REVIEW REPORT

Title: Median nerve diadynamic current stimulation for blood pressure modulation

Authors: Rajan Soundarpandian Senthilkumar, Ramana Kameswaran, Priyadarshini Babu Rajendra Prasad

Reviewer C: Sharmin Afroz, ORCID: 0000-0002-8778-3313, COI: None, **AI disclosure:** None

1. Comment Please remove the word "revival" from the title, as it is a new technique for blood pressure modulation. Rewrite the title with proper grammar.

Response: In order to improve search engine optimisation, we revised the title so that it is clear, succinct, and adequately captures the substance of the publication. we also included the study design in the title itself. The intervention is included in three thematic words in the title.

2. Comment Line 42, the reference regarding "axon reflex" is incorrect. Please verify it.

Response: We checked the text and substituted the appropriate source that describes the axon reflex mechanism.

3. Comment Line 46, "influencing autonomic nervous system", is a broad term; please use a more specific expression.

Response: The wording has been modified to "reducing the sympathetic outflow."

1. Lujan HL, Kramer VJ, DiCarlo SE. Electroacupuncture decreases the susceptibility to ventricular tachycardia in conscious rats by reducing cardiac metabolic demand. American Journal of Physiology-Heart and Circulatory Physiology. 2007 May;292(5):H2550-5.
2. Bang SK, Ryu Y, Chang S, Im CK, Bae JH, Gwak YS, Yang CH, Kim HY. Attenuation of hypertension by C-fiber stimulation of the human median nerve and the concept-based novel device. Scientific Reports. 2018 Oct 8;8(1):14967.

See the second paragraph of the discussion in the first reference and the second paragraph of the discussion on page 6 in the second reference for further details.

4. Comment Line 53, were the electrodes inserted or placed on the skin, considering it is described as a non-invasive method (Line 46)?

Response: The electrodes were placed on the skin surface, as the method is completely non-invasive. An error in wording occurred when the word 'inserted' was used and has been corrected. For further clarity, we have also included an image illustrating the placement of the electrodes and the device used.

5. Comment Please provide detailed information about the method of electrical stimulation, including duration, frequencies, and electrode placement.

Response: The detailed parameters of the electrical stimulation were added in the case description and management section (Lines 100–105).

6. Comment Line 58, specify the variable's name that was measured.

Response: Blood pressure was the variable monitored throughout the study, as detailed in lines 94 and 95, and it served as the primary outcome measure.
as seen in the image, the blood pressure was measured by using a digital sphygmomanometer, as seen in figure 1 of the manuscript.

7. Comment Lines 58–59 contain repeated content; please eliminate the redundancies.

Response: The repeated content in lines 58–59 has been removed.

8. Comment Lines 61–63 should clearly state the results of the electrical stimulation.

Response: Whereas lines 61–63 had requested that the outcomes of the electrical stimulation intervention be clarified, these are now explicitly presented in lines 125–136.

9. Comment Line 66 states "an effect on blood pressure regulation", but in this case report, only the effect of diadynamic current stimulation on a normotensive subject's blood pressure was observed, which showed a "steady increasing trend". How might this contribute to blood pressure regulation?

Response: Although there was a steady increase in systolic pressure, this reflects that the stimulation elicited a consistent hemodynamic response rather than random variation. However, the increase in systolic blood pressure seen in Week-3 was partly due to one confounding variable, namely low-dose caffeine taken one hour prior to testing, which is known to transiently raise systolic pressure. Altogether, the pattern of variation indicates that while caffeine would play a role in the magnitude of change, the reproducible shifts over different sessions still point to the fact that stimulation can modulate blood-pressure dynamics even in a normotensive subject.

10. Comment Line 73, the mention of "increased parasympathetic activity" appears inconsistent with the findings of this experiment. Please clarify.

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Response: Refer the page 80 ,4th edition in this book "Singh J. Textbook of Electrotherapy. JAYPEE BROTHERS PUBLISHERS; 2012". It has lines stating that "The diadynamic diphase type of current primarily affects the autonomic nervous system in the sense of lowering the increased sympathetic tone". Thus, the balance will shift to increased parasympathetic and reduced sympathetic activity

11. Comment In line 77, "management of hypertension by utilising diadynamic current stimulation" does not align with the observed steadily increasing trend in blood pressure following electrical stimulation of the median nerve in this case report.

