Reviewer's report

Title: Association of extracellular signal-regulated kinase expression with anti-allodynic effect in spared nerve injury rats by applying immediate pulsed radiofrequency

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Reviewer: jana sawynok

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This manuscript examines the effects of pulsed radiofrequency, applied adjacent to a site of injury (spared nerve injury or SNI), on manifestations of neuropathic pain (mechanical and cold allodynia) and ERK expression in ipsilateral the spinal cord. It examines two settings (45V and 60V), and observes similar behavioural effects for both settings. SNI induces an increase in ERK1/2 expression (over 2-fold) and PRF restores this to almost normal levels.

The observations in this study are original and address an aspect of the mechanism by which this procedure might lead to alleviation of neuropathic pain in humans. The paper is generally well written, and it adds to an emerging body of preclinical information on how this technique might potentially lead to pain relief. However, it does need some attention to specific details.

1) The data in the tables looks to supplementary information. It should be included in the main body of the manuscript.

2) The authors apply the PRF immediately following nerve injury. However, in humans this procedure would be applied well after a pain condition has become chronic, and is likely quite remote from the inciting injury. The authors refer to unpublished observations (page 16, line 2) in which PRF 14 days after SNI produces less effect than applying it immediately. This biases the observations towards seeing an effect, yet may bias it against clinical relevance. At the very least, the authors need to discuss the issue of immediate vs delayed application of PRF.

3) In figure 2, why was there no data for the 60V condition shown?

Several minor details also need attention.

p.3, line 7: Neuropathic pain was achieved in a SNI model in Wistar rats by ligation and … (then delete “was ligation and cut” line 8-9); line 9: Rats were divided (Wistar strain is now mentioned in methodology sentence; see above); line 10: treatment conditions (both are the same” modality” but differ in intensity); line 14: measurements included mechanical; line 15: and were examined

p.4, line 8: in the ipsilateral spinal; line 9: in the SNI_PRF; line 11: application on the proximal…
p.5, line 5: reduction of pain, and frequently there is unsatisfactory; line 7: and has been used; line 10: shown to be safe and helpful; line 12: stimulation adjacent to

p.6, line 2: The oncogene information looks out of place (it is molecular) as the sentence is referring to anatomical sites, check this sentence carefully. Line 5: systems within the spinal cord which provide...; line 11: In the present study, we examine the...

page 8, line 6: Antinociception (correct the spelling)

Page 13. Line 20: in the ipsilateral spinal ... and this was effectively reduced...

Page 15. Line 8: Refs 34-35. There are other clinical studies that should be listed here. In preclinical studies, in a rabbit neuropathic pain model induced by...; line 16:P We observed 45V and PRF 60V ... provided a (not an) similar; line 19: allodynia developed at day 1

Page 16. Line 1: ...SNI and lasted up to 28 days. Line 5: Furthermore, an animal study... line 7: Our study is the first to apply; line 13-14. For future – this sentence does not make sense, revise the wording. Line 16: which interferes with sensory; line 17: In other studies,

Page 17. Line 4: shown to be...; line 7: that SNI induces ERK; line 8: ipsilateral spinal dorsal horn; line 9: was found to be increased 2.3-fold compared to; line 12: we conclude that the ; line 13: Furthermore, in neuropathic; line 17: our results strongly suggest; line 19: rats, and this reduces ...

Level of interest: An article of importance in its field

Quality of written English: Acceptable

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

Declaration of competing interests:

I have no competing financial interests.