Reviewer's report

Title: Evidence for placebo effects on physical but not on biochemical outcome parameters. A review of clinical trials

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Reviewer: Ted J Kaptchuk

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General
This reviewer enjoyed reading this thoughtful, well-performed and well-written study. The question addressed, to what extent does placebo treatment effect physically defined measures of peripheral disease process as opposed to biochemical parameters is important and timely. This reviewer has several minor questions and comments.

1. In abstract, in the conclusion, the discussion of visceral reward learning should not be there and rather confined to the discussion. The points are important but this discussion is an interpretation of results and not a conclusion for abstract.

2. page 4. Medline does include “untreated control groups” but there is no regular or established way to search for this condition.

3. page 5. The biggest concern I have is what is called “stable disease.” What exactly is meant seems to be judgment call and might be defined with some examples. See below.

4. page 6. Besides unblinding, I think a second reason to only first phase of cross-over is that there may be a carry-over effect from the drug.

5. page 7. Please check the sentence that concerns 56 trials and only 13. Is there an error here?

6. Discussion. I’d make the caveats and limitations stronger. Again, what is stable disease? For example, fistula is considered stable. But some the improvement in physical could be observer bias. Also, I think many of these conditions are subjected to variability and regression. If the definition or caveats were clear, I think the category of “stable” would be ok.

7. Good discussion of operant condition and summary of recent studies.

Major Compulsory Revisions (that the author must respond to before a decision on publication can be reached)

Minor Essential Revisions (such as missing labels on figures, or the wrong use of a term, which the author can be trusted to correct)

Discretionary Revisions (which the author can choose to ignore)

Which journal?: Appropriate or potentially appropriate for BMC Medicine: an article of outstanding merit and interest in its field

What next?: Accept for publication in BMC Medicine after discretionary revisions

Quality of written English: Acceptable

Statistical review: No

Declaration of competing interests:
I declare that I have no competing interests.