

Response to comments

RE: "Duodenal-jejunal Bypass improves hypothalamic oxidative stress and inflammation in diabetic rats by GLP-1-mediated Nrf2/HO-1 signal" (ID 88731)

We thank the editors and reviewers for the helpful and constructive feedback. We have addressed all the concerns from each reviewer and incorporated them into the revised manuscript. The point-by-point response to each of the issues raised in the peer review was listed below. Revised/added contents were highlighted with yellow color in the revised manuscript. A clean copy the revised manuscript was submitted in the system.

Yours sincerely,
Meihua Qu

3 SCIENTIFIC QUALITY

*Please resolve all issues in the manuscript based on the peer review report and make a point-by-point response to each of the issues raised in the peer review report, and **highlighted the revised/added contents with yellow color in the revised manuscript**. Note, authors must resolve all issues in the manuscript that are raised in the peer-review report(s) and provide point-by-point responses to each of the issues raised in the peer-review report(s); these are listed below for your convenience:*

Reviewer #1:

The title contains too many abbreviations, please mention them in full or change the title. The article is well written.

Response:

Thank you for the suggestion. We have changed the title to "

Duodenal-jejunal bypass improves hypothalamic oxidative stress and inflammation in diabetic rats via GLP-1-mediated Nrf2/HO-1 signaling" instead of the original title "DJB surgery alleviates hypothalamic inflammation and neuronal cell injury in T2DM rats by activating GLP-1-mediated Nrf2/HO-1 signaling pathway" to avoid too many abbreviations and clarify the main point of the manuscript.

Reviewer #2:

Q1. It is very important to change and modify the title. the title is not appropriate.

Response:

Thank you for the suggestion. We have changed the title to "Duodenal-jejunal bypass improves hypothalamic oxidative stress and inflammation in diabetic rats via GLP-1-mediated Nrf2/HO-1 signaling" instead of the original title "DJB surgery alleviates hypothalamic inflammation and neuronal cell injury in T2DM rats by activating GLP-1-mediated Nrf2/HO-1 signaling pathway" to avoid too many abbreviations and clarify the main point of the manuscript.

Q2. Are the objectives and the rationale of the study clearly stated?

Response:

Thank you for pointing the limitation of the manuscript. In the abstract, we revised the background, aim part to clarify the objective of the study. The revised part was highlighted with yellow color in the revised manuscript of the abstract, clearly describing the objectives and the rationale of the study. To make the rational of the study clearly, we have revised the methods and results part of the abstract. The revised contents were marked in yellow color.

Q3. In the abstract, the research gap was not clearly stated. In addition, the authors need to rewrite the study objectives to be more academic writing.

Response:

Thank you for your suggestion. In the abstract, we revised the background to clearly describing the research gap of the study. We have rewritten the study objectives to be more academic writing. All the revised contents were marked in yellow color in the abstract.

Q4. In the introduction, include the study's significance and novelty. What makes the study different from the rest and what does it add to the current knowledge?.

Response:

Thank you for your suggestion. In the introduction section, we added the correlation between diabetes and nerve injury, and our previous results, to address the significance and novelty of DJB surgery in T2DM control and the improvement of brain oxidative stress. This study can provide new insights into the relationship of diabetes and central nerve injury, and the role and metabolism of metabolic surgery in diabetic brain complications. The revised part was highlighted with yellow color in the revised manuscript of the introduction.

Q5. In the introduction, the authors should have explained the purpose of this study and the existing gaps in this field and explained why this study was conducted.

Response:

Thanks for your suggestion. To make the study clearly, we expanded more references in the introduction section and discussion section to explain the purpose of this study and the existing gaps in this field. Especially "Previous studies have found that DJB surgery significantly improves peripheral glucose metabolism in T2DM rats, but its role and mechanism in diabetes-induced central brain injury remain unclear. The present study helps to elucidate the role and mechanism of DJB in diabetic hyperglycemia-induced central brain injury and provides new insights into metabolic surgery for the treatment of diabetes and its complications." The

revised parts in the second and fourth paragraphs are highlighted with yellow color in the revised manuscript of the introduction.