Response: Accordingly, line 77 targeted not asserting that single instance as an efficient hypertension control but based on theoretical possibility as discussed within previous research. Although no consistent hypotensive effect on systolic pressure emerged, most probably due to several cofounders like caffeine ingestion, the importance of diastolic pressure measurement brings forth an insightful observation: it confirms that diadynamic current could affect autonomic control despite changes within systolic pressures.
Therefore, it is pertinent to read line 77 as an analogy and not as a conclusion reached from this instance. To remove any ambiguity and bias, these lines have been removed as per requirement to remain consistent with facts.

12. Comment Figure 1, the title is incomplete. Please include axis titles and other relevant information.

Response: Figure 1 was removed due to incompleteness of information with lack of titles for axes. For the purpose of clarity and accuracy, the visual representation has been replaced by Table 1, in which the blood pressure values are expressed numerically in an interpretable manner. Further, in order to analytically enrich this with more robustness than that provided by visual interpretation, a Tau-U statistical analysis was conducted and the results presented in Table 2.

Reviewer D: **Mehedi Hasan,** ORCID: **0000-0002-0762-1462,** COI: None, **AI disclosure:** None

13. Comment The abstract is missing, which is a fundamental requirement.

Response: The abstract has now been added and structured according to the required sub-headings (Background, Case description and management, and Conclusion), with a total length of 213 words.

14. Comment The scientific rationale is underdeveloped. The introduction and discussion do not clearly explain the physiological mechanism by which median nerve stimulation could influence blood pressure regulation, nor do they justify why the median nerve was selected over other nerves with established autonomic or cardiovascular relevance.

Response: We have now described the scientific rationale for the choice of the median nerve and its theoretical potential in regulating blood pressure. The mechanism of blood pressure inhibition via the median nerve is hypothesised to stimulate similar neural pathways activated by electroacupuncture at points that are anatomically close to the median nerve. Evidence from experimental neurophysiology has shown that the afferent signaling from the median nerve excites a central autonomic loop that includes stimulation of the arcuate nucleus of the hypothalamus, the ventral periaqueductal gray, and the nucleus raphe obscurus, which project to the rostral ventrolateral medulla (rVLM), a major center that controls sympathetic efferent activity. In this loop, stimulation-induced release of neurotransmitters such as endorphins, serotonin, and γ-aminobutyric acid engulfs presympathetic neurons within the rostral ventrolateral medulla, thus suppressing cardiac sympathetic activity and peripheral resistance. The choice of the median nerve is based on the stimulation of known central autonomic inhibitory pathways, which is a physiologically valid mechanism that can support regulatory effects on blood pressure control.

15. Comment The methodology is insufficiently described and difficult to reproduce. The authors do not explain why healthy individuals were chosen for a blood pressure–management intervention, and key stimulation parameters—such as intensity, duration, frequency/pulse width, and overall protocol—are not provided. The device used for stimulation is also not identified. In addition, the results section lacks essential outcome data, including baseline and post-stimulation blood pressure values, making the effect of the intervention impossible to evaluate.

Response: For this reason, all methodological information, such as participant selection justification, identification of the used device, and complete stimulation parameters (including intensity, duration, frequency, and protocol), have been fully inserted into the case description and management section. Also, baseline and post-stimulation blood pressure values were added in table 1 and table 2 for the sake of intervention transparency and reproducibility.

16. Comment Figure 1 has multiple problems: It is not cited in the text, and its labeling and interpretation are unclear, so its contribution to the findings cannot be assessed.

Response: Figure 1 was removed due to incompleteness of information with lack of titles for axes. For the purpose of clarity and accuracy, the visual representation has been replaced by Table 1, in which the blood pressure values are expressed numerically in an interpretable manner. Further, in order to analytically enrich this with more robustness than that provided by visual interpretation, a Tau-U statistical analysis was conducted and the results presented in Table 2.

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