

RESPONSE TO LETTER

Pulsed Radiofrequency 2 Hz Preserves the Dorsal Root Ganglion Neuron Physiological Ca2+ Influx, Cytosolic ATP Level, $\Delta \psi m$, and pERK Compared to 4 Hz: An Insight on the Safety of Pulsed Radiofrequency in Pain Management [Response to Letter]

Ristiawan Muji Laksono [D], Taufiq Agus Siswagama , Fa'urinda Riam Prabu Nery , Walter van der Weegen 102, Willy Halim³

Correspondence: Ristiawan Muji Laksono, Department of Anesthesiology and Intensive Therapy, Faculty of Medicine, Brawijaya University, Jl. Jaksa, Agung Suprapto No. 2, Malang, East Java, Indonesia, Tel +62 812-3377-3593, Email ristiawanm@ub.ac.id

Dear editor

We appreciate the letter sent by Prof. Russo that points out our latest study on the pulsed radiofrequency 2 Hz that preserves the dorsal root ganglion neuron physiological Ca²⁺ influx, cytosolic ATP level, Δψm, and phosphorylated extracellular signal-regulated kinase (p-ERK) compared to 4 Hz¹ and gives his positive suggestion that 2 Hz 20 millisecond pulsed radiofrequency neurotomy, as currently practiced clinically, may continue to be the best option for

Regarding our thoughts on the potential optimization of pulsed radiofrequency neurotomy parameters, we have also performed an in-vitro study by measuring pERK, a sensitization biomarker expressed during pain, following pulsed radiofrequency exposure on the sensitized dorsal root ganglion neuron model induced by N-Methyl-D-Aspartate (NMDA). Our study found that 2Hz 20-millisecond pulsed radiofrequency for 600 seconds significantly decreased the pERK level compared to the control, indicating decreased sensitization.² This result shows the scientific evidence that pulsed radiofrequency could directly reduce one of the biological processes of pain generation. However, in clinical practice, the overall outcome of PRF is achieved at two weeks, one month, three months, or six months after the procedure.³ The time range raises a question on how pulsed radiofrequency clinically works. Therefore, more complex biological parameters related to pain, such as α-amino-3-hydroxy-5-methyl-4-isoxazolepropionic acid receptor (AMPAR) level, transcription factors (ie, neurokinin-1, Cox-2, c-Fos, and TrkB), or pain-related neuropeptides can be assessed to understand the whole pulsed radiofrequency mechanism and obtain potential biological targets to expedite the PRF effect. A time-series study comparing 2 and 4-Hz pulsed radiofrequency can also be done to monitor the parameter's dynamic during a certain time range according to the pulsed radiofrequency clinical efficacy. A study using neuron models induced by other substances, ie, Glutamate, can also be performed to understand the different mechanisms of 2Hz 20 millisecond pulsed radiofrequency.

We thank Prof Russo for his interest in pulsed radiofrequency neurotomy, and we hope that further studies will be done to uncover the pulsed radiofrequency mechanism and provide scientific evidence of pulsed radiofrequency application in pain management.

Department of Anesthesiology and Intensive Therapy, Faculty of Medicine, Brawijaya University, Dr. Saiful Anwar General Hospital, Malang, Indonesia; ²Sports & Orthopedics Research Centre, St. Anna Hospital, Geldrop, the Netherlands; ³Medical Department, Faculty of Medicine, Brawijaya University, Malang, Indonesia

Laksono et al **Dove**press

Disclosure

The authors report no conflicts of interest in this communication.

References

1. Laksono RM, Siswagama TA, Nery FRP, van der Weegen W, Halim W. Pulsed radiofrequency 2 Hz preserves the dorsal root ganglion neuron physiological Ca2+ Influx, Cytosolic ATP level, Δψm, and pERK compared to 4 Hz: an Insight on the safety of pulsed radiofrequency in pain management. J Pain Res. 2023;16:3643-3653. doi:10.2147/JPR.S424489

- 2. Laksono RM, Kalim H, Rohman MS, Widodo N, Ahmad MR, Halim W. Pulsed radiofrequency decreases pERK and affects intracellular Ca2+ Influx, cytosolic ATP level, and mitochondrial membrane potential in the sensitized dorsal root ganglion neuron induced by N-Methyl D-Aspartate. J Pain Res. 2023;16:1697–1711. doi:10.2147/JPR.S409658
- 3. Kwak SG, Lee DG, Chang MC. Effectiveness of pulsed radiofrequency treatment on cervical radicular pain. Medicine. 2018;97(31):e11761. doi:10.1097/MD.0000000000011761
- 4. Gao YJ, Ji RR. c-Fos or pERK, which is a better marker for neuronal activation and central sensitization after noxious stimulation and tissue injury? Open Pain J. 2009;2(1):11-17. doi:10.2174/1876386300902010011
- 5. Chen SH, Lin YW, Tseng WL, Lin WT, Lin SC, Hsueh YY. Ultrahigh frequency transcutaneous electrical nerve stimulation for neuropathic pain alleviation and neuromodulation. Neurotherapeutics. 2024;e00336. doi:10.1016/j.neurot.2024.e00336

Dove Medical Press encourages responsible, free and frank academic debate. The contentTxt of the Journal of Pain Research (letters to the editor' section does not necessarily represent the views of Dove Medical Press, its officers, agents, employees, related entities or the Journal of Pain Research editors. While all reasonable steps have been taken to confirm the contentTxt of each letter, Dove Medical Press accepts no liability in respect of the contentTxt of any letter, nor is it responsible for the contentTxt and accuracy of any letter to the editor.

Journal of Pain Research

Dovepress

Publish your work in this journal

The Journal of Pain Research is an international, peer reviewed, open access, online journal that welcomes laboratory and clinical findings in the fields of pain research and the prevention and management of pain. Original research, reviews, symposium reports, hypothesis formation and commentaries are all considered for publication. The manuscript management system is completely online and includes a very quick and fair peer-review system, which is all easy to use. Visit http://www.dovepress.com/testimonials.php to read real quotes from published authors.

Submit your manuscript here: https://www.dovepress.com/journal-of-pain-research-journal





