The effect of top-down attention on secondary mechanical hyperalgesia: a reply to Torta & Meyers

Delia Della Porta [a,b]*,
Eléonore Scheirman[a],
Valéry Legrain [a,b,c]

a Institute of Neuroscience, Université catholique de Louvain, Brussels, Belgium.
b Psychological Sciences Research Institute, Université catholique de Louvain, Louvain-la-Neuve, Belgium.
c Louvain Bionics, Université catholique de Louvain, Louvain-la-Neuve, Belgium.

* **Corresponding author**: D. Della Porta.
Address: Université catholique de Louvain, Institute of Neuroscience, Avenue Hippocrate 53, box B1.53.04,1200 Woluwe-Saint-Lambert, Belgium. Tel.: +39 3479978001
E-mail address: delia.dellaporta@uclouvain.be

Page nr: 5
Word nr: 1319

We are pleased to see that our paper has attracted attention from researchers within the field. However, we were surprised to read the reaction from Torta & Meyers, which we believe stems from some misunderstandings about our methodology. In our response, we first address Torta & Meyers's claim that there is no ongoing controversy, showing that this assertion does not align with empirical evidence, and clarify some points about our methods.

In response to the claim that we incorrectly described their findings [10], we wish to clarify that our phrasing accurately and truthfully reflects the conclusions of their paper [10]. This can be found in the authors'own writing: "*Secondary mechanical hypersensitivity is reduced when a high load working memory task is performed concomitantly with the sensitization procedure*" [10]; and "*Torta et al. (2020) showed that performing a high cognitive load task during LFS results in less hypersensitivity, whereas this was not the case for a low cognitive load task*" [9]. Additionnaly, this interpretation can be found in their title too [10].

Evidence for an ongoing controversy

Torta & Meyers open their commentary by stating that "*the previous literature does not align with the narrative of an ongoing controversy*". However, our view was merely echoing that of the authors who themselves introduced their latest paper [8] by stating "*Whether cognitive factors modulate the development of secondary hypersensitivity remains controversial*." Indeed, prior to our manuscript, three papers by Torta and colleagues split the evidence with two papers pointing in one direction [8,9] and one pointing in the opposite direction [10] (see also [3,4] for similarly contradictory results regarding spatial attention). In their letter the authors present evidence from only two of these studies as a definitive answer to a broad and nuanced question: "*our most recent pre-registered studies, using large samples[8,9], a control condition[8], and Bayesian analysis [8,9], show no support for the possibility that engaging in a high-load task during sensitization reduces the development of secondary mechanical hyperalgesia at the group level, rather strong Bayesian evidence against it* ". While these studies are innovative and important to the field, certain limitations —acknowledged by the authors themselves—such as the lack of blinding for participants or researchers [8,9], and the use of a less robust method to induce mechanical hypersensitivity in [6, see 8],—reduce the conclusiveness of their findings and their interpretation of the Bayesian factors. The ongoing controversy is also just a natural consequence of exploring an emerging field where the concepts in question remain open-ended, as seen in discussions about reconceptualizing sensitization in pain [1]. Such controversy is crucial for the continued debate that refines and clarifies concepts, ultimately leading to a more precise understanding of how attention affects mechanical hypersensitivity.

Incremental improvements

The second point Torta & Meyers make is to question the value of some of the improvements that we introduce in our paper [2].

Time locking. Torta & Meyers seem to misunderstand our rationale for time-locking, suggesting we lack evidence that it is superior to non-time-locked presentation. This presents a good opportunity to clarify any potentail ambiguity in our manuscript. First, we never claimed that time-locking could exert a greater effect on the development of central sensitization. We think that the benefit of time-locking is that it allows stricter control over the manipulated mechanism, placing the competition between nociceptive stimuli and visual stimuli – when rehersaed in working memory [7] – within a defined temporal segment of cognitive processing. This aids in interpreting our findings and facilitates future studies to explore different phases of the cognitive process. The influence of cognitive load can be exerted through different mechanisms and at different levels of sensory information processing [6]. Non-time-locked presentations could dilute the experimental effect by applying attentional competition at incorrect stages for some participants, making null results more difficult to interpret. Torta & Meyers also question the ecological validity of time-locking. However, the aim of our study is to understand a mechanism under controlled conditions by maximizing internal validity. A lack of ecological validity is common in fundamental research, such as animal studies, that yet continue to provide valuable insights.

Statistical test. Torta & Meyers question our use of a simpler model. Our study combines a between-subject design with a model using a two-way interaction term, eliminating the need for a three-way interaction, to achieve more interpretable estimates with smaller sample sizes. However, the authors claim that "*the model neglects a more complex picture"* since we did not include the control arm in our interaction term. We respectfully disagree with this statement. Thanks to our block-randomised between-subject design, any site-unspecific increase in mechanical hypersensitivity that is not caused by our manipulation of interest is taken into account by employing a control group. This ensures that any changes due to our manipulation are over and above any changes that may happen due to unrelated sources (e.g., repeated measurements). The inclusion of a control group also removes the need to estimate a difference score between the control arm and the experimental arm. Thus, the authors' suggestion of calculating a difference score would not improve our ability to make inferences. Additionally, we would like to point out that we did not use 2 models to answer our hypothesis as Torta & Meyers state in their letter. To answer our hypothesis we used one preregistered confirmatory model which only included the experimental arm, as stated in [2]. The other model Torta & Meyers are referring to, was simply an exploratory check on the control arm which showed non-significant changes in sensitivity to mechanical stimuli.