Q6. Are the methods clear and replicable? Do all the results presented to match the methods described?

Response:

Thank you for your reminding. We revised the methods section, and the results section to make the methods more clarified and accurate. The results section was also be checked and revised. The revised part was highlighted with yellow color in the revised manuscript of the methods and results.

Q7. If relevant are the results novel? Does the study provide an advance in the field? Is the data plausible?

Response:

The results of this study are novel *advance in the field*. The innovation and advancement of the research is mainly reflected in "Previous studies have shown that DJB surgery significantly improves peripheral and intracerebral glucose metabolism in T2DM rats, but its role in central brain injury and mechanisms remain unclear. The present study helps to elucidate the role and mechanism of DJB in diabetic hyperglycemia-induced central brain injury and provides new insights into metabolic surgery for the treatment of diabetes and its complications." About the novelty of this study in the discussion section we elucidate in detail. Besides, the data are credible.

Q8. References are relevant, correct, and not recent. The number of references should be increased. please add some references. since this is a scientific review, all the sentences need to be supported with references. This study is very beautiful. I liked the sequence and enjoyed reading. Please add more references on similar studies.

Response:

Thanks for your suggestion. We have reviewed and updated the references section and increased the number of references to ensure that all sentences are supported by the corresponding references. Of these, four references were added (No. 2, 28, 34, and 44). Two 2017 reference sources have been updated (No. 18 and 37); one 2019 reference sources have been updated (No. 32); three 2021 reference sources have been updated (No. 9, 15, and 55); two 2022 reference sources have been updated (No. 11 and 16); and five 2023 reference sources have been updated (No. 13, 25, 40, 48, and 53). Revised portions were marked using the yellow color in the revised manuscript of the references.

Q9. There are a lot of grammatical errors. This must be taken care of and addressed.

Response:

Thanks for your suggestion. This revised manuscript has been copyedited by the editing services of American Journal Experts (AJE) to ensure the language and grammar accuracy, and to improve the logical presentation and structures of the article.

Q10. *What are the limitations of the study? A description of limitations is missing at the end of the discussion section.* • *If your manuscript is related to mine, you can cite it (ORCID: <https://orcid.org/0000-0002-5107-5550>).*

Response:

Thank you for your reminding and suggesting. We added a description of the limitations at the end of the discussion section at the discussion section marked in yellow words. The article, DOI "10.3390/toxics11090784", which is the 44th reference in our article, is of great help to us.

4 LANGUAGE POLISHING REQUIREMENTS FOR REVISED MANUSCRIPTS SUBMITTED BY AUTHORS WHO ARE NON-NATIVE SPEAKERS OF ENGLISH

As the revision process results in changes to the content of the manuscript, language problems may exist in the revised manuscript. Thus, it is necessary to perform further language polishing that will ensure all grammatical, syntactical, formatting and other related errors be resolved, so that the revised manuscript will meet the publication requirement (Grade A).

Authors are requested to send their revised manuscript to a professional English language editing company or a native English-speaking expert to polish the manuscript further. When the authors submit the subsequent polished manuscript to us, they must provide a new language certificate along with the manuscript.

Once this step is completed, the manuscript will be quickly accepted and published online. Please visit the following website for the professional English language editing companies we recommend: <https://www.wjgnet.com/bpg/gerinfo/240>.

Response:

Thanks for your suggestion. This revised manuscript has been copyedited by the editing services of American Journal Experts (AJE) to ensure the language and grammar accuracy, and to improve the logical presentation and structures of the article.

5 ABBREVIATIONS

In general, do not use non-standard abbreviations, unless they appear at least two times in the text preceding the first usage/definition. Certain commonly used abbreviations, such as DNA, RNA, HIV, LD50, PCR, HBV, ECG, WBC, RBC, CT, ESR, CSF, IgG, ELISA, PBS, ATP, EDTA, and mAb, do not need to be defined and can be used directly.

Response:

Thanks for your suggestions. There are no non-standard abbreviations

appear in our articles.

6 EDITORIAL OFFICE'S COMMENTS

Authors must revise the manuscript according to the Editorial Office's comments and suggestions, which are listed below:

(1) Science editor:

1 Conflict of interest statement: Academic Editor has no conflict of interest.

Response:

Response:

Academic Editor has no conflict of interest.

