

PEER-REVIEW REPORT

Name of journal: *World Journal of Gastroenterology*

Manuscript NO: 71595

Title: Spinal anesthesia alleviates dextran sodium sulfate-induced colitis by modulating the gut microbiota

Provenance and peer review: Unsolicited manuscript; Externally peer reviewed

Peer-review model: Single blind

Reviewer's code: 05225141

Position: Peer Reviewer

Academic degree: DVM, PhD

Professional title: N/A

Reviewer's Country/Territory: United States

Author's Country/Territory: China

Manuscript submission date: 2021-09-21

Reviewer chosen by: AI Technique

Reviewer accepted review: 2021-09-21 13:50

Reviewer performed review: 2021-09-29 13:38

Review time: 7 Days and 23 Hours

Scientific quality	<input type="checkbox"/> Grade A: Excellent <input type="checkbox"/> Grade B: Very good <input checked="" type="checkbox"/> Grade C: Good <input type="checkbox"/> Grade D: Fair <input type="checkbox"/> Grade E: Do not publish
Language quality	<input type="checkbox"/> Grade A: Priority publishing <input type="checkbox"/> Grade B: Minor language polishing <input checked="" type="checkbox"/> Grade C: A great deal of language polishing <input type="checkbox"/> Grade D: Rejection
Conclusion	<input type="checkbox"/> Accept (High priority) <input type="checkbox"/> Accept (General priority) <input type="checkbox"/> Minor revision <input checked="" type="checkbox"/> Major revision <input type="checkbox"/> Rejection
Re-review	<input checked="" type="checkbox"/> Yes <input type="checkbox"/> No

Peer-reviewer statements	Peer-Review: [<input checked="" type="checkbox"/>] Anonymous [<input type="checkbox"/>] Onymous Conflicts-of-Interest: [<input type="checkbox"/>] Yes [<input checked="" type="checkbox"/>] No
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SPECIFIC COMMENTS TO AUTHORS

In this manuscript, the authors investigated the potential effect of spinal anesthesia on inflammatory bowel disease (IBD) by modulating gut microbiota, suggesting a new treatment option for IBD. Overall, the design and performance are good. However, there are some issues with the result presentation and discussion. Rephrase this sentence 'The composition of the fecal microbiota was determined by analysis of ~30,000 paired reads per mouse of the ~250-bp v4 region of the 16S rRNA gene by Illumina MiSeq sequencing'. In addition, in method V3-V4 region was measured, how do you can analyze the V4 region? Grammar errors: Line 80: co-caged individual > co-caged individuals; Line 86: after approved from > after approval from; microvillus in colon were > was (or microvilli); Line 158: different group > different groups; Line 195: incubated for in the dark, remove for; Line 277: H&E straining > H&E staining; Line 289: the inflammatory response were> was; Line 344: no significantly difference > significant; Line 378: epithelia barrier > epithelial barrier; Line 389: As we known> As we have known; Line 392: which increase gastrointestinal > which increases gastrointestinal; Line 412: relive disease > relieve disease; Line 434: Increasing sympathetic tone have > has; Line 435: development intestinal inflammation > development of intestinal inflammation; etc. Figure 1B and 1C, day 0 to day 14, maybe not count day 15, as well as Figure 5G or 5H. In addition, how to calculate DAI. Figure 2D to 2J order is now correct, context vs figure. Similarly, checking the order of Figure 3B and 3D. The western blotting figure needs semi-quantification, then describes the results. Section 3.6, the result description was not correct. Verrucomicrobia does not decrease in data of Figure 6, induced by FMT. Several studies have reported the beneficial effects of local or systemic lidocaine in



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experimental colitis, Topical treatment with Lidocaine in Patients with Ulcerative Proctitis/Colitis. Discussion should be added to explore the novelty of current study. Minors: The phylum name of bacteria is not italic. Written errors: Line 103: was cut ^and > was cut and; Line 110: 3), , remove one ,; Line 139: andthen blocked > and then blocked; Line 201: and ^the: and the; Line 265: Armonk, NY) ^.; Line 294: the the expression of IL> remove one of the; Line 439: ^Moreover; Number and unit: ml or mL, 1part, 1: 5,000 or 1:5,000

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Reviewer's code: 05662946

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Scientific quality	<input type="checkbox"/> Grade A: Excellent <input checked="" type="checkbox"/> Grade B: Very good <input type="checkbox"/> Grade C: Good <input type="checkbox"/> Grade D: Fair <input type="checkbox"/> Grade E: Do not publish
Language quality	<input type="checkbox"/> Grade A: Priority publishing <input checked="" type="checkbox"/> Grade B: Minor language polishing <input type="checkbox"/> Grade C: A great deal of language polishing <input type="checkbox"/> Grade D: Rejection
Conclusion	<input type="checkbox"/> Accept (High priority) <input type="checkbox"/> Accept (General priority) <input type="checkbox"/> Minor revision <input checked="" type="checkbox"/> Major revision <input type="checkbox"/> Rejection
Re-review	<input checked="" type="checkbox"/> Yes <input type="checkbox"/> No

