Peer Community In Registered Reports

Are there oscillatory markers of pain intensity?

A recommendation by ***Zoltan Dienes*** *based on peer reviews by* ***Bjoern Horing*** *and* ***Markus Ploner*** *of the STAGE 2 REPORT:*

Chiara Leu, Sébastien Forest, Valéry Legrain, Giulia Liberati (2024) The effect of stimulus saliency on the modulation of ongoing neural oscillations related to thermonociception: a Registered Report. OSF, ver. 3, peer-reviewed and recommended by Peer Community in Registered Reports. https://osf.io/98edq

Submitted: 11 November 2024, Recommended: 20 February 2025

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Dienes, Z. (2025) Are there oscillatory markers of pain intensity?. *Peer Community in Registered Reports*, 100940. 10.24072/pci.rr.100940

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Rhythmic changes in pain can lead to corresponding modulations of EEG amplitudes in theta, alpha, and beta bands. But the question remains open as to whether these modulations are actually tracking pain, or maybe rather saliency or stimulus intensity. The question is of some importance because a marker of pain *per se* could be useful for tracking felt pain without a verbal response, and could be useful in investigating interventions for treating pain (such as suggestion). Here, Leu et al. (2025) addressed the question of whether modulations reflect saliency or else the intensity of pain, by using an oddball paradigm in which most trials are a pain stimulus of a certain intensity, and oddball trials will sometimes occur, at either a higher intensity or a lower intensity than the baseline ones. If the modulations reflected salience, the modulation at the frequency of the oddball would be similar for high and low intensity oddballs. However, if the modulations reflected pain intensity, the modulations for the low rather than high oddball condition would be lower. In fact, the baseline and oddball stimulations were found to be perceived significantly differently only in the high oddball condition; and consistantly, the oddballl stimulus significantly modulated ongoing oscillations in only the high oddball condition. Thus, whether oscillations are modulated by pain intensity or salience could not be picked apart in this study. The study does however raise an important isssue, indicate how it could be addressed, and provide data relevant for clearly resolving the issue in the future. The Stage 2 manuscript was evaluated over two rounds of in-depth peer review. Based on detailed responses to the reviewers' comments, the recommender judged that the manuscript met the Stage 2 criteria for acceptance. **URL to the preregistered Stage 1 protocol:** https://osf.io/qbrf2 **Level of bias control achieved:** Level 6. *No part of the data or evidence that was used to answer the research question was generated until after IPA.* **List of eligible PCI RR-friendly journals:**

- Advances in Cognitive Psychology
- Brain and Neuroscience Advances
- Cortex
- F1000Research
- Imaging Neuroscience
- In&Vertebrates
- NeuroImage: Reports
- Peer Community Journal
- PeerJ
- Psychology of Consciousness: Theory, Research and Practice
- Royal Society Open Science
- Studia Psychologica

References:

1. Leu, C., Forest, S., Legrain, V., & Liberati, G. (2025). The effect of stimulus saliency on the modulation of pain-related ongoing neural oscillations: a Registered Report [Stage 2]. Acceptance of Version 3 by Peer Community in Registered Reports. https://osf.io/98edq

Reviews

Evaluation round #2

DOI or URL of the preprint: https://doi.org/10.17605/OSF.IO/S3879
Version of the preprint: 2

Authors' reply, 18 February 2025

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Decision by Zoltan Dienes, posted 17 February 2025, validated 18 February 2025

Minor Revision

Thank you for your revisions. I have just a couple of points:

1) p 6 " Due to non-compliance or artifacted signals, data of some participants were discarded from the analyses." Be clear if these exclusions were based on pre-registered criteria.

2) When a hypothesis predicts an effect, and the power was not there to pick up all effects that were in principle large enough to support the prediction, then a non-significant result does not disconfirm the hypothesis. It leaves it open. Be more clear about this when discussing non-signfiicant results.

best
Zoltan

Evaluation round #1

DOI or URL of the preprint: https://osf.io/6fcge
Version of the preprint: 1

Authors' reply, 03 February 2025

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Decision by Zoltan Dienes, posted 28 December 2024, validated 30 December 2024

Revision invited

The two reviewers are largely positive about your Stage 2, though make some excellent points. Reviewer 1 urges structuring more closely based on the Study Design Table; indeed, as I was reading the Results section, I had to have the Study Design Table up in another window to go through step by step to check, and it still needed a fair amount of cognitive effort. You could go through listing each question given in the Table, and then the relevant test. Likewise the Discussion, as suggested by the Reviewer. Reviewer 2 raises some relevant substantive points to consider.

On the subject of the Table, note how non-significance was declared as not indicating no effect. As the literature almost universally rides roughshod over this point, it can be hard to break habits absorbed from the literature! Go through thoroughly making sure you do not claim there are no effects when there was simply non-significance. For example: p 24 "while no difference was found between oddball and baseline cycles in the low oddball condition stimulation (F(750)=0.0404, p=0.841)"

"no difference" -> "no significant difference"(as you have not established there was no difference.) Same point arises on page 30, 33, 34, 36, 37. There may be other places.

