NeuroImage: Clinical 20 (2018) 875–882

Contents lists available at ScienceDirect

NeuroImage: Clinical

journal homepage: www.elsevier.com/locate/ynicl

Disruption of superficial white matter in the emotion regulation network in bipolar disorder

Shufei Zhang[a,1], Ying Wang[b,c,**,1], Feng Deng[a], Shuming Zhong[d], Lixiang Chen[a], Xiaomei Luo[b,c], Shaojuan Qiu[b,c], Ping Chen[a], Guanmao Chen[b,c], Huiqing Hu[a], Sunkai Lai[d], Huiyuan Huang[a], Yanbin Jia[d], Li Huang[b,c], Ruiwang Huang[a,*]

[a] Center for the Study of Applied Psychology, Key Laboratory of Mental Health and Cognitive Science of Guangdong Province, School of Psychology, Institute for Brain Research and Rehabilitation, South China Normal University, Guangzhou 510631, PR China
[b] Institute of Molecular and Functional Imaging, Jinan University, Guangzhou 510630, China
[c] Medical Imaging Center, First Affiliated Hospital of Jinan University, Guangzhou 510630, China
[d] Department of Psychiatry, First Affiliated Hospital of Jinan University, Guangzhou 510630, China

ARTICLE INFO

Keywords:
Deep white matter (DWM)
Diffusion tensor imaging
Cortico-cortical connection
Tract-based spatial statistics (TBSS)
Probabilistic tractography

ABSTRACT

Bipolar disorder (BD) is characterized by emotion dysregulation and involves changes in the gray matter (GM) and white matter (WM). Although previous diffusion tensor imaging (DTI) studies reported changes in the diffusion properties of the deep WM (DWM) in BD patients, the diffusion properties of the superficial WM (SWM) are rarely investigated. In this study, we tried to determine whether the diffusion parameters of the SWM were altered in BD patients compared to controls and whether the changes were associated with the disrupted emotion regulation of the BD patients. We collected DTI data from 37 BD patients and 42 gender- and age-matched healthy controls (HC). Using probabilistic tractography, we defined a population-based SWM mask based on all the subjects. After performing the tract-based spatial statistical (TBSS) analyses, we identified the SWM areas in which the BD patients differed from the controls. This study showed significantly reduced fractional anisotropy in the SWM (FA_{SWM}) in the BD patients compared to the HC in the bilateral dorsolateral prefrontal cortex (dlPFC), ventrolateral prefrontal cortex (vlPFC), medial prefrontal cortex (mPFC), and the left parietal cortex. Moreover, compared to the controls, the BD patients showed significantly increased mean diffusivity (MD_{SWM}) and radial diffusivity (RD_{SWM}) in the SWM in the right frontal cortex. This study presents altered cortico-cortical connections proximal to the regions related to the emotion dysregulation of BD patients, which indicated that the SWM may serve as the brain's structural basis underlying the disrupted emotion regulation of BD patients. The disrupted FA_{SWM} in the parietal cortex may indicate that the emotion dysregulation in BD patients is related to the cognitive control network.

1. Introduction

Bipolar disorder (BD) (Chang et al., 2013) is characterized by dysfunction in emotion regulation (Phillips and Swartz, 2014), which refers to the ability of an individual to modulate their response to emotional stimuli (Frank et al., 2014). Dysregulation of the emotions may lead to mood disorders (Townsend et al., 2013). Previous studies revealed a neural circuit (Phillips and Swartz, 2014; Phillips et al., 2008), comprising cortical regions that include the ventrolateral prefrontal cortex (vlPFC), dorsolateral prefrontal cortex (dlPFC), and medial prefrontal cortex (mPFC) as well as subcortical regions, including the amygdala and striatum, which may underlie disrupted emotion

Abbreviations: FA_{SWM}, FA, fractional anisotropy; MD_{SWM}, MD, mean diffusivity; RD_{SWM}, RD, radial diffusivity; AD_{SWM}, AD, axonal diffusivity measured in the SWM; WM, white matter; GM, gray matter; HAMD, Hamilton Depression Scale; YMRS, Young Mania Rating Scale; BD, bipolar disorder; HC, healthy controls; dlPFC, dorsolateral prefrontal cortex; vlPFC, ventrolateral prefrontal cortex; mPFC, medial prefrontal cortex; RMF, rostral middle frontal gyrus; SF, superior frontal gyrus; RAC, rostral anterior cingulate gyrus; IP, inferior parietal gyrus; SP, superior parietal gyrus; SM, supramarginal gyrus; Op, pars opercularis gyrus; Tr, pars triangularis gyrus; PoC, postcentral gyrus; PrC, precentral gyrus; CMF, caudal middle frontal gyrus; LOF, lateral orbitofrontal gyrus.

