Author's response to reviews

Title: Alterations of regional homogeneity in pediatric bipolar depression: A resting-state fMRI study

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Author's response to reviews:

Dear Mr Christopher Acuña,

We thank you for providing us the opportunity to revise our manuscript titled: “Alterations of regional homogeneity in pediatric bipolar depression: A resting-state fMRI study”. We also greatly appreciate the reviewer’s comments and suggestions, which have helped to improve the quality of our manuscript. According to the reviewer’s suggestions, we have made significant changes to the manuscript. We are now resubmitting our revised manuscript along with this response letter. The major changes in the revised manuscript are shown in red. Thank you very much!

Enclosed are our point-to-point responses to the Associate Editor’s comments and the reviewer’s critiques.

Reply to reviewer #1

Q1. In the "Introduction" section, the authors describe that “Although many studies have focused on brain functional changes in BD patients, most studies have investigated adult BD, and relatively less research on PBD has been published”. In this manuscript, the fact that there are relatively less research on PBD using fMRI is one of the novelty. Nevertheless, the authors does not refer to these few studies about PBD-fMRI studies. No references are cited.

A1: Thank you very much for your careful review of our manuscript. We have carefully reviewed the literatures on PBD resting state fMRI studies, and we have added the descriptions of these studies. (Please see Introduction section, line 83 – 92, shown in red)
Q2. In this manuscript, the fact that fewer investigations have been conducted on BD patients that carefully stratify groups by mood states is another novelty. Nevertheless, the authors does not refer to these few studies, without citing references. The authors should refer to the details about these few studies.

A2: Thank you for your helpful comments and we agree with your suggestions. In this context, we have added the details about the studies that stratify groups by mood states in adult BD patients, and we have cited these references as well. (Please see Introduction section, line 94 – 99, shown in red)

Q3. In the "Introduction" section, the authors only described the general knowledge about resting state fMRI and only the Regional homogeneity (ReHo) method. The authors should describe clearly the reason of choosing the resting state fMRI method, especially for pediatric subjects. In addition, the authors should further describe past neuroimaging studies which investigated the brain function of child psychiatric disease (especially for mood disorder) using resting state fMRI. (For example, resting state fMRI method was useful for anticipating the response for treatment?) Without these information, readers cannot figure out the importance of this article.

A3: Thank you again for your suggestions. Prior evidence shows that task-related changes in neural activation may just represent less than 5% of the brain’s total activity. While the majority of its resources have been used on task-independent, spontaneous neural activity, and resting state fMRI study is the best approach to evaluate it [1], in that case, we used resting state fMRI to characterize brain function disturbances in PBD-depression. Resting fMRI method (ReHo) is widely used to elucidate the possible pathophysiological mechanisms underlying many child psychiatric disorders, such as PBD-mania [2], attention-deficit/hyperactivity disorder [3], and autism spectrum disorders [4]. Therefore, we are trying to find the possible pathophysiology of PBD-depression through resting fMRI study, which is the importance of this article.

In the revised manuscript, we have added these descriptions. (Please see Introduction section, line 102 – 105 and 113 – 115, shown in red)

Thank you again for your review.

Reply to reviewer #2

Q1: Results of resting state fMRI are significantly affected by the head motion of participants during fMRI scanning; that is, long-distance correlations are decreased by participant motion, whereas many short-distance correlations are increased. This issue should be serious addressed in method before any relevant conclusion and results can be made.

A1: Thank you for your suggestions. In the revised manuscript, we have described the head motion of participants during fMRI scanning, and we did not find any significant difference between two groups in head motion (t = 0.413, p = 0.682).

We have added these information in 2.2.3. Image processing section, line 179 – 181 (shown in red). Thank you again.
Q2: As the authors examined scores of MFQ in the result and discussion, MFQ should be described in more careful manner.

A2: Thank you for your suggestions. MFQ is a well-designed measure that is very widely used to assess the severity of depression symptoms in adolescents. It has 33 items and each item scores as 0 = never, 1 = sometimes, 2 = often. The total score, in general, is associated with severity of depressive symptoms. The Chinese version of MFQ was introduced in our study, which was translated by Cao et al. (2009). The MFQ has good internal consistency (Cronbach’s alpha = 0.93) in a Chinese sample of 2592 middle school students [5].

We have added these descriptions in the revise manuscript. (Please see 2.2.1. Demographic and clinical assessment, line 150-155, shown in red)

References

Besides, we have invited an English native speaker to revise our manuscript and also we would like to make some minor alterations on the affiliations of authors.

Thank you for your hard work again and we hope you will be satisfied with our replies. We are ready to deal with the questions if you have any. Many thanks!

Yours sincerely,
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