

## ANSWERING REVIEWERS

April 26, 2013

Dear Editor,



**Title:** Effect of amitriptyline on gastrointestinal function and brain-gut peptides: A double-blind trial

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The manuscript has been improved according to the suggestions of reviewers:

1 Format has been updated

2 Revision has been made according to the suggestions of the reviewer

Major:

1. I could not follow this manuscript due to deficiency of enough explanation for the method. Definitely, it needs correction of English by native speaker.

Answer: Thanks so much for your good question. The paper has been edited by professional English language editing companies and got the language certificate from the company.

2. The brief review (about the definition and the function) of brain-gut peptide is needed in the Introduction section.

Answer: Thanks so much for your good question. We have provided the brief review of brain-gut peptide in the introduction section (page 4, line 6-11).

3. The dose of amitriptyline and the method of its administration were shortly described in abstract. However, these contents are not shown in materials and methods section. The full description is necessary.

Answer: Thanks so much for your good question. We have described the dose of amitriptyline and the method of its administration in the materials and methods section fully (page 5, line 4-5).

4. The adverse effect of drug should be described and we need information of whether any person was dropped out due to its adverse effect.

Answer: Thanks so much for your good question. We have described the adverse effect of drug, shown in RESULTS Adverse effects and Safety and Table 5. And no subject dropped out of the study due to the adverse effect (in page 9, line 8-11).

Table 5. Adverse effects of AMT and placebo

Adverse effect	AMT(n=28)	placebo(n=28)
Sleepiness	10	2

Bitter taste	7	2
Dry mouth	6	3
Tired in early morning	2	1
Dizziness	2	0
Constipation	1	1

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5. Why the authors measured HAMD and HAMA score again even though the psychiatric illness history was formerly ruled out in the exclusion criteria? In addition, brief explanation of these scores is needed.

Answer: Thanks so much for your good question. Because subjects haven't psychiatric illness history may have such diseases before the experiment, we measured HAMD and HAMA score again to avoid the factor which affect gastrointestinal function. We have shown the brief explanation of the score in materials and methods (Endpoints of the study) section (page 5, the fourth to the fifth line from the bottom).

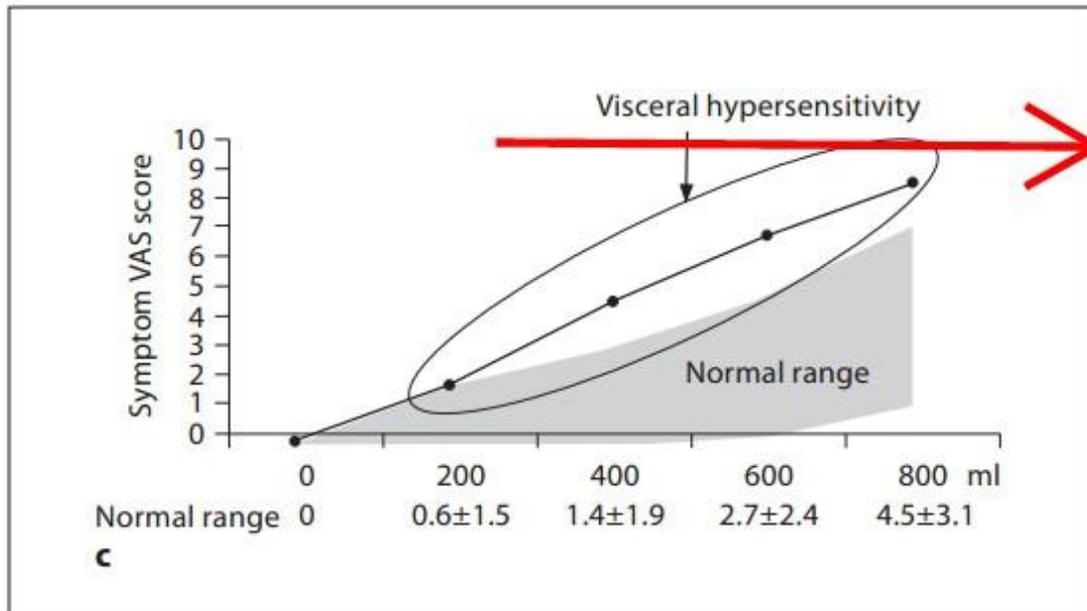
6. Need more detailed instructions about the drinking-ultrasonography. For example, how did volunteers drink water in supine position? By a cup? By a straw? The authors described that the emptying period was calculated 5 and 10 min after drinking the total 800ml of water. This sentence was very ambiguous. How did they calculate the period, by measuring the time or measuring the cross-sectional area of the lumen?

