

Dear reviewers and editors:

Thank you for your great comments and concerning our manuscript entitled “Estrogen augmented visceral pain and colonic neuron modulation in a double-hit model of prenatal & adult stress” to publish in WJG. Those comments are very helpful for revising and improving our paper. However, Dr. Winston and Dr. Li are in USA, the signature may be sent to you in a few days. We have studied comments carefully and have made extensive modification. Revised portion are highlighted in red color in the manuscript. The main corrections in the paper and the response to the reviewers’ comments are as following:

#1 Submitted by: Reviewer 1

Scientific Quality: Grade C (Good)

Language Quality: Grade A (Priority publishing)

Conclusion: Accept (General priority)

Specific Comments to Authors: WELL WORKED UP AND WRITTEN MANUSCRIPT

#2 Submitted by: Reviewer 2

Scientific Quality: Grade B (Very good)

Language Quality: Grade A (Priority publishing)

Conclusion: Accept (General priority)

Specific Comments to Authors:

The problem of visceral hypersensitivity occurs in irritable bowel syndrome, particularly in women has been discussed for several years (including the authors of the current publication).

1. In the literature there are quite a lot of works that discuss of various aspects of this condition. The present publication is a continuation of previous research. The topics are covered very well and thoroughly and literature citations are appropriate. The paper is organized in a clear and easy to understand manner. However, the literature cited is too numerous, especially in the introduction and authors should consider the desirability of citing all papers.

Response: Thanks for the positive comments. The literatures cited in the introduction have been screened and reduced.

2. The Discussion section reiterate some information already presented whereas one

would expect a personal interpretation of the results and some suggestions to move forward. Some of the information from discussion should be included in the introduction of the paper. To sum up, the work provides novel information and deserves publishing after minor essential improvements.

Response: Thanks for the positive comments. According the suggestions, the Introduction and the Discussion sections have been modified, please refer to page 16, 17.

#3 Submitted by: Science editor

Issues raised:

1. The authors did not provide the approved grant application form(s). Please upload the approved grant application form(s) or funding agency copy of any approval document(s).

Response: The approval documents have been uploaded.

2. The authors did not provide original pictures. 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: Done. The PowerPoint has been uploaded.

3. The “Article Highlights” section is missing. Please add the “Article Highlights” section at the end of the main text.

Response: The “Article Highlights” section was added in the manuscript. We also added the Graphical Abstract to the core tips.

Best wishes,

Jinghong Chen, PhD

Prof. in Shanghai Key Laboratory of Psychotic disorders