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# Effects of Transcutaneous Spinal Cord Stimulation on Autonomic Nervous System Regulation

Marcos Sacristán Moraleda
*BSICoS Group, I3A, IIS*
*Universidad de Zaragoza*
Zaragoza, Spain
msacristan@unizar.es

Jaime Ibáñez Pereda
*BSICoS Group, I3A, IIS*
*Universidad de Zaragoza*
Zaragoza, Spain
jibanez@unizar.es

Jesús Lázaro
*BSICoS Group, I3A, IIS*
*Universidad de Zaragoza*, Zaragoza, Spain
*CIBER-BBN*, Madrid, Spain
jlazarop@unizar.es

***Abstract*—This study investigates the impact of transcutaneous spinal cord stimulation (TSCS) on the autonomic nervous system (ANS) by analyzing heart rate variability (HRV) metrics. TSCS, a non-invasive alternative to invasive spinal electrical stimulation, is used to treat motor disability or movement disorders. Despite its usage, the effects of TSCS on the ANS remain unclear, particularly its role in motor rehabilitation. The objective was to understand TSCS effects on HRV in healthy individuals. Electrocardiograms (ECGs) were recorded from 7 participants during baseline and tSCS stimulation periods at 7 Hz, 20 Hz, and 45 Hz. Significant differences were found in parasympathetic markers between the control and 7 Hz stimulation, and between the control and 45 Hz stimulation. However, these differences disappeared when trimming the signal to eliminate start and end effects of stimulation blocks. This suggests that TSCS effects on ANS activity are transient, warranting further time-frequency analyses.**

***Index Terms*—Transcutaneous spinal cord stimulation (TSCS), Autonomic nervous system (ANS), Heart rate variability (HRV)**

## I. Introduction

Invasive spinal electrical stimulation is an effective technique for treating patients with motor disorders due to neuronal injury or disease [1]. However, its invasiveness has associated risks making its use justifiable only in highly impaired patients and it also has high associated costs. A possible alternative is using transcutaneous (noninvasive) spinal cord stimulation, which is a non-invasive type of intervention based on the delivery of electrical currents to specific spinal cord areas using surface stimulation electrodes. This alternative method has lower specificity, so it can produce unspecific effects over the stimulated area of the spinal cord. The main objective of this work is to analyze the effects of transcutaneous spinal cord stimulation on the function of the autonomic nervous system (ANS). Since spinal neurostimulation has been used as potential treatment for ANS pathologies [2], alterations in ANS are expected during its use. Exploring the ANS changes related to spinal stimulation will improve the understanding of the effects of this treatment.

## II. Materials and methods

### A. Materials

A total of 7 healthy individuals were recruited to participate in the study (ages 22-40 years, 4 male subjects). The study conducted has the approval of the local ethics committee (PI23/536).

The electrocardiogram (ECG) of the subjects was acquired at a sampling rate of 10240 Hz using a high-density electrophysiological signal amplification and recording system with an integrated band-pass filter set to 10-500 Hz (*Quattrocento* OT Bioelettronica, IT). A bipolar lead placed on the subject's torso was used, following the main line of the heart from V1 (in the fourth intercostal space, to the right of the sternum) to V4 (fifth intercostal space, in the left mid-clavicular line).

An electrical stimulator (DS8R, Digitimer Ltd., Uk) was used for the transcutaneous spinal cord stimulation. A 50x50mm anodic electrode was placed in the posterior neck region at C6 level, and one 50x90mm cathodic electrode was placed on the clavicle of the dominant side.

The stimulation protocol consisted of the administration of 1 ms stimulation pulses modulated with a carrier frequency of 5 kHz, resulting in five biphasic pulses of 200 $\mu$s in a row. These pulse trains were applied at modulating frequencies of 7 Hz (typical tremor frequency in patients), 20 Hz (beta band oscillations), and 45 Hz (gamma band). These frequencies were chosen because they are the ones used in most tSCS protocols.

To determine the stimulation intensity prior to recording, electrical stimulation was started at 5 mA and it was gradually increased in 5 mA intervals until the appearance of an evoked muscle response (identified in the electromyogram of the first dorsal interosseous muscle) or until a level at which the stimulated subject manifested discomfort or pain. Then, in the main recording and stimulation blocks of the experiment, 90% of the estimated intensity was used for the stimulation.

We then proceeded with the experimental protocol, consisting of 5-minute blocks, separated by 1-minute rest periods. In each block, stimulation was applied at a given frequency (No stimulation, 7 Hz, 20 Hz and 45 Hz). The order of the blocks was determined by a controlled randomization process, in order to minimize possible biases and maximize the internal validity of the study.