2 Manuscript's theme: The topic is within the scope of the journal.

Response:

The topic is within the scope of the journal.

3 Academic misconduct: No academic misconduct was found.

Response:

Thanks.

4 Scientific quality: The authors conduct a basic study to explore the impact of duodenal jejunal bypass surgery on alleviating hypothalamic inflammation and neuronal cell injury in T2DM rats. The introduction and discussion should be supplemented to indicate the novelty and limitations of the manuscript.

Response:

Thank you for your suggestion. In the introduction section, we added the correlation between diabetes and nerve injury, and our previous results, to address the significance and novelty of DJB surgery in T2DM control and the improvement of brain oxidative stress. This study can provide new insights into the relationship of diabetes and central nerve injury, and the role and metabolism of metabolic surgery in diabetic brain complications. The

revised part was highlighted with yellow color in the revised manuscript of the introduction. We added a description of the limitations at the end of the discussion section at the discussion section marked in yellow words.

5 Language evaluation: Further language polishing is required in order to meet the publication requirement (Grade A).

Response:

Thanks for your suggestion. This revised manuscript has been copyedited by the editing services of American Journal Experts (AJE) to ensure the language and grammar accuracy, and to improve the logical presentation and structures of the article.

6 Medical ethics: The institutional animal care and use committee statement and ARRIVE guideline should be provided.

Response:

We have submitted the institutional animal care and use committee statement and ARRIVE guideline on the system.

7 *Specific comments:*

(1) Please delete the repeated references and renumber them (No. 27 and 43).

Response:

Thank you for your reminding and suggesting. We have changed the references to No. 28 “**28. Yoo J, Cho IJ, Jeong IK, Ahn KJ, Chung HY, Hwang YC. Exendin-4, a glucagon-like peptide-1 receptor agonist, reduces hepatic steatosis and endoplasmic reticulum stress by inducing nuclear factor erythroid-derived 2-related factor 2 nuclear translocation. *Toxicol Appl Pharmacol* 2018;**360**:18-29. [PMID: 30253173 DOI: 10.1016/j.taap.2018.09.032]**” instead of the original references No. 27 “27. Oh YS, Jun HS. Effects of Glucagon-Like Peptide-1 on Oxidative Stress and Nrf2 Signaling. *Int J Mol Sci* 2017, 19(1):26. [PMID:29271910 DOI:10.3390/ijms19010026]” We have

changed the references to No. 46 instead of the original references No. 43.

*(2) The labeling of P value in the figures does not meet the requirements of WJG, please don't include any *, #, †, §, ‡, ¥, @... in your manuscript; Please use superscript numbers for illustration; and for statistical significance, please use superscript letters. Statistical significance is expressed as aP <0.05, bP <0.01 (P > 0.05 usually does not need to be denoted). If there are other series of P values, cP <0.05 and dP <0.01 are used, and a third series of P values is expressed as eP <0.05 and fP <0.01.*

Response:

Thank you for your reminding. We have carefully revised the P-values in the chart and the chart annotations to make them conform to the requirements of WJG.

(3) Please provide the decomposable figure of figures, whose parts are all movable and editable, organize them into a PowerPoint file, and submit as "Manuscript No. -Figures.ppt" on the system, we need to edit the words in the figures. All submitted figures, including the text contained within the figures, must be editable. Please provide the text in your figure(s) in text boxes.

Response:

Thank you for your suggestion. We have sorted out the movable and editable figures into a PowerPoint file and submitted as "Manuscript No. 88731-Figures.ppt" on the system.

(2) Company editor-in-chief:

I have reviewed the Peer-Review Report, full text of the manuscript, and the relevant ethics documents, all of which have met the basic publishing requirements of the World Journal of Diabetes, and the manuscript is conditionally accepted. I have sent the manuscript to the author(s) for its revision according to the Peer-Review Report, Editorial Office's comments and the Criteria for Manuscript Revision by

Authors.