* Corresponding author.
** Corresponding author at: Institute of Molecular and Functional Imaging, Jinan University, Guangzhou 510630, China.
E-mail addresses: johneil@vip.sina.com (Y. Wang), ruiwang.huang@gmail.com (R. Huang).
[1] These authors contributed equally to this work.

https://doi.org/10.1016/j.nicl.2018.09.024
Received 5 March 2018; Received in revised form 3 August 2018; Accepted 25 September 2018
Available online 26 September 2018

regulation in BD patients. Recent meta-analyses (Zilverstand et al., n.d.; Buhle et al., 2014) that summarized previous studies of emotion regulation suggested that this emotion regulatory network largely overlaps with the cognitive control network and indicated that abnormalities in the parietal regions, especially in the inferior parietal (IP) and superior parietal (SP) gyrus, may also indicate a deficit in emotion regulation.

Although the pathology of BD remains unknown, white matter (WM) abnormality is believed to be related to the disease mechanism (Mahon et al., 2010). Brain WM can be classified into two systems, the superficial WM (SWM) and the deep WM (DWM), based on differences in their morphological features, including size, arrangement, and distribution (Oishi et al., 2008). WM studies in BD have primarily considered the DWM, which comprises large WM bundles and enables long-range connections between gray matter (GM) regions. In contrast, the SWM enables local connections between cortico-cortical regions. The SWM is located below the cortex (Oishi et al., 2008) and consists of short cortico-cortical fibers, such as U-shaped and intra-lobar fibers (Nazeri et al., 2013).

Although less is known about the specific functions of the SWM, several studies have indicated that the SWM is related to human cognitive functions. For example, Nazeri et al. found that the SWM contributes to cognitive performance in patients with schizophrenia (Nazeri et al., 2013) and in aging populations (Nazeri et al., 2015). Recently, Liu et al. (Liu et al., 2016) reported that in temporal lobe epilepsy the SWM serves as an important link between the functional and structural networks. These findings suggest an important role for the SWM, but an effective tractography for SWM fibers has not yet been fully identified.

Because of the complexity of the brain's cortical folding patterns (Chen et al., 2013; Nie et al., 2012), compared to the DWM, the SWM is more complex, which impede reconstructing long-range connections near the cortical regions (Reveley et al., 2015) using tractography. For example, the fractional anisotropy (FA) and curvature measured at the white/gray matter boundary (WGB) are respectively lower and sharper than those measured in the DWM. Additionally, in a given fiber bundle, it is difficult to distinguish between the fibers (Nazeri et al., 2013) that belong to the DWM and those that belong to the SWM. However, with more advanced fiber-tracking algorithms (Behrens et al., 2007), researcher can use “waypoint mask” or “exclusion mask” to constrain fibers to those near the cortex and remove the long-range fibers passing through the exclusion regions, if the seeds were selected at the WGB.

In this study, our goals were to determine whether the SWM is altered in BD patients compared to healthy controls (HC) and to determine whether these SWM alterations are associated with the disrupted emotion regulation of BD patients. In the calculations, we adopted probabilistic tractography (Behrens et al., 2007) to reconstruct a population-based SWM mask and used a tract-based spatial statistics (TBSS) (Smith et al., 2006) analysis to assess the differences of diffusion parameters in the SWM regions between the BD patients and the HC group.