Peer-reviewer statements	Peer-Review: <input checked="" type="checkbox"/> Anonymous <input type="checkbox"/> Onymous
	Conflicts-of-Interest: <input type="checkbox"/> Yes <input checked="" type="checkbox"/> No

SPECIFIC COMMENTS TO AUTHORS

General comments: This manuscript "Spinal anesthesia alleviated DSS-induced colitis by modulating gut microbiota" revealed that spinal anesthesia alleviates DSS-induced colitis in mice by affecting the microbiota. Spinal anesthesia reduced increased noradrenaline levels in DSS-induced mice, which may be one of the mechanisms underlining the effect on gut microbiota. This is a new method to reduce colitis and impressive me. The experiment is well designed and the presented data support the conclusion. However, some specific details and mismatch or between figure and text should be revised to improve the quality of the manuscript. Major Revision. Questions: Why is the quantitative statistical result of Fig. 7B inconsistent with the information shown in Fig. 7A? Is there no more specific picture of saline+DSS group in HE staining? From the picture of HE staining, we can only see intestinal villi fracture in the saline+DSS group, but there are no other clear inflammatory indicators. Please provide more specific pictures. Can you provide the Venn diagram of OTUs in microbial analysis? It is suggested to refer to the article "Dietary Taxifolin enhances the intestinal barrier and regulates intestinal flora to prevent sodium dextran sulfate induced colitis through NF-KB signaling". Spinal anesthesia is a novel approach to alleviate DSS-induced colitis by modulating gut microbiota, however, some discussion of its comparison with other ways should be added, such as bioactive peptides and taxifolin: "Dietary Bioactive Peptide Alanyl-glutamine Attenuates Dextran Sodium Sulfate-induced Colitis by Modulating Gut Microbiota. Oxidative Medicine and Cellular Longevity", "Dietary Taxifolin Protects Against Dextran Sulfate Sodium-induced Colitis via NF-κB Signaling, Enhancing Intestinal Barrier and Modulating Gut Microbiota. Frontiers in Immunology",

"The Potential of Food Protein-derived Bioactive Peptides against Chronic Intestinal Inflammation. Mediators of Inflammation". Line 32-35: Rewrite this sentence. Line 35: Change "reducing" to "reduce". Line 46: Change "inflammation" to "inflammatory". Line 98: Change "mg/kg" to "mg/kg BW". Line 130: Delete "blank". Line 119: Change "microvillus" to "Microvillus". Line 131: Change "was" to "were". Line 139: Change "andthen" to "and then". Line 252: Delete ")". Line 257: Change ";" to ":". Line 265: Change "NY) ." to "NY)". Line 275: Change "stool consistency" to "stool consistency reduce". Line 289: Change "were" to "was". Line 294: Change "the the expression" to "the expression". Line 294: Change "TNF- α in" to "TNF- α in". Line 294: Rewrite all "induced by DSS" in this manuscript. Line 331-334: Supplement the figure of PCoA. Line 332-334: Supplement the description about the figure. Line 349-350: Rewrite this sentence. Line 367: Please add some references to prove "Several studies ". Line 370: Change "Figure 1A" to "Figure 7A". Line 374: Change "underline" to "underlining". Line 392: Change "increase" to "increases". Line 414: Change "is" to "are". Line 422: Change "main catecholamine" to "the main catecholamines". Line 440: Write the full name of "BCA". Line 443: Supplement "NC" manufacturer information. Line 444: Delete "a degree of". Line 434: Change "have" to "has". Line 435: Delete "by". Line 439: Change " β -Actin" to "Occludin". Line 441: Change "was" to "were". Line 449: Change "underline" to "underlining". Line 583: The pictures in "Figure Legends" are seriously inconsistent with the description in the manuscript, PCoA pictures are missing, and the meaning of pictures 5A and 6A is unclear. Please check and modify carefully. Line 628: Change "(DAI) (F)" to "(DAI), (F)". Line 638-639: Supplement the figure of PCoA. Line 643: Change "(DAI) (F) colon length" to "(DAI) (F), colon length". Line 653-654: The quantitative statistical results of Figure 7B are inconsistent with the information shown in Figure 7A. Please provide the data (including peak area) used for quantification.

RE-REVIEW REPORT OF REVISED MANUSCRIPT

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Author's Country/Territory: China

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Scientific quality	<input type="checkbox"/> Grade A: Excellent <input checked="" type="checkbox"/> Grade B: Very good <input type="checkbox"/> Grade C: Good <input type="checkbox"/> Grade D: Fair <input type="checkbox"/> Grade E: Do not publish
Language quality	<input checked="" type="checkbox"/> Grade A: Priority publishing <input type="checkbox"/> Grade B: Minor language polishing <input type="checkbox"/> Grade C: A great deal of language polishing <input type="checkbox"/> Grade D: Rejection
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Peer-reviewer	Peer-Review: <input checked="" type="checkbox"/> Anonymous <input type="checkbox"/> Onymous



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statements

Conflicts-of-Interest: [] Yes [Y] No

SPECIFIC COMMENTS TO AUTHORS

The authors revised the comments according to reviewer's suggestion. Good job.