Schizophrenia Research xxx (2016) xxx–xxx

Contents lists available at ScienceDirect

Schizophrenia Research

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

Letter to the Editor

Common and diagnosis-specific fractional anisotropy of white matter in schizophrenia, bipolar disorder, and major depressive disorder: Evidence from comparative voxel-based meta-analysis

Dear editors,

Recently, genetic analyses have identified highly shared overlaps in polymorphisms across three major psychiatric disorders: schizophrenia (SCZ), bipolar disorder (BD) and major depressive disorder (MDD) (Cross-Disorder-Group, 2013). Also, clinical analyses find similarities in some psychotic symptoms across three disorders and high comorbidity between diagnoses (Borsboom et al., 2011). Collectively, this evidence possibly suggest there exists a common neurobiological mechanism across three related disorders.

In our recent meta-analysis of comparing the fractional anisotropy (FA) of white matter between SCZ and BD, we found shared impairments of FA at left genu of corpus callosum (GCC) and left posterior cingulum fibers (Dong et al., 2017). Meanwhile, Wise et al. (2016) found MDD and BD are both characterized by FA abnormalities in left GCC, and BD showed more reduced white matter integrity in the left posterior cingulum when comparing to MDD. Combining with the two meta-analysis studies, we hypothesized that a) the GCC will represent common alterations in FA across the three disorders and b) that SCZ and BP will show significantly reduced FA in the left posterior cingulum relative to MDD. However, these presumptions lack direct comparison among three conditions. As an extension and integration, we performed the voxel-based meta-analytic comparison of whole-brain FA evaluated by diffusion approach to identify the common or disorder-specific structural abnormalities among three illnesses.

For whole-brain Diffusion tensor imaging literature in SCZ and BD, we used our previous datasets, i.e., 24 datasets for SCZ; 23 datasets for BD (Dong et al., 2017). In accordance with our previous inclusion and exclusion criteria for study selection, thirty studies of MDD were included in following analyses (Table S1). Descriptive Information for each Sample was summarized in supplementary material. All analyses were performed using anisotropic effect-size-based algorithms (AES-SDM) software (http://www.sdmproject.com) in a standard process. First, separated analyses were conducted to investigate the impairments of FA within each disorder group ($P < 0.005$, shown in Fig. S1 and Table S2). We also did some additional analyses to guarantee the stability and replicability with each patient group, see Supplementary material for details. Secondly, we conducted three voxel-wise quantitative comparisons between each pair with controlling for age, gender ($P < 0.0005$). Thirdly, three separate conjunction analyses for each pair were conducted ($P < 0.0025$). Finally, another conjunction analysis of three separate conjunction maps were conducted to identify common FA alterations (see Dong et al. (2017) for more details).

In line with our presumptions, we identified a shared pattern of white matter FA decrease across three major psychiatric disorders only located in left GCC (Fig. 1) which connects bilateral prefrontal and orbitofrontal cortices. These areas are central to current model of physiopathology across three conditions. More importantly, this concordance provided further evidence for shared endophenotypes across psychiatric disorders (Goodkind et al., 2015). Future studies should determine if FA reductions of the GCC may be present in every psychiatric disorder.

As well as shared FA reductions between these disorders, we also observed diagnosis-specific effects, distinguishing MDD from SCZ and BD (Fig. 1). There were no FA differences between SCZ and BD. In comparison to the MDD group, SCZ and BD were associated with significantly reduced white matter integrity in the posterior cingulum which plays an important role in neurocognitive functions (Corbetta and Shulman, 2002). This may underlie the more observed impairment of cognitive functions present in SCZ and BD (Barch et al., 2003; Xu et al., 2012). In comparison to SCZ, MDD showed significantly reduced FA in left anterior limb of the internal capsule (ALIC), a region that is heavily involved in motivation and reward, meanwhile, we noted that the FA of ALIC was significantly reduced in MDD, but not in SCZ when compared with controls (Fig. S1). Combining these evidence, our results indicated ALIC pathway may represent MDD-specific impairment and this impaired pathway may further contribute to abnormal reward processing in MDD (Henderson et al., 2013), although this is worthy of further exploration. MDD also showed greater reductions in FA of the middle GCC. This may indicate that white matter alterations of the GCC are bilaterally located in MDD, with more left lateralization in SCZ (Park et al., 2004).

Although significant, there are some limitations associated with the preliminary comparative meta-analyses, including the use of different processing pipelines (VBM, TBSS), different image acquisition parameters between studies, different clinical populations and clinical states, potential effects of medication, duration of illness and symptom severity at time of scanning. These factors can potentially influence the results. Future researchers should collected the multi-cites, large numbers of homogeneous samples, which would validate reliability and stability of our results and shed more light on our standing of the etiology of the three conditions.

To conclude, present results highlight white matter FA decrease in left GCC may constitute a common pathophysiological pathway among three major psychiatric disorders. By contrast, there were also a few diagnosis-specific effects, distinguishing only MDD from SCZ and BD. Most importantly, these findings concur with previous studies to provide further evidence of both shared and distinct endophenotypes across psychopathology.

