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Research paper

White matter microstructural differences across major depressive disorder, bipolar disorder and schizophrenia: A tract-based spatial statistics study

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A B S T R A C T

Background: White matter abnormalities have been implicated in mental disorders including major depressive disorder (MDD), bipolar disorder (BD), and schizophrenia (SZ); however, the shared and distinct white matter integrity across mental disorders is still unclear.
Methods: A total of 290 participants (MDD = 85, BD = 42, SZ = 68, and healthy controls = 95) were included in the present study. Tract-based spatial statistics were performed to measure fractional anisotropy (FA) and characterize shared and distinguishing white matter changes across mental disorders.
Results: We found that decreased FA converged across MDD, BD and SZ in the body and genu of the corpus callosum, bilateral anterior and posterior corona radiata, and right superior corona radiata. By contrast, diagnosis-specific effect was only found in MDD in the anterior portion of anterior corona radiata.
Limitations: The small and imbalanced sample size, and possible confounding effects of medication.
Conclusions: Our findings suggest that abnormally reduced white matter integrity in the interhemispheric and thalamocortical circuit could be consistently involved in the pathogenesis of MDD, BD and SZ.

1. Introduction

Major depressive disorder (MDD), bipolar disorder (BD) and schizophrenia (SZ) are severe and highly complex mental disorders with remarkable heterogeneous symptoms characterized by combinations of dysfunctions in thoughts, perceptions, emotions and behavior. Studies illustrate mental disorders are substantial causes of the global growing disability and mortality (Vigo et al., 2016; Walker et al., 2015).

Although MDD, BD and SZ are clinically distinct disorders, convergent evidence suggests that there are no clear distinguishing borders between diagnostic categories for patients with mental disorders (Baker et al., 2019). Specifically, patients show overlapping clinical characteristics (Keshavan et al., 2011), including disturbances in mood, perception, and cognitive deficits. They share transcriptional dysregulation at molecular level (Gandal et al., 2018), and the molecular convergence is associated with the substantial overlap of genetic factors that increase risk for mental disorders (Cross-Disorder Group of the Psychiatric Genomics Consortium 2013). Consistent with behavioral and genetic studies, neuroimaging research suggests that common neurobiological alterations may be implicated in mental disorders, including neuroanatomical (Goodkind et al., 2015) and functional (Yang et al., 2019; Xia et al., 2018; Wei et al., 2018) abnormalities across MDD, BD and SZ. For instance, Goodkind et al. identified a shared pattern of gray matter loss in the anterior insula and dorsal anterior cingulate across psychiatric disorders using voxel-based morphometry meta-analysis studies (Goodkind et al., 2015). Another research group

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examined local (Wei et al., 2018) and large-scale (Xia et al., 2018) functional connectivity and identified shared and distinct functional features across MDD, BD and SZ.

Compared to transdiagnostic gray matter atrophy and functional connectivity disruption studies, there are no structural connectivity studies across three mental disorders that we are aware of. Structural connectivity may serve as the structural substrate of information flow over which the functional networks can unfold, and provide highly valuable insights into the neurobiological mechanisms underlying disorders. Mental disorders are reported to be abnormality of fiber-track connectivity (Pasternak et al., 2018), characterized by disruptions of afferent and efferent connections between regional neocortical areas associated with establishing and pruning of axonal connections (Garey et al., 1998). Diffusion magnetic resonance imaging (dMRI) provides microstructural information about white matter integrity and coherence by assessing fractional anisotropy (FA). Tract-based spatial statistics (TBSS) allows for the detection of subtle fiber tract changes across the whole brain. The TBSS method has been used to provide accurate voxel-based evidence of structural dysconnectivity in MDD (Won et al., 2016; Korgaonkar et al., 2011), BD (Bauer et al., 2015; Benedetti et al., 2011) and SZ (Kelly et al., 2018; Lee et al., 2013), with consistent reports of aberrant white matter integrity in fiber tracts such as corpus callosum (CC) (Lee et al., 2013; Benedetti et al., 2011; Won et al., 2016) and corona radiata (CR) (Kelly et al., 2018; Benedetti et al., 2011; Xiao et al., 2015). In addition, conjunction analyses of two diagnostic disorders also revealed shared white matter abnormalities between MDD and BD (Wise et al., 2016), or between SZ and BD (Squarcina et al., 2017; Cui et al., 2011; Li et al., 2014). For instance, the CC is consistently altered in both MDD and BD (Wise et al., 2016), and in both SZ and BD (Squarcina et al., 2017; Li et al., 2014) in previous studies.

The aim of the present study is to examine the convergent and divergent white matter microstructural changes across MDD, BD and SZ using TBSS. We hypothesized that, compared with healthy controls, patients with MDD, BD and SZ would show a transdiagnostic pattern of white matter alterations in CC and CR.