For all changes to IPA, note them in a footnote at the point they are first mentioned, together with when the change was approved by PCI RR.

best
Zoltan

Reviewed by Markus Ploner, 04 December 2024

The stage 2 manuscript mostly follows the outlines of the stage 1 manuscript. Different than initially planned, the stimulation hardly elicited painful sensations. Therefore, the title and the abstract have been changed to account for this lack of pain induction. Beyond that, the main finding is that high oddball stimuli elicited painful sensations and neural responses, which differed from baseline stimuli. In contrast, the low oddball stimuli did not. Thus, no definite conclusion can be drawn regarding the relationship between stimulus saliency, stimulus intensity, pain perception, and ongoing oscillations.

The manuscript presents the results mostly clearly and discusses the findings extensively. Some revisions might further improve the manuscript:

1. Title and abstract. Unlike initially planned, the stimulation hardly elicited painful sensations, which changed the title and the abstract from pain perception to thermonociception. I'm wondering whether this

tacit focus change is in accordance with the idea of a registered report. The authors might consider presenting and explaining this change in the abstract.

2. Results. The presentation of the results does not clearly relate them to the hypothesis table. I understand the hypothesis table as a core part of a registered report that should guide the analysis and interpretation. Thus, the authors should explicitly relate the findings to the hypothesis table.

3. Discussion. The discussion is quite long and discusses many details of the paradigm, but the results and their interpretation are less discussed along the hypothesis table. The authors might significantly shorten the discussion and change the focus from discussing methodological details to the main topic and the interpretation of the main results.

Reviewed by Bjoern Horing, 22 December 2024

Let me first say that I am excited that the results are in! Thank you for a well thought-out and informative study, it's been a pleasure accompanying this process.

In the following, page numbers refer to the clean PDF. All comments are rather minor, but I would strongly argue for a re-reading of the discussion that seems a bit frayed occasionally.

GENERAL COMMENTS

- The abstract does not mention the (final) sample size which seems like a relevant information for me; furthermore, it is not clear from the descriptions in 2.1 versus 3. whether the final sample size is 35 or 33 (for behavioral data) and 31 (for EEG data), respectively - or if the sample was expanded considering the drop-outs
- 3.1, paragraph 1: The authors suggest to "see Supplementary Material for single subject average examples"; later it more specifically points to "see Supplementary Materials S.IV for single subject average examples"; however, that section seems not to exist, at least not in the two PDFs provided (RR_Saliency Stage II_clean, RR_Saliency Stage II_marked)
- 3.1, paragraph 2: It is quite surprising that the (ostensibly) high temperatures employed did not yield robust pain; it would be an interesting data point exactly what these temperatures were, so could the authors provide at least the descriptives (calibrated mean±SD), at best a plot showing perception threshold, pain threshold, and max temperature (possibly akin to Fig 5)? This may seem pedantic at this point, but I feel it's pertinent given that the thermal stimulation seems to have been one of the big issues during actual empiry.
- 3.3.2, line 7, "considering the first two harmonics in the high oddball condition" is unfortunately phrased, you mean "including the first two harmonics…" (in addition to the oddball frequency itself), right? So FOSagg is 0.125+0.25+0.375, not just 0.25+0.375. This confusion also exists on p. 35, line 2 (it's activity at the first 2 harmonics AND the oddball frequency).
- 4.1, the high oddball supposedly was "the only stimulation that was consistently perceived as painful" seems to be a stretch: Fig 5 and the top mean±SD of 5.5±2.4 VAS (5 being pain threshold) clearly indicate that large portions of the sample did not in fact perceive them as painful. I suggest replacing "consistently" with "on average".
- Parts of the discussion have a rushed feel and should be revisited, e.g.
- p. 32 line 7f., "known to be the primarily" => do you mean primary contributors/afferents/some such notion?
- p. 32 I would think it's a "heat sink-effect", not a "heat sink"? Also use "larger" instead of "worse"?
- p. 32 remove the ", which" after "Wang et al. (2022)"
- p. 34 "… following the oddball stimulation in the low oddball condition", the wording here and in the following is a bit ambiguous and you shift from referencing high oddball/low oddball/unspecified oddball results; can you revisit this?
- All heat sink-related or neuronal temporal filtering aside (enjoyable as the discussion is), it seems to me that another explanation of high oddball-salience and the absence of low oddball-salience is simply that only the high oddball recruited nociceptors to begin with. Hypothetically, assuming an absence of pain perception

for the baseline stimulus (VAS 4.6/VAS 5.0 depending on calculation) chiefly due to an absence of nociceptive drive, the high oddball-related temperature increase might have pushed the stimulus above the pain threshold, leading to a discrete and very salient percept (as in, a new sensory modality arises), whereas baseline/low oddball fluctuations all remain within the non-noxious heat range. This interpretation is tempered, of course, by the fact that roughly half the sample would have actually perceived the baseline peaks as painful (>5.0), as well, without modality-related salience of the high oddball.

- Another alternative interpretation the authors may or may not want to explore is an accumulating offset effects from the downward slopes, maybe fostering a larger antinociceptive tone of the descending modulation (they already point to the comparatively short time spent ”at peak”, by nature of the stimulation).

MINOR FORMAL ISSUES

- p. 23 has at least 2 FOSoddball subscript issues
- p. 29 line 5 subscript period [sub].[/sub]
- p. 31 probably => probable