Author's response to reviews

Title: Enhanced sensitivity to punctate painful stimuli in female patients with chronic low back pain

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Author's response to reviews: see over
**Point-by-Point Reply to the Reviewers’ Comments**

First of all, we thank the reviewers for their constructive comments. We have provided a point-by-point reply (see below) and include several changes into the manuscript. As a result, we believe that the manuscript has improved considerably.

**Reviewer: 1**

This study demonstrates punctate hyperalgesia in female patients with low back pain compared to matched healthy controls. The investigators followed the protocol put forward by the German Research Network on Neuropathic Pain, and this is a strength of the study. The work has no significant flaws and the study is a valuable contribution to the literature on low back pain. There are no major compulsory revisions.

**Minor Essential Revisions**

The paper needs some improvements before it is ready for publication.

Under Participants, please specify gender and offer some rationale for not using both sexes.

**Response:** We included information on gender to the method section as suggested.

During the recruitment of patients, we primarily found female volunteers for our study (14 females, 2 men). So there was no rationale to specifically recruit female volunteers, but rather the situation during recruitment of patients. While the 2 men principally show the same behavior of SR function, we decided not to include their data due to this imbalance in numbers.

As a result, we were not able to include a specific rationale for not including men; instead, we have included this as a limitation of the study to the discussion section (see p. 13, §2).

In Methods, it is unclear whether the investigators performed the stimulation unilaterally or bilaterally.

**Response:** We included this information (now p. 5; §2).

In Discussion, Limitations and Further Directions, sentence two mentions effect sizes but unless I am missing a table, the text does not report effect sizes. It might be a good idea to do so in light of the small sample sizes (discretionary).

**Response:** We included Cohen’s d as a measure of effect size to the results including factor Group throughout the MS.
Writing quality is uneven. …

Response: A native speaker (Dr. Jeremy Thorne, see Acknowledgements) has now approved the text.

… While the results are quite lucid, the Background needs improvement. The last sentence in the first paragraph is nonsensical.

Response: We have changed the sentence.

Paragraph 2 line one, replace “was shown being” with “is.”

Response: We have changed the phrase according to the suggestion.

Line 6 in the same paragraph, replace “was demonstrated being” with “is.”

Response: We have changed the phrase according to the suggestion.

In the same line, “Unexpectedly” seems out of place and would read better as “However.”

Response: We have changed the phrase according to the suggestion.

Last sentence, “reduces” should be “reduced.” The final paragraph in Background is difficult to read, and it is very important because it states the hypothesis. I suggest: “We hypothesized that CLBP patients exhibit increased sensitivity to punctate mechanical stimuli on both paraspinal lumbar areas and dorsal and palmar aspects of the hand compared to matched healthy controls.”

Response: Thank you for this advice. We have changed this according to the suggestion.

Perhaps it should say noxious punctate mechanical stimuli.

Response: We have changed the phrase according to the suggestion.

Methods, Participants, paragraph two, line one, I suggest, “To evaluate our hypothesis we tested pain sensitivity to…”

Response: We have changed the phrase according to the suggestion.

Sentence 2, delete “also recruited that were…”

Response: We have changed the phrase according to the suggestion.
**Discretionary Revisions**

Finally, in Discussion, Limitations and Further Directions, it might be useful to say more. Testing only females is unusual and there may be concerns about how well the results will generalize to males. There is no report of tracking menstrual cycle or testing at only specific phases of it as many investigators do. This may merit a comment.

**Response:** Thank you for this suggestion. We have included statements with respect to the concern to generalize data to males as well as to the restrictions concerning menstrual cycle (p. 13, § 2).
Reviewer: 2

This study used pinprick stimuli to determine if there is higher sensitivity to noxious stimulation in chronic low back pain patients than matched controls. The authors report enhanced sensitivity to both low and moderate pinprick stimuli at the back and a remote site (the hand) suggesting alterations in higher level processing or an enhanced vulnerability.

The introduction covers the most important materials but disregards the older literature on perceptual deficits in CLBP, which is quite extensive and also covers the topic of habituation. 

Response: According to the reviewer’s suggestion, we have included additional statements and some pieces of the older literature on perceptual deficits (last § on page 3 to §1 on page 4).

Throughout the paper a number of grammatical errors can be found that need to be corrected in a revised version (for example, replace subjects’ characteristics by subject characteristics or 6 months history by six month history; each stimuli should be each stimulus; stimulation side should be stimulation site.)

Response: We have performed all changes requested. Additionally, a native speaker (Dr. Jeremy Thorne) has now checked the text (see acknowledgement).

Although the subjects were without medication at the time of the testing it would be good to know what medication they were using. With the small N of subjects this could be given per subject and medication aftereffects could be tested.

Response: We have changed table 1 and present now detailed data for each patient including the requested information on medication.

We have performed additional ANOVAs similar to our statistical approach comparing CLBP patients without any medication vs. CLBP patients with medications (instead of all CLBP patients vs. HC). There was no significant main effect of Group and no significant interaction including factor Group. Furthermore we selectively excluded CLBP patient No 7 (flupirtin) from the analysis: all reported significant changes remain the same without this patient. So we concluded that medication did not significantly influence the results.

The time the patients were off medication was very short. How was compliance tested?

Response: Patients were informed and asked directly before the examination. We have included statements in the MS (p. 4; last paragraph).
The methods and results are otherwise adequately described but the authors should give exact
p-values for non-significant comparisons.

Response: We have now included exact p-values for all non-significant comparisons.