2. Materials and methods

2.1. Participants

We recruited patients with MDD ($n = 85$), BD ($n = 42$), and SZ ($n = 68$) from Second Affiliated Hospital of Xinxiang Medical University between March 2013 and October 2017. MDD, BD and SZ were confirmed by psychiatrists using the Structured Clinical Interview for DSM-IV-TR (Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition, Text Revision) Axis I Disorders (SCID-I, patient edition). The exclusion criteria included a diagnosis of other mental illness, organic causes of depression include heart, liver or kidney disease. The Beck Depression Scale (BDI) (Beck et al., 1961) and Beck Anxiety Scale (BAI) (Beck et al., 1988) were used to assess symptoms in patients with MDD and BD. The scale of Young Mania Rating Scale (YMRS) (Young et al., 1978) was used to assess the symptoms in BD patients. BD patients were further diagnosed into mania ($n = 25$) and depression ($n = 15$) subtypes based on BDI and YMRS scales at the time of the scan. Two BD patients had no subtype diagnoses because of missing BDI and YMRS scales. SZ patients were evaluated using the Positive and Negative Syndrome Scale (PANSS) (Kay et al., 1987). A group of 95 healthy controls (HCs) were recruited from the local community through advertisements. None of the HCs had a history of mental or neurological disease. All participants were right-handed, and had no contraindications to magnetic resonance imaging (MRI) scanning. The study was approved by the Ethics Committee of the Second Affiliated Hospital of Xinxiang Medical University and all participants gave written informed consent.

2.2. Image acquisition

MRI scans were acquired by a 3 Tesla Siemens Verio scanner at the Second Affiliated Hospital of Xinxiang Medical University. The participants were instructed to be awake, keep their eyes closed and not to think about anything in particular during the scan. The acquisition parameters for dMRI data included: repetition time (TR)/echo time (TE) = 8400/91 ms, thickness/gap = 3.0/0 mm, flip angle = 90°, matrix size = 128 × 128 × 50, voxel size = 2 × 2 × 3 mm^3. For each participant, a total of 65 vol were acquired, including 1 non-diffusion-weighted volumes ($b = 0\ s/mm^2$) and 64 non-collinear gradient directions ($b = 1000\ s/mm^2$). Sagittal T1-weighted MRI scans were obtained using the following optimized parameters: TR/TE = 2530/2.43 ms, flip angle = 7°, FOV = 256 × 256 mm^2, matrix size = 256 × 256, 192 sagittal slices, voxel size = 1 × 1 × 1 mm^3.

2.3. Diffusion MRI data preprocessing

The preprocessing of dMRI data was performed using the FMRIB's Software Library (FSL, version 5.0.10, https://fsl.fmrib.ox.ac.uk/fsl). Preprocessing included the following stages. Firstly, eddy current and head movement were corrected by registering all diffusion weighted images to the non-diffusion-weighted image (b0 image). Brain extraction was then performed on the non-diffusion-weighted image to remove non-brain structures and create each participant's brain mask. Finally, the FA maps for each participant were estimated using the FSL FDT tool.

2.4. Voxelwise TBSS

Voxelwise statistical analyses of FA images were performed using the TBSS toolbox in FSL. In brief, the FA images of all participants were spatially transformed to a 1 × 1 × 1 mm^3 FMRIB58 FA standard space by a nonlinear registration algorithm. A mean FA image was then created by averaging the nonlinearly registered FA images of all participants. A template FA skeleton which represented the center of the white matter fiber bundle of this cohort of participants was extracted from the mean FA image. Only voxels with FA greater than 0.30 on the skeleton were included in statistical analysis, because this could exclude the interference of gray matter and cerebrospinal fluid. Individual FA skeleton images in the standard space were then generated based on the template FA skeleton mask.

2.5. Statistical analysis

We analyzed the main effects of groups (i.e. MDD, BD, SZ, and HC) using one-way ANCOVA at each voxels on the individual FA skeleton images, controlling the effects of age and gender. To correct for multiple comparisons, a family-wise error (FWE) approach with a threshold of $p < 0.05$ was performed on the threshold-free cluster enhancement statistic image (5000 random permutations). Subsequent post-hoc comparisons between each pair of four groups were performed in the regions with significant group effects and cluster size >50, using general linear model controlling for the effects of age and gender with FWE threshold of $p < 0.05$.

The regions showing significant group differences were then located and labeled using JHU ICBM white matter atlas, and the median FA values within each region were calculated for each participant. We used the median values of the FA rather than the arithmetic mean because the median has been reported to be more robust to noise, registration, and segmentation errors (Xie et al., 2019). We used linear mixed model (LMM) to test the effects of symptom severity (measured by BDI, BAI, YMRS, PANSS scales in MDD, BD and SZ), duration of illness, and medication status for MDD, BD and SZ, respectively. LMM is a commonly used method to measure the relationship between a dependent variable (e.g., FA) and independent variables (e.g., symptom/duration/

Table 1
Demographic characteristics and clinical scales of participants.

