

Dear Editors and Reviewers:

On behalf of my co-authors, we thank you very much for giving us an opportunity to revise our manuscript, we appreciate editor and reviewers very much for their positive and constructive comments and suggestions on our manuscript entitled "The Effect of Lactobacillus Rhamnosus GG Supernatant on Serotonin Transporter Expression in Rats with Post-Infectious Irritable Bowel Syndrome"(Manuscript NO: 36608). Those comments are all valuable and very helpful for revising and improving our paper, as well as the important guiding significance to our researches. We have studied comments carefully and have made correction which we hope meet with approval.

Revised portion are marked in red (response to the reviewers) and blue (response to the editors) in the paper. The main corrections in the paper and the responds to the reviewer's comments are as following:

Responds to the reviewer' s comments:

Reviewer #1 (Reviewer's code: 01047616):

1. **Comment:** The timing and age of the rats to conduct AWR for evaluation of visceral hypersensitivity is unclear.

Response: As two consecutive tests with negative culture, rats were considered to get rid of infection. Rats without infection were kept separately from infected rats. At the 42th day, 95% of the C. jejuni rats were no longer infected. At the 56th and 70th day, all C. jejuni rats were test negatively. Then the AWR test was done to evaluate the visceral hypersensitivity. On account of gavaged with C. jejuni at the same time, the period of C. jejuni colonization phase were likely. (Page 8 line 24-26; Page 11 line 20-22)

2. **Comment:** Discuss the gender issue in the discussion section.

Response: The gender was discussed in the discussion section, and more

references were added to support the validity of the use of male animals for PI-IBS study. (Page 16 line 7-17)

3. Comment:

- ① The use of undiluted, double-diluted, and triple-diluted LGG supernatant did not result in a dose-response of the expression of SERT. The authors should provide their speculation in the discussion section.
- ② Have the authors looked at the SERT levels in control rats (similar to control mice data)?
- ③ Whether LGG supernatant relieve pain in the PI-IBS model by Campylobacter infection?

Response:

- ① Different contents of supernatant and each substance with different concentration in undiluted, double-diluted, and triple-diluted LGG supernatant, combined with prior *C. jejuni* intestinal infection, may lead to different expressions of inflammatory factors, results in undoes-response of expression of SERT. (Page 15 line 18-20)
- ② We are very sorry for our negligence of research the SERT levels in control rats. Our previous study had found that LGG-s could up-regulated the SERT levels in wild-type mouse. The focus of this study was to build the model of PI-IBS, and on this basis, evaluate the effect of LGG-s on SERT levels.
- ③ The study did not do the AWR test after LGG-s gavage. The AWR was used only in the determination of PI-IBS. Because the rats need to be anesthesia and the AWR may induce mucosal injury, the SERT levels of intestinal may be affected. According to our experience, the treatment of LGG-s should be controlled within a certain time range and intestinal specimens should be taken immediately after the rats decapitated. The aim of the study was to research the SERT levels in PI-IBS. The effect of LGG-s for relieve symptoms will be done in our next work.

4. **Comment:** There is no line numbers or page numbers in the manuscript.
Response: Page numbers were added to the footer.
5. **Comment:** The figure numbers stated in the result text should be at the end of the paragraph, but not at the title
Response: The figure numbers were adjusted to the end of the paragraph. (Page 7 line 29; Page 11 line 16; Page 11 line 27; Page 12 line 29; Page 13 line 7)
6. **Comment:** The number of animals used must be added at the end of the figure legend of each figure
Response: The figure legend has been revised.

Reviewer #2 (Reviewer's code: 02821831):

1. **Comment:** In section Materiel and Method, the authors must explain the control model used in one sentence.
Response: During the modeling period, the rats were grouped into two groups, control group (normal and healthy) and PI-IBS model group (C. jejuni infection). Then, after the model evaluation, the rats were regrouped. The control group still was normal and healthy rats, and the model group was divided into four groups, in order to evaluate the effect of LGG-s on SERT levels. (Page 7 line 8; Page 7 line 17-18)

Response to the Editors:

Attachment of supplementary material (PPT) and image file (Visio) were used to provide the decomposable figure of Figures. The audio file was to describe final core tip.

We are very sorry for our incorrect sequencing of authors. The second and the third author, Li-Juan Feng and Yuan-Yuan Liu, needed to be exchanged. At the page 1 line 11 the authors' names were exchanged, but they were still make a significant contribution to this study.

We tried our best to improve the manuscript and made some changes in the manuscript. These changes will not influence the content and framework of the paper.

We appreciate for Editors and Reviewers' warm work earnestly, and hope that the correction will meet with approval.

Once again, thank you very much for your comments and suggestions.

Best regards!

Yanan Cao

Corresponding author:

Name: Yuming Wang.

E-mail: ywang12@tmu.edu.cn