Accuracy. In our discussion [2], we share the authors' sentiment that accuracy might not be a good proxy for attentional engagement. However, the composite scores we used were not intended to assess the evolution of the participants' performance over time but to verify whether they were able to remain focused on the visual task during the application of HFS. Analyzing accuracy in distinct phases is intriguing, but the evidence the authors show to motivate this idea is based on exploratory analyses that need replication; especially since the authors themselves have not replicated this pattern in other studies [9,10]. If we give a closer look at their latest results [8], using a composite score would yield similar inferences: a significantly higher pre-HFS score and significantly higher post-HFS score (with the post-HFS score being lower) would combine into a significant composite score with an effect size between that of the pre-HFS and post-HFS differences.

No-task control. The authors suggest that using a control group with no task, as they did in study [8], could have helped in the interpretation of our results. However, assuming that participants do nothing in a control group can result in heterogeneity in the imposed load [5]. This is a sentiment echoed by the authors: "*Whereas it is clear that the working memory task necessitates executive control, one could argue that the non-working memory task and even the distraction techniques used to cope with the pain in the control condition also require top-down processes to promote more adaptive functioning. If participants used top-down attentional regulation to cope with the pain in all three conditions, it could explain the lack of difference in the perception of the electrical stimulation and the development of hypersensitivity*" [8]. Moreover, participants in a no-task control group are more susceptible to expectancy effects, as it is possible to infer that one is not partaking in an experiment [5]. Thus, an active control condition allows for stricter control over the cognitive load and enhances blinding when, as in our study, it is coupled with a double-blind between-subject design [2].

Conclusion

In conclusion, while we acknowledge the merits of previous studies, the complexity of central sensitization and cognitive interactions warrants ongoing investigation. Our study aimed to contribute to the cumulative understanding of these complexities by combining different refinements in one robust design. Similarly we hope that future studies will build on our work.

Acknowledgements

We wish to express our gratitude to Michael Aristodemou for their insightful feedback on our response.

D.D.P. and V.L. were supported by the Funds for Scientific Research of the French-speaking Community of Belgium (F.R.S.-FNRS). We have no conflicts of interest to declare.

References

[1] van den Broeke EN, Crombez G, Vlaeyen JWS. Reconceptualizing sensitization in pain: back to basics. PAIN Rep 2024;9:e1125.

[2] Della Porta D, Scheirman E, Legrain V. Top-down attention does not modulate mechanical hypersensitivity consecutive to central sensitization: insights from an experimental analysis. Pain 2024. doi:10.1097/j.pain.0000000000003225.

[3] Della Porta D, Vilz M-L, Kuzminova A, Filbrich L, Mouraux A, Legrain V. No evidence for an effect of selective spatial attention on the development of secondary hyperalgesia: a replication study. Cogn Neurosci 2022:754.

[4] Filbrich L, van den Broeke EN, Legrain V, Mouraux A. The focus of spatial attention during the induction of central sensitization can modulate the subsequent development of secondary hyperalgesia. Cortex 2020;124:193–203.

[5] Kazdin, A. Research design in clinical psychology 4th ed. Boston, MA Allyn and Bacon 2003.

[6] Lavie N. Distracted and confused?: Selective attention under load. Trends Cogn Sci 2005;9:75–82.

[7] Legrain V, Damme SV, Eccleston C, Davis KD, Seminowicz DA, Crombez G. A neurocognitive model of attention to pain: Behavioral and neuroimaging evidence. Pain 2009;144:230–232.

[8] Meyers E, Alves M, Teugels A, Torta DM. No Evidence that Working Memory Modulates the Plasticity of the Nociceptive System, as Measured by Secondary Mechanical Hypersensitivity. J Pain 2023:S152659002300425X.

[9] Meyers E, Vlaeyen JWS, Van Den Broeke EN, Von Leupoldt A, Palmer AJ, Torta DM. The effect of high versus low cognitive load on the development of nociceptive hypersensitivity: The roles of sympathetic arousal, sex and pain-related fear. Eur J Pain 2023:ejp.2098.

[10] Torta DM, De Laurentis M, Eichin KN, von Leupoldt A, van den Broeke EN, Vlaeyen JWS. A highly cognitive demanding working memory task may prevent the development of nociceptive hypersensitivity. Pain 2020;161:1459–1469.

[11] Van Den Broeke EN, Gousset S, Bouvy J, Stouffs A, Lebrun L, Van Neerven SGA, Mouraux A. Heterosynaptic facilitation of mechanical nociceptive input is dependent on the frequency of conditioning stimulation. J Neurophysiol 2019;122:994–1001.