	MDD (n = 85)	BD (n = 42)	SZ (n = 68)	HC (n = 95)	F/χ^2 values	P-values
Age, years	32.44 (8.79)	32.88 (8.79)	28.58 (4.66)	30.21 (6.85)	4.77	.003[a]
Male	51 (60.0%)	19 (45.2%)	38 (55.9%)	48 (50.5%)	3.08	.379
Education, years	11.5 (3.60) (n = 84)	10.50 (3.83) (n = 40)	11.46 (2.75) (n = 63)	13.80 (2.90) (n = 94)	13.75	<.001
Age of onset, years	29.18 (9.32) (n = 84)	26.25 (8.88) (n = 40)	24.40 (4.85) (n = 63)	–	6.63	.002
Duration, months	40.81 (55.87) (n = 84)	77.10 (77.16) (n = 40)	43.83 (43.67) (n = 63)	–	5.86	.003
Medication, yes	66 (77.6%)	37 (88.1%)	42 (61.8%)	–	10.30	.006
Antipsychotics, yes	5 (5.9%)	24 (57.1%)	42 (61.8%)	–	60.89	<.001
Antidepressants, yes	64 (75.3%)	15 (35.7%)	0	–	89.38	<.001
Mood stabilizer, yes	1 (1.2%)	24 (57.1%)	0	–	94.13	<.001
BDI	18.97 (7.24) (n = 66)	10.95 (11.60) (n = 38)	–	–	19.26	<0.001
BAI	39.69 (12.12) (n = 48)	31.87 (13.82) (n = 39)	–	–	9.24	.003
YMRS	–	24.67 (10.96) (n = 39)	–	–	–	–
PANSS positive	–	–	22.80 (3.79) (n = 64)	–	–	–
PANSS negative	–	–	19.97 (5.22) (n = 64)	–	–	–

Data presented as either n (%) or mean (SD).
BAI, Beck Anxiety Inventory; BD, Bipolar disorder; BDI, Beck Depression Inventory; HC, Healthy control; MDD, Major depressive disorder; PANSS, Positive and Negative Syndrome Scale; SZ, Schizophrenia; YMRS, Young Mania Rating Scale.
[a] P-values of post hoc results for age: MDD vs. HC, BD vs. HC, and SZ vs. HC, all $p > 0.05$; MDD vs. SZ, $p = 0.001$; BD vs. SZ, $p = 0.001$.

medication, age, and gender) (Yan et al., 2019). Both voxelwise and ROI-based analyses were performed in the regions with significant main effects of group for FA across MDD, BD, SZ and HC groups. For FA values in a voxel or a ROI, we used MATLAB's command fitlme to test the model: y ~ 1 + Symptom + Age + Gender. We obtained t and p values for the fixed effect of Symptom, and a FDR approach was used to correct for multiple comparisons. In order to examine the effect of duration of illness or medication status, we replaced Symptom with Duration or Medication (yes/no, assessed at time of scan) in the LMM model.

3. Results

3.1. Demographic and clinical characteristics

Demographic and clinical characteristics of MDD, BD, SZ and HC groups are presented in Table 1. There were no statistically significant differences in age or gender distribution between any patient group and HCs, but both the MDD and BD groups were older than SZ group (post hoc results for MDD vs SZ, $p = 0.001$; BD vs SZ, $p = 0.001$). All of the MDD, BD and SZ groups had fewer years of education compared with HC groups, but no significant differences in years of education were observed among MDD, BD, and SZ groups. Significant differences were also observed in duration of illness, age of onset, and medication status across patient groups. Detailed characteristics of BD subtypes are presented in Supplementary Table 1. There were no statistically significant differences in age, gender distribution, years of education, age of onset, duration of illness, or medication status between two BD groups.

3.2. Fractional anisotropy comparisons

We found main effects of group for FA across MDD, BD, SZ and HC groups, mainly in the body, genu and splenium of CC, and bilateral anterior, posterior and superior CR (Fig. 1A and Supplementary Fig. 1A). Post hoc analyses revealed significant reduced FA in MDD (Fig. 1B), BD (Fig. 1C), and SZ (Fig. 1D) groups compared with HCs (see also Supplementary Figs. 1B–D). Specifically, all three mental disorders showed reduced FA in the body, genu, and splenium of CC, and anterior, posterior and superior CR, and MDD group exhibited a more widespread implicated pattern than BD and SZ patients. Consistent FA decreases in patients were found in the body and genu of CC, bilateral anterior and posterior CR, and right superior CR (Fig. 1E and Table 2). Bar plots of the white matter regions with consistent reduced FA were shown in Fig. 2. Compared with SZ group, the MDD group had significantly reduced FA measurements in bilateral anterior portion of the anterior CR (Fig. 3). In contrast, the overlapping region with decreased FA across MDD, BD and SZ groups was mainly in the posterior portion of the anterior CR.

The average median FA values of three mental disorders were generally a gradient trend in the body and genu CC and bilateral anterior CR, with the SZ group has greater FA than the BD group, while the BD group has greater FA than the MDD group (MDD < BD < SZ; Fig. 2). The effects of symptom severity and duration of illness did not survive correction for multiple comparisons in either voxelwise or ROI-based analyses. We found medicated MDD patients had significantly lower FA values than non-medicated MDD patients in the left anterior corona radiata (cluster size = 78, Supplementary Fig. 2). In addition, no significant differences were found between mania and depression subtypes in BD patients in either voxelwise or ROI-based analyses.

4. Discussion

In the present study, we identified a transdiagnostic pattern of white matter microstructural alterations in the body and genu of CC and bilateral anterior, posterior, and right superior CR across patients with MDD, BD and SZ. A gradient in the common alterations were observed in FA with MDD < BD < SZ. In contrast to the shared structural dysconnectivity, diagnosis-specific effects were only found in MDD in the anterior portion of anterior CR. To the best of our knowledge, this is the first study employing TBSS to investigate the global white matter alterations to identify transdiagnostic abnormalities across major mental disorders using dMRI.

