Format for ANSWERING REVIEWERS

June 08, 2016

Dear Editor,

Please find enclosed the edited manuscript in Word format (file name: 26634-review.doc).

Title: Comparative effects of $\alpha_2\delta$-1 ligands in mouse models of colonic hypersensitivity

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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
This preclinical study demonstrates a2δ-1 ligands efficacy on inflammation-associated CHS, showing their potential clinical interest for patients with chronic abdominal pain and moderate intestinal inflammation.

1. The authors state that low-doses of DSS probably do not induce severe tissue lesion and subsequent desensitization. I would like to know how did they prove the severity of the tissue lesions during the experiment? What they used for the evaluation of the severity of tissue damage, microscopic or microscopic evaluation? Accordingly if they performed a pathological evaluation, did they observe any different finding regarding tissue damage between groups?

We thank the reviewer for this comment and in order to clarify how we quantified the severity of the tissue lesions during the experiment, we performed some measurement to assess intestinal inflammation: histological score and MPO activity (lines 213-228). As expected, low-dose 1% DSS treatment induced moderate alterations of colonic mucosa characterized by a few focused epithelium disorganization and inflammatory cell infiltration (Supplemental Figure 1). A histological score was calculated on a range of 0 to 12. Thus, a slight but significant increase of the histological score was observed in the low-dose 1% DSS-treated mice (Supplemental Table 1). Moreover, MPO activity was not significantly modify in low-dose 1% DSS-treated mice compared to control water-treated mice (Supplemental Table 1). All together, these results tended to highlight a moderate colonic inflammatory impairment associated to CHS. Thus, in our study, low-dose of DSS probably does not induce severe tissue lesion and subsequent desensitization but are sufficient to enhance colonic

primary afferents response to colorectal distension (lines 273-281).

2. The grammatical and typo grammatical errors should be corrected.

After a careful reading of the text by MG Translate, a few grammatical and typo grammatical errors has been corrected.

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