Reviewer’s report

Title: Clinical relevance of contextual factors as triggers of placebo and nocebo effects in musculoskeletal pain

Version: 0 Date: 02 Nov 2017

Reviewer: Przemysław Babel

Reviewer’s report:

This is a nice and comprehensive review paper dealing with the effects of contextual factors on musculoskeletal pain. I do appreciate extensive work done by the authors, however I have some important conceptual concerns.

1. The authors do not use the term placebo, but they use the terms placebo and nocebo effects as resulting from contextual factors, and it is not clear what is the relationship between placebo and contextual factors. Are they synonyms or are there any differences between both phenomena?

2. Contextual factors are considered either as a cause of the placebo and nocebo effects ("The presence of the CFs triggers psycho-neurobiological responses (placebo and nocebo effects"; "when the presence of positive CFs produces placebo effects or when the presence of negative CFs produces nocebo effects"), or mediators of the placebo and nocebo effects ("the study of CFs as mediators of placebo and nocebo effects"; "The impact of CFs as mediators of pain outcome"; "the different CFs as modulators of therapeutic outcome"). These are not the same.

3. It should be clarified what authors mean by "patients that are not influenced by the therapeutic context (the so called "placebo non-responders")", One may assume that there are some people who never response to placebos, although in fact there are neither placebo responders nor placebo non-responders - everybody can sometimes respond to placebos and sometimes not.

4. Trying to explain the mechanisms of the effects of the contextual factors, the authors refer to the mechanisms of the placebo effects (page 9) without having acknowledged that.

5. The presentation of the expectancy theory seems to be at odds with the theory. It is not the treatment to be expected, but the treatment activates the expectancy of relief.

6. Although the authors refer to some theories as psychological ones (page 9), in fact all of the theories they discuss are psychological. Moreover, those so called psychological theories are just the factors affecting the effects of the placebo administration rather than theories.
7. Studies cited in the context of musculoskeletal pain conditions do not always refer to musculoskeletal pain; sometimes they refer to pain in general or other pain conditions.

8. The authors seem to consider brain as a homunculus (e.g. "CFs influence the patient's brain"; "CFs are actively interpreted by the patient's brain"; "How do the contextual factors modify the patient's brain?"). This should be avoided.

9. Although the authors avoid the term placebo and use the term contextual factors instead, most of the cited literature refer to the placebo effects, not to the contextual factors.

10. The Figure 1 is at odds with the text of the manuscript. According to the Figure 1 there is only one mechanism of the placebo and nocebo effects, i.e. expectancy. However, in fact, there are a few mechanisms proposed, which is clearly acknowledged in the text of the manuscript (page 9).

In summary, some work is needed to make the paper clearer. First, it should be clarified what is the topic of the paper (contextual factors, placebo effects or maybe placebo-related effects?), or - at the very least - it should be clarified when the authors refer to the studies/theories on the contextual factors, and when to the studies/theories on the placebo effects. Second, it should be clarified whether this is a paper on pain in general, with some references to musculoskeletal pain, or a paper on musculoskeletal pain only. If the latter, the authors should always acknowledge when they refer to the studies on pain in general, not to musculoskeletal pain.

Are the methods appropriate and well described?
If not, please specify what is required in your comments to the authors.

Unable to assess

Does the work include the necessary controls?
If not, please specify which controls are required in your comments to the authors.

Unable to assess

Are the conclusions drawn adequately supported by the data shown?
If not, please explain in your comments to the authors.

Yes

Are you able to assess any statistics in the manuscript or would you recommend an additional statistical review?
If an additional statistical review is recommended, please specify what aspects require further assessment in your comments to the editors.

Not relevant to this manuscript

Quality of written English
Please indicate the quality of language in the manuscript:

Acceptable

**Declaration of competing interests**
Please complete a declaration of competing interests, considering the following questions:

1. Have you in the past five years received reimbursements, fees, funding, or salary from an organisation that may in any way gain or lose financially from the publication of this manuscript, either now or in the future?

2. Do you hold any stocks or shares in an organisation that may in any way gain or lose financially from the publication of this manuscript, either now or in the future?

3. Do you hold or are you currently applying for any patents relating to the content of the manuscript?

4. Have you received reimbursements, fees, funding, or salary from an organization that holds or has applied for patents relating to the content of the manuscript?

5. Do you have any other financial competing interests?

6. Do you have any non-financial competing interests in relation to this paper?

If you can answer no to all of the above, write 'I declare that I have no competing interests' below. If your reply is yes to any, please give details below.

I declare that I have no competing interests.

I agree to the open peer review policy of the journal. I understand that my name will be included on my report to the authors and, if the manuscript is accepted for publication, my named report including any attachments I upload will be posted on the website along with the authors' responses. I agree for my report to be made available under an Open Access Creative Commons CC-BY license (http://creativecommons.org/licenses/by/4.0/). I understand that any comments which I do not wish to be included in my named report can be included as confidential comments to the editors, which will not be published.

I agree to the open peer review policy of the journal

Do you want to get recognition for reviewing this manuscript? Add a record of this review to Publons to track and showcase your reviewing expertise across the world's journals. Signing up is quick, easy and free!

Yes