We found convergent white matter loss in the CC including the body and genu across MDD, BD and SZ. White matter FA differences in CC are consistently reported in MDD (Wise et al., 2016; Jiang et al., 2017), BD (Wise et al., 2016; Yang et al., 2018) and SZ (Kelly et al., 2018). Specifically, reduced FA in CC especially the body and genu, showed greatest effects in SZ in a large-scale prospective meta-analysis study (Kelly et al., 2018). The CC as the largest white matter tract, connects the bilateral cerebral hemisphere and enables communication between hemispheres. The genu of the CC in particular connects the prefrontal cortex and was also identified as the shared reduced FA between BD and SZ (Dong et al., 2017), and between BD and MDD (Wise et al., 2016). Aberrant white matter microstructure in genu and body of CC in our findings suggests abnormal interhemispheric information flow play a role in the pathogenesis of MDD, BD and SZ. Our results suggest a common structural substrate of interhemispheric connectivity across major mental disorders.

We identified consistent white matter abnormalities across MDD, BD, and SZ in CR, including anterior, posterior and superior portions.

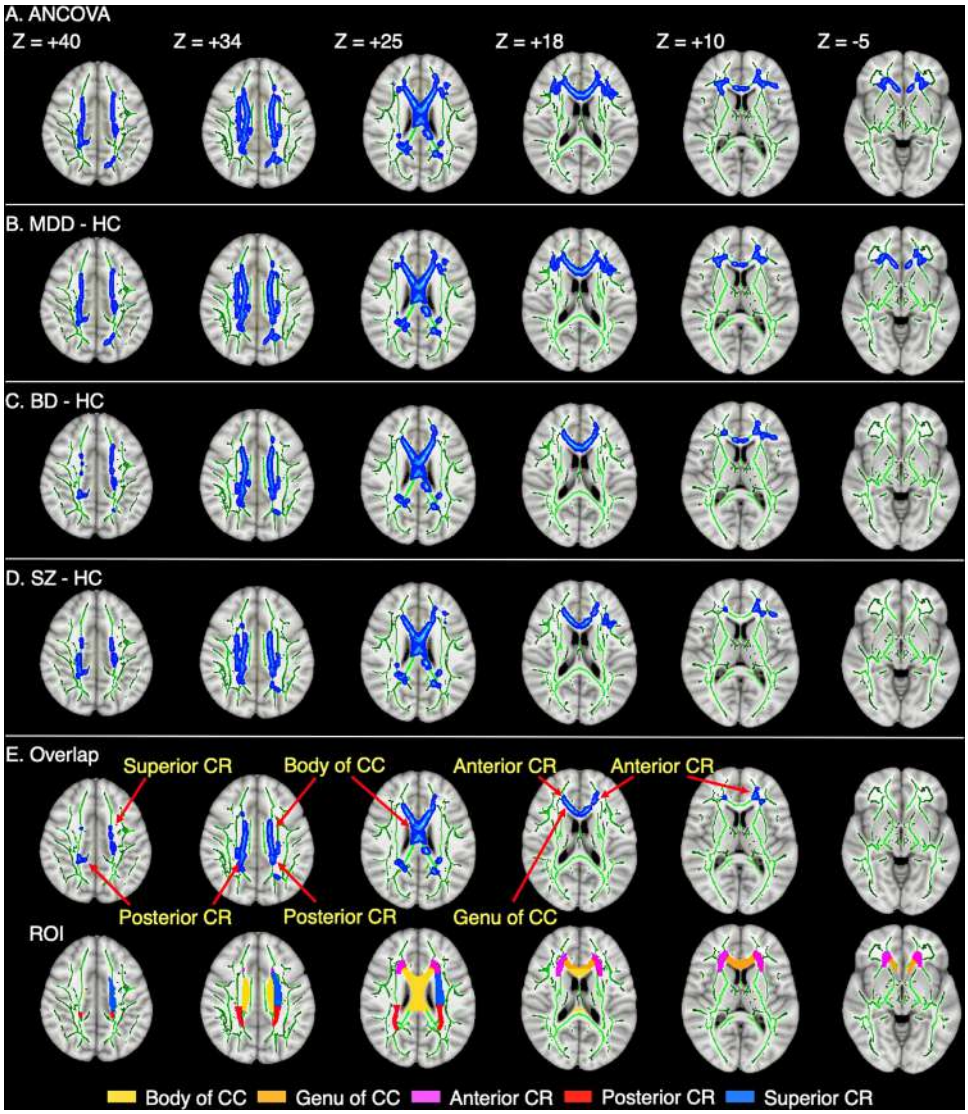

Fig. 1. Voxel-wise TBSS analysis results of fractional anisotropy (FA) images across mental disorders and healthy controls (HCs). A, significant fractional anisotropy differences across major depressive disorder (MDD), bipolar disorder (BD), schizophrenia (SZ) and HCs ($p < 0.05$, FWE corrected based on the threshold-free cluster enhancement statistic image). Post hoc analyses revealed significant FA reductions in MDD (B), BD (C), and SZ (D) compared with HCs. E, the overlapping regions across B, C, and D. The corresponding JHU ICBM white matter ROIs were shown in the last row. Green represents the mean white matter skeleton of all participants. The left side of the image corresponds to the right hemisphere of the brain. ANCOVA, analysis of covariance; CC, corpus callosum; CR, corona radiata.

