Reviewer's report

Title: Pain disorder leads to a frequency shift in the anterior default mode and the salience network

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Reviewer: Karin Jensen

Reviewer's report:

1. Is the question posed by the authors well defined?

Major revision: Not really, since the distinction between “explained” pain and “unexplained” pain is confusing. It is not true that the pain in previous studies, mentioned in the introduction, have “a convincing organic correlate”. Chronic low back pain, for example, is often idiopathic and not more organic than the pain described by the authors in this manuscript. The point is that previously “unexplained” pain syndromes have become medically explainable due to scientific progress. The cause for pain is often impossible to determine in chronic pain disorders and comorbidity with psychiatric diagnoses is high. High correlation doesn’t mean that there is a given causality where negative affect leads to pain. The authors should have adapted a more dynamic approach to the definition of “unexplained chronic pain” and psychiatric symptoms. How many patients with musculoskeletal pain such as Fibromyalgia, or IBS, would fulfill the inclusion criteria in this study? In spite of the point about “explained” versus “unexplainable” pain in the introduction, the discussion seems to include both types of pain without any mechanistic distinction. Very confusing.

2. Are the methods appropriate and well described?

Major revision: Methods are generally well described but the practical steps around fMRI scanning are poorly described. The multiple comparison correction in the less stringent fMRI analysis (threshold at p=0.005) needs to defined: Was it voxel-wise or cluster-wise? Is there a z-value threshold that the authors can describe in the methods section, instead of p-values? How was the functional connectivity in relation to depression and anxiety scores performed? Dual regression? This needs to be described in the methods section.

3. Are the data sound?

Major revision: Six minutes of BOLD fMRI for resting state is normal and the analyses used in this study are standard. However, the comparisons of power spectra seem to suffer from a multiple comparison problem. Do the results survive Bonferroni correction?

4. Does the manuscript adhere to the relevant standards for reporting and data deposition?
Minor revision: Yes, but data is not detailed. Only the main results are reported and there could have been more elaborate investigations of data by using plots or looking at functional connectivity that controlled for ongoing clinical pain etc. P-values should be mentioned in the tables.

5. Are the discussion and conclusions well balanced and adequately supported by the data?

Major revision: Some points in the discussions are presumptuous, for example the section about “our findings reflect one neurobiological facet of the strong clinical impression that patients who suffer from pain disorder often show reduced subjective emotional awareness and impaired social understanding”. The discussion should mirror the line of thought used in the introduction, where somatoform disorder is thought to be different from pain syndromes with a clear etiology.

6. Are limitations of the work clearly stated?

Major revision: Yes. However, the theoretical limitations of this work are not considered. The distinction “medically explained” and “unexplained” needs to be addressed.

7. Do the authors clearly acknowledge any work upon which they are building, both published and unpublished?

Yes.

8. Do the title and abstract accurately convey what has been found?

Major revision: NO. The title implies causality, which has not been investigated in this study. “Pain disorder leads to…” This has to be changed into a more appropriate title.

9. Is the writing acceptable?

Minor essential revision: Acceptable but needs revision and language check.

**Level of interest:** An article whose findings are important to those with closely related research interests

**Quality of written English:** Needs some language corrections before being published

**Statistical review:** No, the manuscript does not need to be seen by a statistician.

**Declaration of competing interests:**

I declare that I have no competing interests