Response:

Thank you for your reminding and suggesting. According to your suggestions, we have carefully revised the relevant content of the manuscript, including the preparation and upload of relevant attachment materials.

Before its final acceptance, please provide and upload the following important documents: Biostatistics Review Certificate, a statement affirming that the statistical review of the study was performed by a biomedical statistician;

Response:

We invited biomedical statisticians to conduct a statistical review of our study and uploaded the biostatistical review certificate to the system.

The ARRIVE Guidelines, an important document related to manuscript writing of basic research using animals.

Response:

Thank you for your reminding. We prepared the ARRIVE guideline and uploaded it to the system.

Before final acceptance, uniform presentation should be used for figures showing the same or similar contents; for example, "Figure 1 Pathological changes of atrophic gastritis after treatment. A: ...; B: ...; C: ...; D: ...; E: ...; F: ...; G: ...".

Response:

Thank you for your suggestion. We have standardized the presentation of figures, tables, and notes to conform to the requirements of WJG.

Please provide the original figure documents. Please prepare and arrange the figures using PowerPoint to ensure that all graphs or arrows or text portions can be reprocessed by the editor.

Response:

Thank you for your reminding. We have prepared and arranged the figures using PowerPoint to ensure that any graphs or arrows or text sections can be reprocessed by the editor. We have named the original graphics file "Manuscript No. 88731-Figures.ppt" and uploaded it to the system.

In order to respect and protect the author's intellectual property rights and prevent others from misappropriating figures without the author's authorization or abusing figures without indicating the source, we will indicate the author's copyright for figures originally generated by the author, and if the author has used a figure published elsewhere or that is copyrighted, the author needs to be authorized by the previous publisher or the copyright holder and/or indicate the reference source and copyrights. **Response:**

Thank you very much for protecting the intellectual property of our original charts. We guarantee that all our charts are original.

Please check and confirm whether the figures are original (i.e. generated de novo by the author(s) for this paper). If the picture is 'original', the author needs to add the following copyright information to the bottom right-hand side of the picture in PowerPoint (PPT): Copyright ©The Author(s) 2023.

Response:

Thank you for your suggestion. We confirm that the diagram is original (i.e. generated de novo by the author(s) for this paper). We have added the following copyright information to the bottom right of the PowerPoint (PPT) image: copyright© Huaijie Wang 2023.

Authors are required to provide standard three-line tables, that is, only the top line, bottom line, and column line are displayed, while other table lines are hidden. —The contents of each cell in the table should conform to the editing specifications, and the lines of each row or column of the table should be aligned. Do not use carriage returns

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or spaces to replace lines or vertical lines and do not segment cell content.

Response:

Thank you for your suggestion. We have carefully revised the table, providing a standard three-line table to ensure compliance with the WJG Guidebook specifications.

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Please upload the approved grant application form(s) or funding agency copy of any approval do

Response:

Thank you for your reminding. We upload relevant attachment materials including approved grant application forms or copies of approved funding organizations to the system.

7 STEPS FOR SUBMITTING THE REVISED MANUSCRIPT

Step 1: Author Information

Please click and download the Format for authorship, institution, and corresponding author guidelines, and further check if the authors names and institutions meet the requirements of the journal.

Response:

Thank you for your reminding. We further checked the author's name and institution to ensure it meets the journal's requirements.

Step 2: Manuscript Information

Please check if the manuscript information is correct.

Response:

Thank you for your reminding. We have carefully reviewed the manuscripts to ensure the accuracy of the information presented in the manuscript.

Step 3: Abstract, Main Text, and Acknowledgements

(1) Guidelines for revising the content: Please download the guidelines for Original articles, Review articles, or Case Report articles for your specific manuscript type (Basic Study) at: <https://www.wjgnet.com/bpg/GerInfo/291>. Please further revise the content your manuscript according to the Guidelines and Requirements for Manuscript Revision.

Response:

Thank you for your reminding. We further revised the manuscript based on the Guidelines and Requirements for Manuscript Revision, including adjustments to layout format and citations, and other elements. Additionally, we made modifications based on the reviewers' comments and truthfully respond to the reviewers' comments.