CR includes descending and ascending fibers with the thalamus and cerebral cortex and is thought to be involved in a variety of functions, including emotion regulation (Drevets et al., 2008), executive function (Etkin et al., 2013) and cognition. These are typical transdiagnostic domain of impairments across major disorders (Sloan et al., 2017). CR is involved in the top-down regulation systems that organizing emotion processing which is closely related to medial prefrontal cortex and anterior cingulate that have been consistently implicated in previous morphological (Goodkind et al., 2015) and functional (Wei et al., 2018) studies. CR is also in the pathway with anterior insula (Nomi et al., 2017), which has been identified as a region with consistent gray matter loss across mental illness (Goodkind et al., 2015), and associated with emotional and executive dysfunction in disorders. The results of previous studies suggest that FA reductions in CR were detected in MDD (Cole et al., 2012), BD (Benedetti et al., 2011) and SZ (Kelly et al., 2018), and dMRI measures in CR are associated with speed of

Table 2
Regions showing consistent reduced fractional anisotropy for MDD, BD, and SZ patients compared with healthy controls (i.e., overlap), and the regions showing significant fractional anisotropy differences between SZ and MDD.

	Regions	Cluster size (mm^3)	Peak MNI coordinate			*P*-value (minimum)
			X	*Y*	*Z*	
Overlap	Body of corpus callosum	2016	4	18	18	.0046
	Genu of corpus callosum	303	−16	24	23	.0044
	L Anterior corona radiata	365	−17	35	12	.0044
	R Anterior corona radiata	216	17	22	25	.0055
	L Posterior corona radiata	190	−19	−30	34	.0079
	R Posterior corona radiata	282	20	−49	30	.0055
	R Superior corona radiata	50	17	15	30	.0055
SZ - MDD	L Anterior corona radiata	50	−25	37	0	.0408
	R Anterior corona radiata	393	25	32	−4	.0210

BD, bipolar disorder; L, left; MDD, major depressive disorder; MNI, Montreal Neurological Institute; R, right; SZ, schizophrenia.

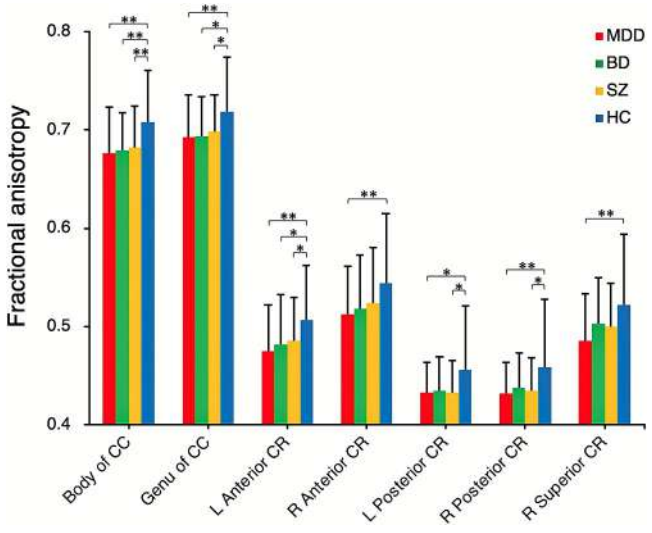

Fig. 2. The overlapping regions with consistent reduced fractional anisotropy for major depressive disorder, bipolar disorder, and schizophrenia compared with healthy controls. CC, corpus callosum; CR, corona radiata; L, left; R, right; *, $p < 0.05$; **, $p < 0.01$, after false discovery rate correction for multiple comparisons.

information processing and working memory performance in patients with mental disorders (Poletti et al., 2015). In particular, the anterior CR which contains reciprocal connections between the anterior thalamus and prefrontal cortex plays a role in neural circuitry of emotion regulation (Goodkind et al., 2015). Consistent with previous findings, we identified the bilateral anterior CR, especially the posterior portion of anterior CR consistently implicated in MDD, BD and SZ, suggesting a common pattern of substrate shared by major mental disorders. In contrast to the convergent white matter integrity abnormalities in the posterior portion of anterior CR, we found the MDD specific pattern in the bilateral anterior portion of the anterior CR, suggesting that the anterior portion of anterior CR may be a potential biomarker for the identification of MDD. In addition, we identified a gradient of FA alterations in body and genu of CC and bilateral ACR among disorders, with MDD having the worst FA integrity and BD in the middle between MDD and SZ. This is in accordance with previous report of SZ has higher FA measures than bipolar disorder in the body of callosum (Kumar et al., 2015). A functional study examined response to the negative feedback processing revealed BD patients had better signal changes than MDD in lateral prefrontal cortex (Tavares et al., 2008). The present study did not find significant correlations between FA reductions and symptom severity measures, similar to previous studies (Squarcina et al., 2017; Kelly et al., 2018).

