

## OPEN PEER REVIEW REPORT 1

**Name of journal:** Neural Regeneration Research

**Manuscript NO:** NRR-D-21-00335

**Title:** Efficacy and safety of transcutaneous auricular vagus nerve stimulation paired with conventional rehabilitation training in acute stroke patients

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**Reviewer's country:** Italy

### COMMENTS TO AUTHORS

This is a very interesting randomized controlled trial aimed at testing the efficacy and safety of transcutaneous auricular vagus nerve stimulation in the recovery of motor and sensory functions and emotional response in acute ischemic and haemorrhagic stroke patients.

I suggest reviewing the following points:

- Page 3, Line 36-37: much safer, better-tolerated method. Please specify compared to what, and please provide a specific supporting reference.
- Page 5, line 30: "and so on". Please, use a more formal expression
- Paragraph "interventions":
  - o please specify if the participants were hospitalized during all the stimulation period (20 days)
  - o please specify the frequency of the rehabilitation therapy (daily for 20 days?)
- "The intensity of stimulation was individually adjusted by the patients according to their tolerance". Please provide in the results the data about mean stimulation intensity, if available
- For a more standardized data reporting, please provide data about electrode composition and attachment method, pulse duty cycle
- Page 11: "The control ta-VNS group received intense rehabilitation similar to the active ta-VNS group, rather than typical standard of care.". Please clarify what the intensive and the standard of care rehabilitation protocols involve
- Page 11: "In conclusion, this is the first study mainly aimed to demonstrate the clinical effect and safety of ta-VNS.". Previous studies have been already published to this aim. Please, rephrase this sentence
- Measures of baseline stroke severity, such as NIHSS and mRS could be added, if available, to better describe the enrolled population. Similarly, for a better interpretation of the results about the emotional effects of ta-VNS, it could be useful to report if patients were on pharmacologic treatment for anxiety/depression.
- The discussion could be further ameliorated: some useful references: 10.1007/s00702-014-1299-7; <https://doi.org/10.3389/fnhum.2020.568051>
- Please, review the grammar and syntax of the manuscript. Some examples: one of a leading cause (page 3, line 15); as one such potential targeted plasticity therapy (page 3, line 30); assigned participants to intervention or control group in a 1:1 ratio (page 4, line 20); stimulations were all blinded (page 4, line 38); Only two cases ... was found (page 8, line 30).