

## **Responses to the peer reviewers' comments**

RE: Manuscript No.: 60960

Title: Altered spontaneous brain activity in patients with diabetic optic neuropathy: a resting-state functional MRI study using regional homogeneity

Dear editors:

Thank you very much for making suggestions for the above-mentioned manuscript. We have revised the paper according to the Editor ' s and reviewer ' s suggestions. Attached please find the revised version of the paper, with highlighting where changes have been made in the revised manuscript.

Below are our specific responses to the reviewers ' comments.

### **Reviewer 1:**

**Q1:** Please, discuss in more details the results regarding the anxiety and depression

**RE1:** Done, thanks for your suggestions. Some details about the relationship between anxiety and depression and diabetic optic neuropathy have been added to the abstract and discussion.

**Q2:** Please, provide more details about patients with diabetes (type of diabetes, duration of diabetes, antidiabetic treatment, diabetes complications, comorbidities, etc.)

**RE2:** Thanks for your suggestions. In diabetic optic neuropathy group, some patients only use hypoglycemic drugs or insulin injection, but some patients need oral hypoglycemic drugs and insulin injection to maintain blood glucose level. Because this study is mainly to observe the abnormal neural activity in different brain regions of diabetic optic neuropathy patients, we are very sorry that our team did not record the detailed treatment and other complications of diabetes. In the future research, we will use your suggestion to explore the complications of diabetes and record the specific treatment plan of patients, so as to obtain more comprehensive research results.

**Q3:** Please, revise the whole manuscript and remove typos and grammar errors

**RE3:** Done, thanks for your suggestions. We have revised the manuscript.

**Q4:** Please, revise the list of references and make it uniform in style

**RE4:** Done, thanks for your suggestions. We have revised the manuscript.

**Reviewer 2:**

**Q1:** Please proofread and copyedit the text. There are numerous typing errors that make the text difficult to read. Use the free version of Grammarly to check the manuscript.

**RE1:** Done, thanks for your suggestions. We have revised the manuscript.

**Q2:** This does not seem to be a clinical trial and it is definitely not a RCT. Maybe a case-control study?

**RE2:** Thanks for your suggestions. This is a case-control study.

**Q3:** You also investigated anxiety and depression but you did not mention anything about it in the introduction, abstract or discussion. Please discuss these results as well and why you decided to perform this investigation. Maybe your findings are related to your patients' anxiety/depression rather than DON? Please argue about this issue.

**RE3:** Done, thanks for your suggestions. Some details about the relationship between anxiety and depression and diabetic optic neuropathy have been added to the abstract and discussion.

**Q4:** Revise the references for uniformity.

**RE4:** Done, thanks for your suggestions. We have revised the manuscript.

**Q5:** Regarding the figures, did you use copyrighted images or did you prepare them? Please check whether you are allowed to use those images.

**RE5:** Thanks for your suggestions. The figures were made by our team.

**Q6:** In diabetes and diabetes (the association of diabetes and obesity) oxidative stress seems to be an important putative mechanism. The adipose tissue is a source of pro-inflammatory adipocytokines and reactive oxygen

species and might contribute to the ocular complications, including the development of DON. Please see the following paper published in the World Journal of Diabetes this year:

<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7243484/>

<https://www.tandfonline.com/doi/abs/10.1080/10408398.2020.1821166>

**RE6:** Thanks for your suggestions. In this study, almost all patients in the DON group cannot control blood sugar well, some patients only use hypoglycemic drugs or insulin injection, but some patients need oral hypoglycemic drugs and insulin injection to maintain blood glucose level. Because this study is mainly to observe the abnormal neural activity in different brain regions of diabetic optic neuropathy patients, we are very sorry that our team did not pay close attention to macrovascular and microvascular complications in these patients and their treatment. In the future study, we will adopt the reviewer's opinions to explore the macrovascular and microvascular complications of diabetes, and record the treatment plan of patients, so as to obtain more comprehensive research results.