There are several limitations of the present study that need to be considered. First, the number of patients included in the analysis is relatively small and imbalanced, and the validity of our findings remains uncertain without replication in larger samples. Second, the cross-sectional cross-diagnostic design cannot rule out the potential medication effects on dMRI measures. Therefore, the observed differences may be possibly confounded by medication status across diagnoses. Future studies are needed to confirm our findings in treatment-naïve patients with disorders. In addition, our investigation of the effects of medication status in MDD patients revealed that the medicated MDD patients had significantly lower FA values than non-medicated MDD patients in the left anterior corona radiata. Our finding is consistent with previous studies that MDD patients taking antidepressants showed significantly reduced FA (Cole et al., 2012) or a trend of reduction (Bessette et al., 2014). Another study also found that the use of any antidepressants in the elderly was associated with worsening white matter (Steffens et al., 2008). Our findings suggest a modification of white matter integrity in medicated MDD patients, however, the present study is limited in the specification of type, dosage and duration of taking antidepressants. Future investigations are warranted to validate these findings in longitudinal designs in MDD patients.

In conclusion, the present study demonstrated a shared white matter loss in the boy and genu of CC and CR in MDD, BD and SZ patients. The results provide insight into the similarities and differences of spatial patterns of white matter damage in major mental disorders. Our findings enhance our understanding for common neural substrate of interhemispheric and thalamocortical connectivity disruptions and provide insights to underlying neural mechanisms and the possibility interventions for mental disorders.

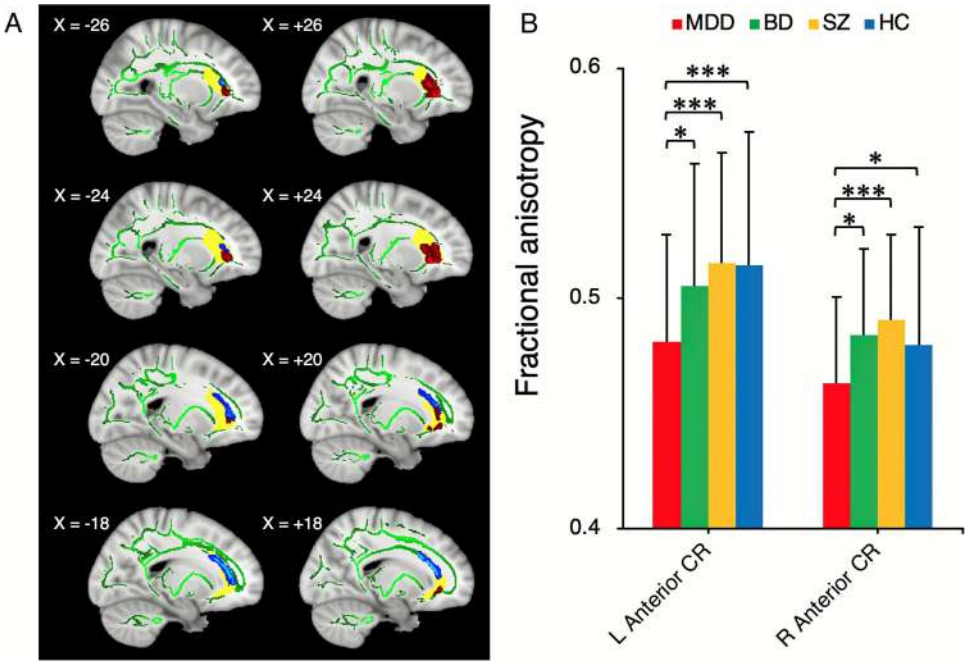

Fig. 3. FA differences between MDD and SZ groups. A, anterior portion of anterior CR showing significantly reduced FA in MDD patients compared with SZ patients (red), posterior portion of anterior CR showing consistently reduced FA for MDD, BD, and SZ patients compared with healthy controls (blue), and the region of interest of anterior CR (yellow). B, bar plots of bilateral anterior CR showing FA differences between MDD and SZ groups. CR, corona radiata; FA, fractional anisotropy; MDD, major depressive disorder; SZ, schizophrenia. *, $p < 0.05$; **, $p < 0.01$; ***, $p < 0.001$ after false discovery rate correction for multiple comparisons.

CRediT authorship contribution statement

Cui Yue: Conceptualization, Writing - original draft. **Dong Jiahao:** Data curation, Writing - original draft. **Yang Yongfeng:** Data curation. **Yu Hongyan:** Data curation. **Li Wenqiang:** Data curation. **Liu Yang:** Investigation. **Si Juanning:** Investigation. **Xie Sangma:** Data curation, Writing - original draft. **Sui Jing:** . **Lv Luxian:** Data curation. **Jiang Tianzi:** Conceptualization, Writing - original draft.

Declaration of Competing Interest

None.

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Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.jad.2019.09.029.

