862	<0.001**
	4.03	19.03 <sup>a</sup>	4.07 <sup>ab</sup>		
Range	5–20	8–95	2–17		

F-one way analysis of variance.

p-Value>0.05 NS; statistically significance \*=p<0.05; high statistical significance = \*\*p=<0.001.

Post HOC test: a: significant difference with Bipolar I group; b: significant difference with the Psychotic group.

(Cui et al., 2011; Costafreda et al., 2009; Hall et al., 2010).

Additionally, numerous fMRI studies (Palaniyappan and Liddle, 2014; Argyelan et al., 2014; Brandt et al., 2014), revealed that if the neural impairments associated with schizophrenia and BD occur on a spectrum, schizophrenia typically exhibits more pronounced or extensive aberrations.

In comparison to ours, several investigations revealed no differences between bipolar and psychotic groups (Sussmann et al., 2009; Cui et al., 2011; Kumar et al., 2015), While Lu et al. (2011) observed that BD had the cingulum FA less than SCZ (Table 5).

Nonetheless, confounding variables such as cumulative drug dose and patient age may impact the pattern of white matter architecture. Variability among studies may also result from differences in motion correction, scan acquisition, and analysis methodologies.

These white matter deficiencies are almost certainly the result of a consistent format, including a genetic etiology (Hakak et al., 2001; Karoutzou et al., 2008) such as a polymorphism within some of the genes involved in myelination or a malfunction of the immune system (Muller and Schwarz, 2010), which may be induced by an inflammatory response (Müller et al., 2012).

Regarding executive functions, the psychotic and bipolar group showed statistically significant impairment than the control group regarding trail making test part B, WCST (category completed and Perseverative errors) with considerably greater deficits in the psychotic group than the bipolar group.

Similar to our findings, bipolar patients showed impairment in executive functions in multiple prior studies (Clark et al., 2002; Kolur et al., 2006; Elshahawi et al., 2011; Lee et al., 2014).

Likewise, cognitive patterns in individuals with schizophrenia and BD have been observed, but the level of dysfunction seems to be larger in schizophrenia (Bearden et al., 2001; Martinez-Aran et al., 2002; Seidman et al., 2002). These findings may support the arguments of opponents of the kraepelinian dichotomy, who concurs that the similarities between these two disorders imply they exist on continuity (Crow, 1990).

As one group (both psychotic and bipolar groups), there were statistically significant negative associations between FA of the left superior longitudinal fasciculus and trail making test B and perseverative errors. Moreover, there is a strong relation between FA and category fulfilled. Also, FA of right superior longitudinal fasciculus was adversely associated with trail-making test B.

A correlation between altered SLF and specific cognitive patterns in both disorders has been established (Oertel-Knöchel et al., 2014; Bauer et al., 2015; Karbasforoushan et al., 2015).

# Significant outcomes

Both groups of patients have significant deficits than the control group regarding	the
integrity of SLF and cingulum and executive functions.	

The study revealed statistically significant deficits of SLF bilaterally, left cingulum, and executive functions in the psychotic group than the bipolar group. Thus, both diseases exhibit abnormalities in white matter integrity and executive

functioning, with the psychotic group suffering more significant disability than the bipolar group.

#### Limitations

- Despite the fact that we assessed individuals early in the course of the condition following a single episode, we cannot rule out the impact of treatment on the FA of the chosen tracts.
- Small sample size.
- Localized examination of white matter as we investigated only two tracts (SLF and cingulum). Due to their anatomical location, we limited our studies to these tracts depending on prior literature and their postulated role in executive processes. We need a widespread

#### Table 5

Correlation between DTI findings and executive functions, using in both psychotic and bipolar groups.

Executive functions		DTI findings (FA)			
		Right superior longitudinal fasciculus	Left superior longitudinal fasciculus	Right cingulum	Left cingulum
Trail making part A	R	-0.078	-0.058	0.109	-0.112
	p-Value	0.631	0.723	0.504	0.490
Trail making test B	R	-0.368	-0.421	-0.126	0.265
	p-Value	0.020	0.007	0.438	0.099
Wisconsin card sorting test (WCST)					
Categories completed	R	0.261	0.365	0.288	0.104
	p-Value	0.103	0.020	0.072	0.523
Conceptual level	R	0.234	0.283	0.185	0.019
	p-Value	0.146	0.076	0.254	0.909
Preservative errors	R	-0.302	-0.394	-0.215	0.214
	p-Value	0.058	0.012	0.183	0.186

t-Pearson correlation coefficient; p-value >0.05 NS; statistically significance \*=p< 0.05; high statistical significance = \*\*p=<0.001.

examination of white matter as we expect diffuse white matter abnormalities in both disorders.

#### **Ethical approval**

Each parent was notified of the study's purpose and provided informed consent was taken from all individuals prior to recruitment. The Ain Shams University Hospital Ethics Board accepted this study with a particular statement that included the following information; the study's justification was that enrollment was purely voluntary and provided no immediate advantage to the individual, although the data collected may be utilized to assist other individuals, they may be revoked at any time without explanation and without impairing their care. The study's findings may be published in scientific journals, but the sufferers' identities will remain fully anonymous.

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## CRediT authorship contribution statement

- 1. Zeinab Mohamed El Nagar: recruitment of patients, analysis and interpretation of data, and critical revision of the manuscript.
- 2. **Heba Hamed El-Shahawi:** study concept, and design, and critical revision of the manuscript.
- 3. **Safeya Mahmoud Effat:** study concept, and design, and critical revision of the manuscript.
- 4. Hossam Moussa Sakr: made substantial contributions to the design of the present study and DTI data interpretation.
- 5. **Yosra Abdelzaher Ibrahim:** made substantial contributions to the design of the present study and DTI data interpretation.
- 6. **Mona El-sheik:** study concept, and design, analysis and interpretation of data, and critical revision of the manuscript.
- 7. **Ahmed Adel:** study concept, analysis and interpretation of data, and critical revision of the manuscript.
- 8. **Ola Mohamad Aufa:** recruitment of patients, analysis and interpretation of data, and writing and editing the manuscript.

All authors read and approved the final manuscript.

# Declaration of competing interest

The authors declare that research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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