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Optimizing Dosing of Vagus Nerve Stimulation for Stroke Recovery

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Abstract

Vagus nerve stimulation (VNS) paired with rehabilitative training enhances recovery of function in models of stroke and is currently under investigation for use in chronic stroke patients. Dosing is critical in translation of pharmacological therapies, but electrical stimulation therapies often fail to comprehensively explore dosing parameters in preclinical studies. Varying VNS parameters has non-monotonic effects on plasticity in the central nervous system, which may directly impact efficacy for stroke. We sought to optimize stimulation intensity to maximize recovery of motor function in a model of ischemic stroke. The study design was preregistered prior to beginning data collection (DOI:

https://doi.org/10.17605/OSF.IO/BMJEK). After training on an automated assessment of forelimb function and receiving an ischemic lesion in motor cortex, rats were separated into groups that received rehabilitative training paired with VNS at distinct stimulation intensities (sham, 0.4 mA, 0.8 mA, or 1.6 mA). Moderate-intensity VNS at 0.8 mA enhanced recovery of function compared with all other groups. Neither 0.4 mA nor 1.6 mA VNS was sufficient to improve functional recovery compared with equivalent rehabilitation without VNS. These results demonstrate that moderate-intensity VNS delivered during rehabilitation improves recovery and defines an optimized intensity paradigm for clinical implementation of VNS therapy.

Data and Code Availability

All data and analysis code from this study have been made available on Github (https://github.com/davepruitt/OptimalDosingIntensityVNS).

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Contributions

DTP participated in study design, surgeries, data acquisition, data analysis, data interpretation, and software development and wrote the manuscript. TTD participated in study design, surgeries, and data acquisition. ML/NP/PR/VW/AP participated in data acquisition, surgeries, tissue processing, and histological analysis. RLR participated in study design. MPK participated in study design and data interpretation. SAH participated in study design, data interpretation, and writing of the manuscript.

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Ethics declarations

Conflict of Interest

MPK is a consultant for MicroTransponder which develops VNS-related technologies.

Ethical Approval

All applicable international, national, and/or institutional guidelines for the care and use of animals were followed. All experimental procedures were approved by the University of Texas Institutional Animal Care and Use Committee.

Additional information

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