References

Baker, J.T., Dillon, D.G., Patrick, L.M., Roffman, J.L., Brady, R.O., Pizzagalli, D.A., et al., 2019. Functional connectomics of affective and psychotic pathology. Proc. Natl. Acad. Sci. USA 116 (18), 9050–9059.
Bauer, I.E., Ouyang, A., Mwangi, B., Sanches, M., Zunta-Soares, G.B., Keefe, R.S., et al., 2015. Reduced white matter integrity and verbal fluency impairment in young adults with bipolar disorder: a diffusion tensor imaging study. J. Psychiatr. Res. 62, 115–122.
Beck, A.T., Epstein, N., Brown, G., Steer, R.A., 1988. An inventory for measuring clinical anxiety: psychometric properties. J. Consult. Clin. Psychol. 56 (6), 893.
Beck, A.T., Ward, C., Mendelson, M., Mock, J., Erbaugh, J., 1961. Beck depression inventory (BDI). Arch. Gen. Psychiatry 4 (6), 561–571.
Benedetti, F., Yeh, P.-H., Bellani, M., Radaelli, D., Nicoletti, M.A., Poletti, S., et al., 2011. Disruption of white matter integrity in bipolar depression as a possible structural marker of illness. Biol. Psychiatry 69 (4), 309–317.
Bessette, K.L., Nave, A.M., Caprihan, A., Stevens, M.C., 2014. White matter abnormalities in adolescents with major depressive disorder. Brain Imaging Behav. 8 (4), 531–541.
Cole, J., Chaddock, C.A., Farmer, A.E., Aitchison, K.J., Simmons, A., McGuffin, P., et al., 2012. White matter abnormalities and illness severity in major depressive disorder. Br. J. Psychiatry 201 (1), 33–39.
Cross-Disorder Group of the Psychiatric Genomics Consortium, 2013. Identification of risk loci with shared effects on five major psychiatric disorders: a genome-wide analysis. Lancet 381 (9875), 1371–1379.
Cui, L., Chen, Z., Deng, W., Huang, X., Li, M., Ma, X., et al., 2011. Assessment of white matter abnormalities in paranoid schizophrenia and bipolar mania patients. Psychiatry Res. 194 (3), 347–353.
Dong, D., Wang, Y., Chang, X., Jiang, Y., Klugah-Brown, B., Luo, C., et al., 2017. Shared abnormality of white matter integrity in schizophrenia and bipolar disorder: a comparative voxel-based meta-analysis. Schizophr. Res. 185, 41–50.
Drevets, W.C., Price, J.L., Furey, M.L., 2008. Brain structural and functional abnormalities in mood disorders: implications for neurocircuitry models of depression. Brain Struct.Funct. 213 (1–2), 93–118.
Etkin, A., Gyurak, A., O'Hara, R., 2013. A neurobiological approach to the cognitive deficits of psychiatric disorders. Dialogues Clin. Neurosci. 15 (4), 419.
Gandal, M.J., Haney, J.R., Parikshak, N.N., Leppa, V., Ramaswami, G., Hartl, C., et al., 2018. Shared molecular neuropathology across major psychiatric disorders parallels polygenic overlap. Science 359 (6376), 693–697.
Garey, L., Ong, W., Patel, T., Kanani, M., Davis, A., Mortimer, A., et al., 1998. Reduced dendritic spine density on cerebral cortical pyramidal neurons in schizophrenia. J. Neurol. Neurosurg. Psychiatry 65 (4), 446–453.
Goodkind, M., Eickhoff, S.B., Oathes, D.J., Jiang, Y., Chang, A., Jones-Hagata, L.B., et al., 2015. Identification of a common neurobiological substrate for mental illness. JAMA Psychiatry 72 (4), 305–315.
Jiang, J., Zhao, Y.-J., Hu, X.-Y., Du, M.-Y., Chen, Z.-Q., Wu, M., et al., 2017. Microstructural brain abnormalities in medication-free patients with major depressive disorder: a systematic review and meta-analysis of diffusion tensor imaging. J.Psychiatry Neurosci. 42 (3), 150.
Kay, S.R., Fiszbein, A., Opler, L.A., 1987. The positive and negative syndrome scale (PANSS) for schizophrenia. Schizophr. Bull. 13 (2), 261–276.
Kelly, S., Jahanshad, N., Zalesky, A., Kochunov, P., Agartz, I., Alloza, C., et al., 2018. Widespread white matter microstructural differences in schizophrenia across 4322 individuals: results from the ENIGMA Schizophrenia DTI Working Group. Mol. Psychiatry 23 (5), 1261.
Keshavan, M.S., Morris, D.W., Sweeney, J.A., Pearlson, G., Thaker, G., Seidman, L.J., et al., 2011. A dimensional approach to the psychosis spectrum between bipolar disorder and schizophrenia: the Schizo-Bipolar Scale. Schizophr. Res. 133 (1–3), 250–254.
Korgaonkar, M.S., Grieve, S.M., Koslow, S.H., Gabrieli, J.D., Gordon, E., Williams, L.M., 2011. Loss of white matter integrity in major depressive disorder: evidence using tract-based spatial statistical analysis of diffusion tensor imaging. Hum. Brain. Mapp. 32 (12), 2161–2171.
Kumar, J., Iwabuchi, S., Oowise, S., Balain, V., Palaniyappan, L., Liddle, P.F., 2015. Shared white-matter dysconnectivity in schizophrenia and bipolar disorder with psychosis. Psychol. Med. 45 (4), 759–770.
