

Answering Reviewers

Dear reviewers,

Thank you very much for your comments on our manuscript entitled *Abnormal Volumetric Brain Morphometry and Cerebral Blood Flow in Adolescents with Depression*. We are very grateful to receive your comments which are very helpful for improving our paper. We have sincerely and carefully considered the comments and revised the manuscript thoroughly. Detailed point-by-point response is given below. Revised portions are highlighted in **RED** in the revised manuscript.

I hope that the revised manuscript is suitable. Thank you again for your help with the manuscript. I am more than happy to provide any further information you may need.

Sincerely yours,

Ren-qiang Yu

May, 10th, 2023

Responses to Reviewer #1:

1.Core tip: Please re-phrase the sentence "Meanwhile we introduced alterations etc. (maybe detected or found?).

Response:

We sincerely thank the reviewer for careful reading. As suggested, we have corrected the "introduced" into "detected".

2.Introduction: Please re-phrase: In addition, there has been some evidence in dicating that depression is associated with functional and structural changes in individuals with depression. This is repeated unnecessarily.

Response:

Thanks for your suggestion, we have deleted this unnecessarily sentence in the revised

manuscript.

3. Were there individuals with suicide ideation? If yes: Were their brain structural (and functional) alterations more pronounced than in non-suicidal individuals?

Response:

Some of MDD patients we recruited may have suicide ideation, but suicidal individuals were not included in this research. Thanks for your comments, we may consider your precious view into the follow-up experiments.

Responses to Reviewer #2:

1. More comprehensive background of the earlier studies on voxel based morphometry in depression, e.g. <https://doi.org/10.1017/neu.2019.20>

Response:

Thank you for your positive comments. As suggested by the reviewer, we have added more reference to introduce background of the VBM in depression. (Reference: 24-28)

2. Detailed explanation on the role of multimodal approaches to combine structural and functional MRI data as possible diagnostic instruments: <https://doi.org/10.3390/diagnostics12020469>

Response:

Thanks for your advice. We have re-written this part, added some evidence supporting VBM in combination with CBF as a diagnostic tool. (Location: page6, line22)

3. Addressing in the conclusion the critical question about incorporation of neuroimaging data into standard diagnostic procedures in psychiatry.

Response:

We think this is a professional advice, which acquires multicenter neuroimaging data. It is a pity that our single center exploration is unable to be qualified to this task. Your advice is the development direction of imaging examination in the diagnosis of mental diseases and this is also the direction of our future efforts.

We tried our best to improve the manuscript and made some changes marked in red in revised paper which will not influence the content and framework of the paper. We appreciate for Editors and Reviewers warm work earnestly and hope the correction will meet with approval. Once again, thank you very much for your comments and suggestions.