Answer: Thanks so much for your good question. Volunteers drunk water in supine position by a straw. We calculated the period by measuring the time. We have corrected it in the materials and methods (Drinking-ultrasonography test) section (page 6, line 7, line 14-16).

7. The authors scored the discomfort (such as 'abdominal fullness', not separating the symptoms) of volunteers to drink water in supine position by VAS analogue. It would be reasonable to check subdivided symptoms (abdominal pain, abdominal fullness, regurgitation etc.) and add up each score (Aliment Pharmacol Ther 2011; 34: 638-648).

Answer: Thanks so much for your good question. We used the same method to evaluate gastric accommodation from reference 10, and the author did not subdivided the symptoms in the experiment (See Figure 1 from reference 10. ), so we didn't neither. We directly asked the subjects symptoms all together and didn't subdivide them.

Figure 1



8. It is not common to use one way ANOVA to compare two groups. The results could be the same. However, using student t-test in comparing the continuous variables between two groups is necessary.

Answer: Thanks so much for your good question. We have used student t-test compared the two groups, and the result were the same. We have corrected it in the Statistical analysis section (page 7, line 8-10).

9. In Discussion section, the authors cited reference 19 to compare the author's results with this article. However, citalopram is a SSRI that has different mechanism with TCA. I think it is not appropriate to compare these two drugs. Thus, the authors should modify the present manuscript, somehow

Answer: Thanks so much for your good question. As we know, there was no study reported the effect of TCA on the level of ghrelin. According to your suggestion, we have deleted the reference 19, and cited reference 6 in discussion section (in page 10, the third to the last line from the bottom).

10. The authors must comment the limitation of this study before the conclusion. For instance, total number is quite small because the subjects were healthy volunteers. etc.

Answer: Thanks so much for your good question. We have commented the limitation of our study in discussion section (page 11, line 8-13).

Minor:

1. More detailed descriptions about the exclusion criteria are needed.

Answer: Thanks so much for your good question. We have corrected the text in the paper (page 5, line 16-22).

2. The last paragraph of method section, the explanation of table 1, was a mention about the result. It would be better to comment them in the result section.

Answer: Thanks so much for your good question. We have corrected the text in the paper (page 7, line 13-22).

3. OCTT also reflect small bowel transit time. It should be clarified.

Answer:Thanks so much for your good question.We have clarified OCTT also reflect small bowel transit time(page 10, line 8-9).

4. The abbreviation in the figure 1 such as AMT should be fully described. And it would be better to indicate 'two weeks wash out period' in figure 1. In table 1-4, it is correct to change '10 mm VAS' to '100 mm (10 cm) VAS'.

Answer:Thanks so much for your good question.We have corrected the text in the paper.

5. There must be the standardization of the terms. The authors are using 'serum level' mixed with 'plasma level' or 'blood level', 'analogue' with 'analog'.

Answer:Thanks so much for your good question. We have corrected the text in the paper.

6. Please correct many typing errors, spacing errors and expression errors. For example; Page 3, line 5, there will be ";" instead of ","; Page 4, line 11, neuropeptide Y Page 4, line 14, AMT instead of ATM Page 9, line 14, moreover instead of morever Page 11, line 3 and 8, elevated instead of evaluated Page 11, line 15, marks of parenthesis is missing

Answer:Thanks so much for your good question. We have corrected the text in the paper.

3 References and typesetting were corrected

Thank you again for publishing our manuscript in the *World Journal of Gastroenterology*.

Sincerely yours,  
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