2. Methods

2.1. Subjects

Thirty-seven BD subjects were recruited from the First Affiliated Hospital of Jinan University (AHJU), Guangzhou. The eligible subjects for this study were right-handed, aged 18–55 years old, and able to read and write. All the patients (26 M/11 F, aged 18–51 years old) completed the Young Mania Rating Scale (YMRS) (Young et al., 1978) and the Hamilton Depression Scale (HAMD) (Whisman et al., 1989). The YMRS was used to measure the manic degree of the BD patients in the week before the scan and the HAMD was used to detect each individual's depression state. The inclusion criteria for the BD group were (i) no long-term history of medication usage and (ii) a YMRS score < 12 and HAMD score > 21. The exclusion criteria for the patients were as follows: patients with other comorbid DSM-IV Axis-I psychiatric disorders or a history of neurological disorders, organic brain disorders, cardiovascular diseases, pregnancy, and alcohol or substance abuse. We also recruited forty-two healthy subjects (26 M/16 F, aged 18–52 years old) as the control group in the hospital. The exclusion criteria for the HC were same as that of the BD patients. In addition, to remove comorbidities we excluded subjects who had a history of or first-degree relatives with psychiatric illness. Table 1 lists the demographic characteristics of the BD patients and the HC group and the clinical performance of the BD patients. This study was approved by the Institutional Review Board of the First Affiliated Hospital of Jinan. Written informed consent was obtained from each subject prior to the study.

Table 1
Demographic characteristics of the patients with bipolar disorder (BD) and the healthy controls (HC).

Parameter	BD (n = 37)	HC (n = 42)	p-value (two-tailed)
Gender	26 M/11 F	26 M/16 F	0.483[a]
Age (years old)	26.3 ± 8.5	27.6 ± 9.0	0.515[b]
Education level (years)	13.7 ± 2.3	15.3 ± 2.5	0.004[**],[c]
Disease exacerbations (times)	3.0 ± 1.9	N/A	
Onset age (years old)	21.7 ± 10.6	N/A	
Duration time (months)	49.6 ± 61.4	N/A	
HAMD	28.8 ± 6.0	N/A	
YMRS	3.0 ± 2.9	N/A	

Abbreviations: HAMD, Hamilton Depression Scale; YMRS, Young Mania Rating Scale.
[a] The p-value was obtained from a χ^2-test.
[b] The p-value was obtained from a two-sample t-test.
[c] The p-value was obtained from a two-sample t-test.
[**] p-value < .01.

2.2. Data acquisition

All MRI data were acquired on a 3 T GE MR750 scanner with 8-channel head coil. The DTI data were obtained using a single-shot diffusion-weighted EPI sequence with the following parameters: repetition time (TR) = 8, 000 ms, echo time (TE) = 68 ms, field of view (FOV) = 256 mm × 256 mm, data matrix = 128 × 128, voxel size = 2 × 2 × 2 mm^3, slice thickness = 2 mm, flip angle (FA) = 90°, 30 diffusion-sensitive directions with b = 1, 000 mm^2/s, 5 volumes with b = 0 mm^2/s, and 75 slices without inter-slice gap. All the DTI data were scanned twice to improve the signal-to-noise ratio (SNR). In addition, we acquired high resolution brain structural images with a T1-weighted 3D Ax FSPGR BRAVO sequence (TR = 8.212 ms, TE = 3.22 ms, inversion time = 450 ms, FA = 12°, data matrix = 256 × 256, FOV = 256 mm × 256 mm, voxel size = 1 × 1 × 1 mm^3, slice thickness = 1 mm, and 136 axial slices covering the whole brain).

3. Data processing

3.1. Image preprocessing

DTI data preprocessing was performed in FDT, a tool implemented in FSL (http://fsl.fmrib.ox.ac.uk/fsl). First, for each subject, the two repeated DTI datasets were concatenated and averaged. Second, non-diffusion-weighted images (b_0) were extracted and non-brain tissues were removed using FSL/bet. Third, head-motion and eddy current-induced distortions were corrected using FSL/eddy_correct, and gradient orientations of the B-matrix were rotated (Leemans and Jones, 2009). Then, the eigenvalues of diffusion tensor were estimated using FSL/dtifit, and fractional anisotropy (FA), radial diffusivity (RD), axonal diffusivity (AD), and mean diffusivity (MD) were generated. Finally, a 2-tensor model was fitted at each voxel for necessary