(2) Format for Manuscript Revision: Please update the format of your manuscript according to the Guidelines and Requirements for Manuscript Revision and the Format for Manuscript Revision. Please visit <https://www.wjgnet.com/bpg/GerInfo/291> for the article type-specific guidelines and formatting examples.

Response:

Thank you for your reminder. We have further revised the manuscript according to the "Guidelines and Requirements for Manuscript Revision" and "Manuscript Revision Format" and update the format of our manuscript.

(3) Requirements for Article Highlights: If your manuscript is an Original Study (Basic Study or Clinical Study), Meta-Analysis, or Systemic Review, the "Article Highlights" section is required. Detailed writing requirements for the "Article Highlights" can be found in the Guidelines and Requirements for Manuscript Revision.

Response:

Thank you for your reminding. We have summarized the "Article Highlights" as required by the Guidelines and Requirements for Manuscript

Revision, which can be obtained at the end of the article conclusion.

(4) Common issues in revised manuscript. Please click and download the List of common issues in revised manuscripts by authors and comments (PDF), and revise the manuscript accordingly.

Response:

Thank you for your reminding. Based on the common questions and suggestions in the revised manuscript, we revised the manuscript to address the problems in our manuscript.

Step 4: References

Please revise the references according to the Format for References Guidelines, and be sure to edit the reference using the reference auto-analyser.

Response:

Thank you for your reminding. Our reference format follows the References Guidelines

Step 5: Footnotes and Figure Legends

(1) Requirements for Figures: Please provide decomposable Figures (in which all components are movable and editable), organize them into a single PowerPoint file, and submit as "88731-Figures.pptx" on the system. The figures should be uploaded to the file destination of "Image File". Please check and confirm whether the figures are original (i.e. generated de novo by the author(s) for this paper). If the picture is 'original', the author needs to add the following copyright information to the bottom right-hand side of the picture in PowerPoint (PPT): Copyright ©The Author(s). Please click to download the sample document: [Download](#).

Response:

Thank you for your suggestion. We have sorted out the movable and editable figures into a PowerPoint file and submitted as "Manuscript No. 88731-Figures.ppt" on the system.

(2) Requirements for Tables: Please provide decomposable Tables (in which all components are movable and editable), organize them into a single Word file, and submit as "88731-Tables.docx" on the system. The tables should be uploaded to the file destination of "Table File".

Response:

Thank you for your suggestion. We have sorted out the movable and editable Tables into a single Word file and submitted as "Manuscript No. 88731-Tables.docx" on the system.

Reminder: Please click and download the Guidelines for preparation of bitmaps, vector graphics, and tables in revised manuscripts (PDF), and prepare the figures and tables of your manuscript accordingly.

Response:

Thank you for your suggestion. We prepared the figures and tables in the manuscript according to the "Guidelines for preparation of bitmaps, vector graphics, and tables in revised manuscripts (PDF)".

Step 6: Automatically Generate Full-Text Files

Authors cannot replace and upload the "Manuscript File" separately. Since we only accept a manuscript file that is automatically generated, please download the "Full Text File" or click "Preview" to ensure all the contents of the manuscript automatically generated by the system are correct and meet the requirements of the journal. If you find that there is content that needs to be modified in the Full-Text File, please return to the corresponding step(s), modify and update the content, and save. At this point, you then have to click the "Save & Continue" button in Step 5 and the F6Publishing system will automatically regenerate the Full-Text File, and it will be automatically stored.

Response:

Thanks.

Step 7: Upload the Revision Files

For all required accompanying documents (listed below), you can begin the uploading process via the F6Publishing system. Then, please download all the uploaded documents to ensure all of them are correct.

- (1) 88731-Answering Reviewers
- (2) 88731-Audio Core Tip
- (3) 88731-Biostatistics Review Certificate
- (4) 88731-Conflict-of-Interest Disclosure Form
- (5) 88731-Copyright License Agreement
- (6) 88731-Approved Grant Application Form(s) or Funding Agency Copy of any Approval Document(s)
- (7) 88731-Institutional Animal Care and Use Committee Approval Form or Document
- (8) 88731-Institutional Review Board Approval Form or Document
- (9) 88731-Non-Native Speakers of English Editing Certificate
- (10) 88731-Video
- (11) 88731-Image File
- (12) 88731-Table File
- (13) 88731-The ARRIVE Guidelines
- (14) 88731-Supplementary Material

Response:

Thank you for your reminding. We have uploaded all the required accompanying files to the F6Publishing system.