Author contributions

Debo Dong and Yulin Wang designed the study, searched the literature, and wrote the manuscript; Debo Dong and Xuebin Chang conducted the statistical analysis; Xi Chen and Xin Chang searched the literature and checked the accuracy of data; Dezhong Yao and

http://dx.doi.org/10.1016/j.schres.2017.07.003
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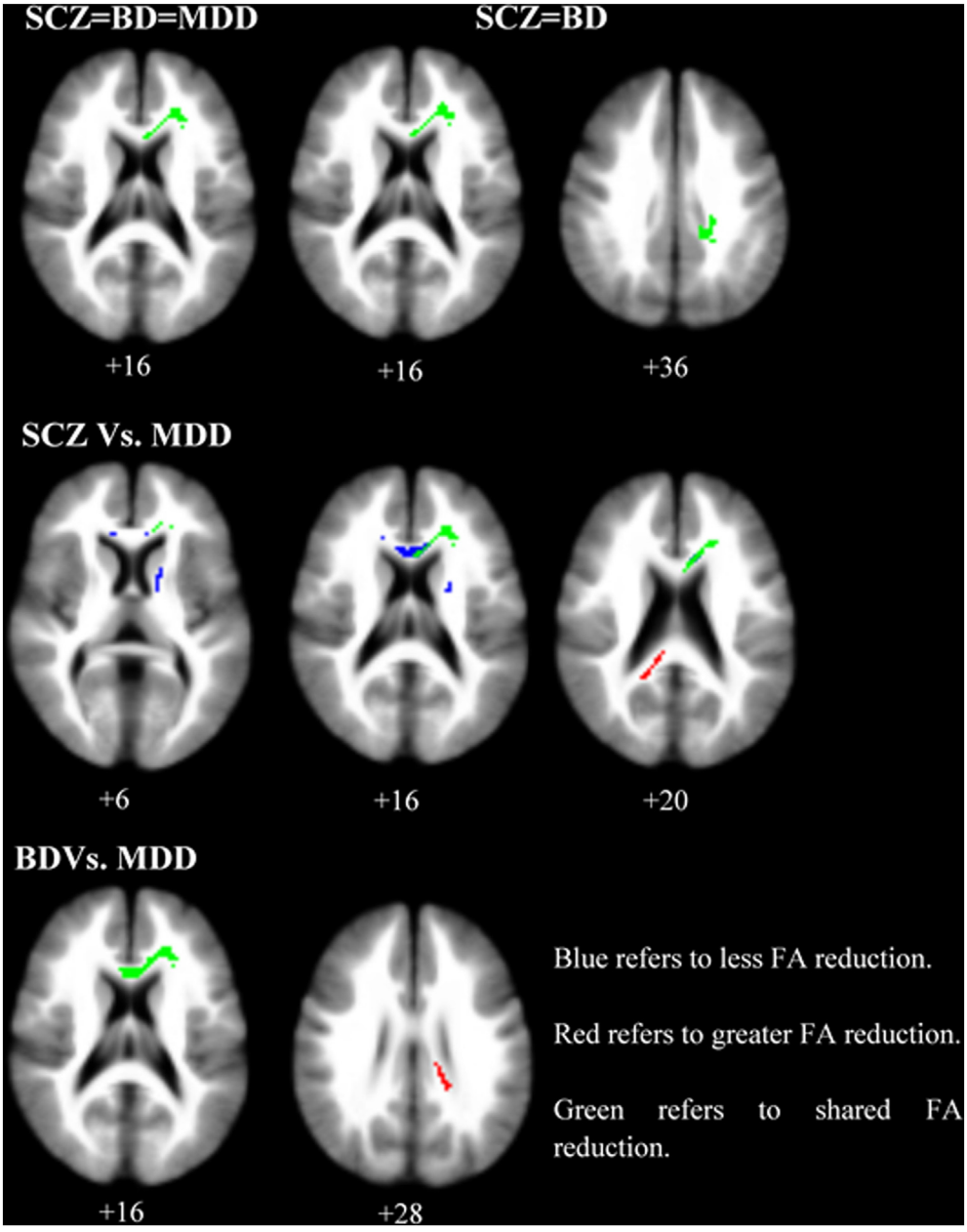

Fig. 1. Comparisons of FA abnormalities across three disorders.

Cheng Luo, who contributed equally to playing the role of corresponding author, conceived, commented and worked on the manuscript.

Conflict of interest

The authors report no biomedical financial interests or potential conflicts of interest.

Acknowledgement

This study was supported by grants from the National Nature Science Foundation of China (grant numbers: 81471638, 81571759); Program for Changjiang Scholars and Innovative Research Team (IRT 0910); and the '111' project (B12027). Our thanks go to the anonymous referee for his (her) valuable comments to improve quality of our paper.

Appendix A. Supplementary data

Supplementary data to this article can be found online at http://dx.doi.org/10.1016/j.schres.2017.07.003.

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Please cite this article as: Dong, D., et al., Common and diagnosis-specific fractional anisotropy of white matter in schizophrenia, bipolar..., Schizophr. Res. (2016), http://dx.doi.org/10.1016/j.schres.2017.07.003

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31 March 2017
Available online xxxx

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Please cite this article as: Dong, D., et al., Common and diagnosis-specific fractional anisotropy of white matter in schizophrenia, bipolar..., Schizophr. Res. (2016), http://dx.doi.org/10.1016/j.schres.2017.07.003