Neuromod+ Project Closure Report

Characterization of the Clinical and Neuromodulatory Effects of Transcutaneous Spinal Cord Stimulation in Essential Tremor

1. Project Information

Funding Programme: Neuromod+ Multi-Investigator Award for Feasibility Studies

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Institutions: Imperial College London (Bioengineering Department) and University College London (UCL Queen Square Institute of Neurology)

2. Main Outcomes and Achievements

2.1 Experimental Protocol and Rationale

Essential tremor (ET) is the most common movement disorder in adults, yet current treatments often provide inadequate relief with significant adverse effects. While Deep Brain Stimulation (DBS) has proven effective for tremor reduction, it requires invasive neurosurgery. Transcutaneous spinal cord electrical stimulation (tSCS) emerged as a potential non-invasive alternative capable of modulating oscillatory activity underlying tremor by influencing spinal circuits and afferent pathways. In this project, we characterized the effects of tSCS on tremor modulation.

The experimental protocol was designed to test the hypothesis that tSCS could disrupt tremor in a frequency-dependent manner. Eighteen patients with ET completed the study, performing 60-second postural tremor recordings under five conditions: no stimulation (baseline), tSCS at the individual patient's tremor frequency, tSCS at 1 Hz, tSCS at 21 Hz, and trapezius stimulation (serving as control). Cervical tSCS was delivered via electrodes positioned over the spinal cord at the C6-C7 level, using biphasic current pulses below motor threshold to avoid muscle activation. Tremor was quantified using accelerometry, with frequency and amplitude analyzed and compared across conditions to identify the most effective stimulation parameters.

2.2 Primary Research Findings

The study with 18 ET patients revealed significant frequency-selective effects of tSCS on tremor amplitude:

(1) tSCS delivered at the individual tremor frequency produced significant tremor amplitude reduction, with effects becoming statistically significant during the second half of the 60-second stimulation period. This stimulation resulted in the highest number of responders among all tested protocols;

(2) Notably, during tremor frequency stimulation, a subgroup of responders exhibited tremor entrainment, demonstrated by consistent synchronization between tremor phase and delivered stimulation. This entrainment phenomenon provides mechanistic evidence that tSCS can directly interact with tremorgenic oscillatory networks.

These findings suggest that the observed changes in tremor amplitude result from modulation of spinal cord circuits by tSCS, which disrupts the oscillatory drive to muscles by affecting afferent pathways or spinal reflexes. The frequency-selectivity of the effect indicates that temporal synchronization between stimulation and tremor oscillations is critical for efficacy. However, the possibility of an interplay between spinal and supraspinal centers in mediating these effects cannot be discounted.

The results from this cohort of 18 patients were published in Movement Disorders Journal (Impact Factor: 7.6, Q1 journal), one of the most prestigious international journals in clinical neurology and movement disorders: Pascual-Valdunciel et al. (2024), "Frequency-Selective Suppression of Essential Tremor via Transcutaneous Spinal Cord Stimulation," Movement Disorders, 39(10), 1817–1828. This publication significantly enhanced the visibility and scientific impact, establishing the scientific credibility and international visibility of the Neuromod+ project outcomes.

2.3 Extended Studies

In addition to postural tremor assessments, further experiments were conducted involving patients with ET and dystonic tremor to evaluate stimulation effects during functional tasks. Open-loop tSCS delivered at tremor frequency was applied while participants performed spiral drawing, nine-hole pegboard tests, and postural arm-holding tasks. The resulting dataset is currently undergoing detailed analysis and is expected to provide further insight into the translational potential of tSCS for functional tremor reduction during real-world activities.

2.4 Strengthened Inter-Institutional Collaboration

The project consolidated collaboration between Imperial College London and the UCL Queen Square Institute of Neurology, integrating bioengineering and clinical neurology expertise within a shared research framework. This collaboration facilitated knowledge exchange in neuromodulation methods, clinical recruitment, and data interpretation, and has established a sustainable platform for future joint research. Building on the success of the present work, the partnership has expanded to investigate spinal circuit excitability in patients with stiff-person syndrome and dystonia, with ongoing planning of further collaborative studies and funding applications.

3. Scientific and Clinical Impact

3.1 Advancement of Scientific Knowledge

By demonstrating frequency-selective tremor suppression in 18 ET patients, the research provides novel evidence that the spinal cord plays an active role in tremor generation and propagation, rather than functioning solely as a passive relay. The research establishes a foundation for developing accessible, non-invasive neuroprosthetic devices for tremor management. Unlike DBS, which requires invasive neurosurgery and carries significant risks, tSCS offers a low-cost, minimal-risk alternative that could be deployed in outpatient settings or potentially as a home-based therapy. The demonstrated safety profile with 18 patients and minimal adverse effects position tSCS as a viable option for patients who cannot tolerate pharmacological treatments or are not candidates for surgical interventions.

4. Conclusions and Future Directions

The Neuromod+ project successfully achieved its stated objectives through rigorous experimental studies with 18 ET patients, delivering outcomes that advance both fundamental neuroscience understanding and clinical translation of non-invasive neuromodulation. This project was directly aligned with and contributed to the core mission of the Neuromod+ network. The project exemplified Neuromod+ network's emphasis on transformative research by demonstrating that non-invasive tSCS can achieve clinically meaningful tremor suppression without the risks associated with invasive procedures. By establishing successful collaboration between Imperial College London (bioengineering) and UCL Queen Square Institute of Neurology (clinical expertise), the project embodied the network's goal of facilitating multidisciplinary partnerships and knowledge exchange across stakeholder groups.

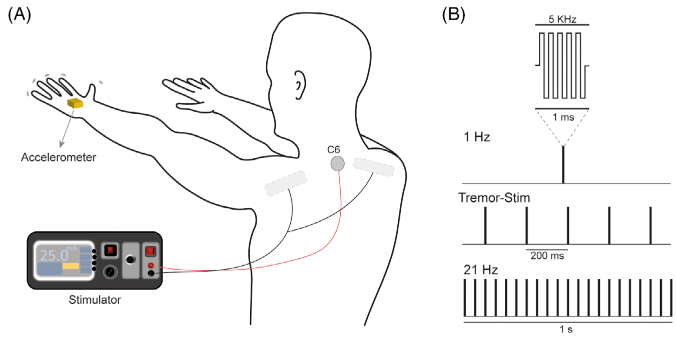

Illustration of tSCS methodology applied during the project