Lee, S.-H., Kubicki, M., Asami, T., Seidman, L.J., Goldstein, J.M., Mesholam-Gately, R.I., et al., 2013. Extensive white matter abnormalities in patients with first-episode schizophrenia: a diffusion tensor imaging (DTI) study. Schizophr. Res. 143 (2–3), 231–238.
Li, J., Kale Edmiston, E., Chen, K., Tang, Y., Ouyang, X., Jiang, Y., et al., 2014. A comparative diffusion tensor imaging study of corpus callosum subregion integrity in bipolar disorder and schizophrenia. Psychiatry Res. 221 (1), 58–62.
Nomi, J., Schettini, E., Broce, I., Dick, A., Uddin, L., 2017. Structural connections of functionally defined human insular subdivisions. Cereb. Cortex 28 (10), 3445–3456.
Pasternak, O., Kelly, S., Sydnor, V.J., Shenton, M.E., 2018. Advances in microstructural diffusion neuroimaging for psychiatric disorders. NeuroImage 182, 259–282.
Poletti, S., Bollettini, I., Mazza, E., Locatelli, C., Radaelli, D., Vai, B., et al., 2015. Cognitive performances associate with measures of white matter integrity in bipolar disorder. J. Affect. Disord. 174, 342–352.
Sloan, E., Hall, K., Moulding, R., Bryce, S., Mildred, H., Staiger, P.K., 2017. Emotion regulation as a transdiagnostic treatment construct across anxiety, depression, substance, eating and borderline personality disorders: a systematic review. Clin. Psychol. Rev. 57, 141–163.
Squarcina, L., Bellani, M., Rossetti, M.G., Perlini, C., Delvecchio, G., Dusi, N., et al., 2017. Similar white matter changes in schizophrenia and bipolar disorder: a tract-based spatial statistics study. PLoS One 12 (6), e0178089.
Steffens, D.C., Chung, H., Krishnan, K.R.R., Longstreth Jr., W., Carlson, M., Burke, G.L., 2008. Antidepressant treatment and worsening white matter on serial cranial magnetic resonance imaging in the elderly: the Cardiovascular Health Study. Stroke 39 (3), 857–862.
Tavares, J.V.T., Clark, L., Furey, M.L., Williams, G.B., Sahakian, B.J., Drevets, W.C., 2008. Neural basis of abnormal response to negative feedback in unmedicated mood disorders. NeuroImage 42 (3), 1118–1126.
Vigo, D., Thornicroft, G., Atun, R., 2016. Estimating the true global burden of mental illness. Lancet Psychiatry 3 (2), 171–178.
Walker, E.R., McGee, R.E., Druss, B.G., 2015. Mortality in mental disorders and global disease burden implications: a systematic review and meta-analysis. JAMA Psychiatry 72 (4), 334–341.
Wei, Y., Chang, M., Womer, F.Y., Zhou, Q., Yin, Z., Wei, S., et al., 2018. Local functional connectivity alterations in schizophrenia, bipolar disorder, and major depressive disorder. J. Affect. Disord. 236, 266–273.
Wise, T., Radua, J., Nortje, G., Cleare, A.J., Young, A.H., Arnone, D., 2016. Voxel-based meta-analytical evidence of structural disconnectivity in major depression and bipolar disorder. Biol. Psychiatry 79 (4), 293–302.
Won, E., Choi, S., Kang, J., Kim, A., Han, K., Chang, H., et al., 2016. Association between reduced white matter integrity in the corpus callosum and serotonin transporter gene DNA methylation in medication-naive patients with major depressive disorder. Transl. Psychiatry 6 (8), e866.
Xia, M., Womer, F.Y., Chang, M., Zhu, Y., Zhou, Q., Edmiston, E.K., et al., 2018. Shared and distinct functional architectures of brain networks across psychiatric disorders. Schizophr. Bul.l 45 (2), 450–463.
Xiao, J., He, Y., McWhinnie, C.M., Yao, S., 2015. Altered white matter integrity in individuals with cognitive vulnerability to depression: a tract-based spatial statistics study. Sci. Rep. 5, 9738.
Xie, S., Liu, B., Wang, J., Zhou, Y., Cui, Y., Song, M., et al., 2019. Hyperconnectivity in perisylvian language pathways in schizophrenia with auditory verbal hallucinations: a multi-site diffusion MRI study. Schizophr. Res. 210, 262–269.
Yan, C.-G., Chen, X., Li, L., Castellanos, F.X., Bai, T.-J., Bo, Q.-J., et al., 2019. Reduced default mode network functional connectivity in patients with recurrent major depressive disorder. Proc.Natl. Acad.Sci. 116 (18), 9078–9083.
Yang, C., Li, L., Hu, X., Luo, Q., Kuang, W., Lui, S., et al., 2018. Psychoradiologic abnormalities of white matter in patients with bipolar disorder: diffusion tensor imaging studies using tract-based spatial statistics. J. Psychiatry Neurosci. 44 (1), 32–44.
Yang, Y., Liu, S., Jiang, X., Yu, H., Ding, S., Lu, Y., et al., 2019. Common and specific functional activity features in schizophrenia, major depressive disorder, and bipolar disorder. Front. Psychiatry 10.
Young, R.C., Biggs, J.T., Ziegler, V.E., Meyer, D.A., 1978. A rating scale for mania: reliability, validity and sensitivity. Br. J. Psychiatry 133 (5), 429–435.