### B. Data analysis and statistics

The stimulation artifact waveform for each recording was defined as the mean of the signal aligned at the stimulation

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instants. Then, considering it as additive noise, this waveform was subtracted from the original signal at the stimulus times, with an amplitude factor proportional to the range of the signal between the nearest stimulation pulses to account for subtle changes in impedance. A low pass Butterworth filter of sixth order at 50 Hz was applied. Then the signal was then resampled at 250 Hz for further analysis.

R-peaks were detected from the ECG signal using a wavelet-based algorithm [3], and the RR series, which represents the intervals between consecutive R-peaks, was subsequently constructed. Subsequently, an instantaneous heart rate signal sampled at 4 Hz was obtained by a methodology based on integral pulse frequency modulation [4].

For each stimulation stage, the following metrics were obtained, based on the time domain analysis of the series of beat occurrence and its previously mentioned correction to define normal beats: Mean heart rate (HRM) (in beats per minute), standard deviation of normal intervals (SDNN) (in ms), standard deviation between adjacent normal beats (SDSD) (ms), and the proportion of normal RR interval differences greater than 50 ms between consecutive beats (pNN50). In addition, the following frequencial indices were also computed: power at low and high frequency bands (PLF (0.04-0.15 Hz) and PHF (0.15-0.4 Hz), respectively), and their versions normalized with respect to the total power PLF + PHF (PLFn, PHFn), and the ratio between low and high frequency (PLF/PHF).

To assess if there were any significant changes across stimulation conditions in the extracted metrics, Wilcoxon signed-rank tests were performed to compare the metrics across different conditions. This test remains a non-parametric paired statistical test. The significance level was set as $p < 0.05$.

In order to avoid potential confounding effects of stimulation-induced surprises, an alternative analysis was performed using a time window of only 3 minutes centered at the middle of each stage, *i.e.*, discarding the first and the last minute of each stage for further analysis.

## III. Results

According to the Wilcoxon test, both SDNN (p=0.015) and pNN50 (p=0.047) were significantly higher during the 45 Hz stimulation stage than during the no stimulation (control) stage. Additionally, PHF was significantly lower during the 7 Hz stimulation stage than during the Control stage (p=0.047). No significant differences were found in other comparisons conducted. However, when only the central part of the stimulation blocks were considered, no significant differences were observed for any of the studied metrics.

## IV. Discussion

We observed a significant increase in SDNN and pNN50 during 45-Hz stimulation blocks compared to the control condition, suggesting an increase of parasympathetic activity. This may be due to a possible stimulation of vagus nerve [5], which may be a side effect of TSCS. However, this behavior of parasympathetic markers has not been observed when stimulating at 7 nor 20 Hz, which sugests a frequency-specific effect. In fact, PHF, which is also a parasympathetic marker, was significantly lower during 7-Hz stimulation than during control stage. These results suggest that TSCS has some effects on ANS activity, and that those effects depend on the frequency of stimulation.

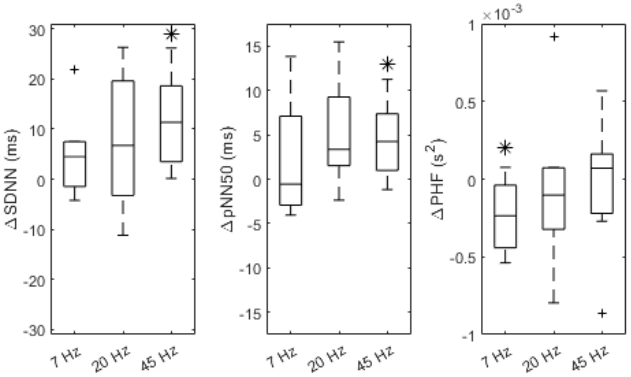


Fig. 1. Boxplots showing the variation of the three statistically different HRV metrics compared to a control value under three different stimulation conditions (7 Hz, 20 Hz, and 45 Hz). The first plot (left) shows the variation in SDNN (ΔSDNN), the second plot (center) shows the variation in pNN50 (ΔpNN50), and the third plot (right) shows the variation in PHF (ΔPHF). Asterisks (*) indicate significant differences from the control value ($p<0.05$).

Nevertheless, no significant differences were observed when discarding the first and the last minutes of each stage. These results suggest that the effects of TSCS in ANS activity are transient and not stationary, encouraging further analyses with a time-frequency approach.


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