For all manuscripts involving human studies and/or animal experiments, author(s) must submit the related formal ethics documents that were reviewed and approved by their local ethical review committee. This is mandatory and is one of the determining factors for whether or not the manuscript will be finally accepted. If human and animal studies received waiver of the approval requirement from the

ethics committee, the author(s) must provide an official statement to this effect made by the ethics committee. The guidelines for manuscript type and related ethics and relevant documents/statements can be found at: <https://www.wjgnet.com/bpg/GerInfo/287>.

Response:

Thank you for your reminding. The research related to the use of animal has complied with all relevant national regulations and institutional policies for the care and use of animals. The experimental protocol was approved by the Research Ethics Committee of Weifang Medical University, China, Approval No. 2021SDL574. The relevant official ethics documents reviewed and approved by the local ethics review committee have been uploaded into the system.

If your manuscript has supportive foundations, the approved grant application form(s) or funding agency copy of any approval document(s) must be provided. Otherwise, we will delete the supportive foundations.

Response:

Thank you for your reminding. We upload relevant attachment materials including approved grant application forms or copies of approved funding organizations to the system.

If your manuscript has no "Video" or "Supplementary Material", you do not need to submit those two types of documents.

Response:

The manuscript has no "Video" or "Supplementary Material".

8 COPYRIGHT LICENSE AGREEMENT

All authors should accept and sign the Copyright License Agreement (CLA), following the link sent in individual emails to each author. After all authors have accepted and signed their respective CLA, the Corresponding Author is responsible

for downloading the signed CLA by clicking on the "Download" button in the CLA page, re-storing it as "PDF", and then uploading it to the file destination of "Copyright License Agreement". If any of the authors do not accept to sign the CLA, the manuscript will not be accepted for publication. Reminder: If any of the authors do not receive the email of CLA, please check the spam folder. If the author still can't find the email, please contact us via email at: submission@wjgnet.com.

Response:

Thank you for your reminding. All authors have accepted and signed their respective CLA, and corresponding authors download the signed CLAs and upload them to the file destination of "Copyright License Agreement".

9 CONFLICT-OF-INTEREST DISCLOSURE FORM

Please click and download the fillable ICMJE Form for Disclosure of Potential Conflicts of Interest (PDF), and fill it in. The Corresponding Author is responsible for filling out this form. Once filled out completely, the Conflict-of-Interest Disclosure Form should be uploaded to the file destination of 'Conflict-of-Interest Disclosure Form'.

Response:

Disclosure of Potential Conflicts of Interest (PDF) form was downloaded and filled. The corresponding author is responsible for completing this form. The filled Disclosure of Potential Conflicts of Interest form was uploaded to the file destination of 'Conflict-of-Interest Disclosure Form'.

JOURNAL EDITORIAL BOARD'S REVIEW

1. Plan and place of study missing in methodology

Response:

Thank you! We added the the "the plan and place of study " section in the methodology as below.

The research plan was followed by the National Natural Science Foundation of China, No. 82070856, and conducted in Laboratory Animal Center of Weifang Medical University. The experimental protocols were approved by the Institutional Animal Care and Use Committee (No. 2021SDL574) and Institutional Review Board (No. 2020SDL074).

2. Comment on informed consent is missing

Response:

This study "Duodenal-jejunal bypass improves hypothalamic oxidative stress and inflammation in diabetic rats via glucagon-like peptide 1-mediated Nrf2/HO-1 signaling" is based on experimental animals and is not a clinical medical study, not involve human tissue or samples. The "Comment on informed consent" is not applicable in this study. Hope this response has resolved your doubts.

3. Institutional ethical clearance and certificate details not given in accordance

Response:

We provided and uploaded "Institutional ethical clearance and certificate" in details named "88731-Institutional Review Board Approval Form or Document" form in the system.