511

Elkelini M[1], Pravdivyi I[1], Hassouna M[1]
1. *Toronto Western Research Institute, University of Toronto*

MECHANISM OF ACTION OF TRANSCUTANEOUS SACRAL NERVE STIMULATION IN SPINAL CORD INJURED RODENT MODEL

Hypothesis / aims of study

Invasive sacral neuromodulation (SNM) has been demonstrated to be effective in the treatment of urge incontinence and detrusor overactivity [1]. The mechanism of action of SNM has implicated the role of C-afferent fibers in a spinal cord injury rodent model [2, 3]. The hypothesis of this study was that a novel, non-invasive, transcutaneous sacral nerve stimulation method has an identical mechanism of action as the invasive SNM.

Study design, materials and methods

The Selective Nerve Stimulation (SNS, known as "Project SyNapSe") device provides non-invasive neurostimulation through a controlled, amplitude-modulated waveform. This carrier waveform is designed to be of sufficient frequency to overcome skin and tissue impedance. The pulse envelope contains selective frequency, pulse width, amplitude, and shape waveform that is designed to stimulate specific nerves. In the present study, 28 female Sprague Dawley rats were stratified into three groups: normal controls (C); spinally transected at T10 (S); and spinally transected and electrically stimulated bilaterally at S1 using the SNS method for 2 hours before sacrifice (N). Three weeks after spinal transection, rats were assessed using urodynamics. In separate groups of rats, calcitonin gene-related peptide (CGRP) was extracted from the dorsal root ganglia (DRG) of the L5 and L6 roots and quantified by radioimmunoassay. Univariate ANOVA was used to analyse the data and statistical significance was set at $P < 0.05$.

Results

Spinally transected rats developed urinary bladder hyperreflexia after 3 weeks indicated by the presence of uninhibited contractions, increased resting pressure, increased threshold pressure and increased maximum voiding pressure. Short term neurostimulation affected urodynamics by significantly reducing the threshold pressure ($p=0.02$) (Table 1). Spinal transection increased CGRP concentration in the L6 DRG compared with the control, while neurostimulation significantly reduced CGRP concentration in L6 ($p=0.03$) (Table 2).

Table 1: Bladder Pressure Parameters

Group	Resting Pressure (cmH2O)	Threshold Pressure (cmH2O)	Maximum Voiding Pressure (cmH2O)	Number of Uninhibited Contractions
Control	3.8 ± 0.6	14.6 ± 2.4	26.2±2.1	0
Spinal transection	9.2 ± 1.2	43.8 ± 6.5	56.5 ± 3.3	5.8 ± 2.6
Neurostimulation	8.6 ± 0.7	30.5 ± 2.9	54.3 ± 6.2	4.6 ± 3.1

Table 2: CGRP concentration fmol/ml (mean ± SD)

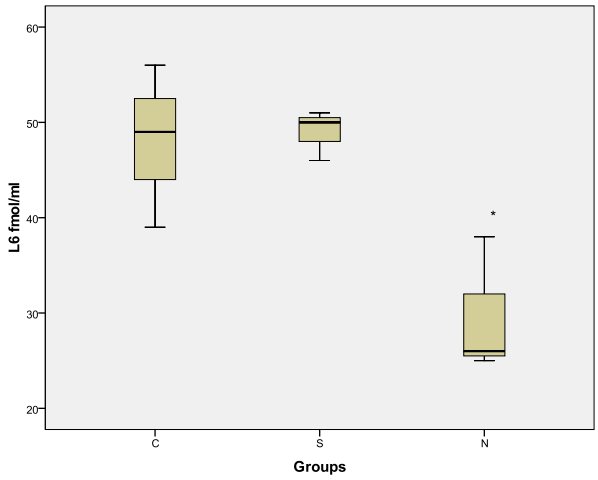
Group	L5	L6
Control	48.67 ± 6.11	48.00 ± 8.54
Spinal transection	50.00 ± 7.93	49.00 ± 2.64
Neurostimulation	40.33 ± 1.15	29.67 ± 7.23

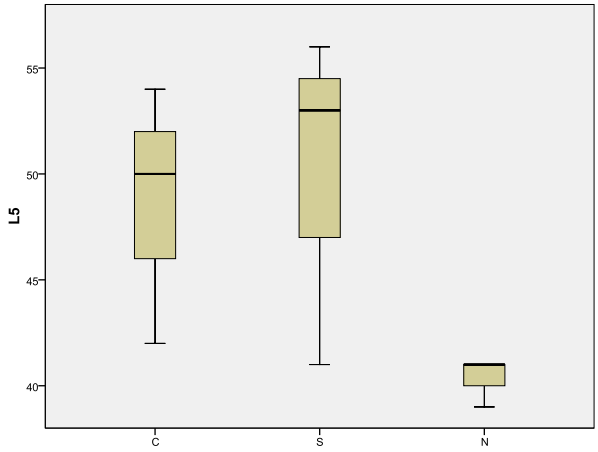
Interpretation of results

Neurostimulation at S1 has been shown to improve voiding behaviour following spinal cord injury by inhibiting the activity of the reflex arc conveyed by the C-afferent fibers [2, 3]. In this study, using non-invasive neurostimulation, a similar response to invasive neurostimulation was achieved. Furthermore, the changes in voiding parameters could be also related to inhibiting C-fiber activity as evidenced by the significant reduction of CGRP concentration in L6 dorsal root ganglia.

Concluding message

This study demonstrates a good bladder response in spinalized rats after non-invasive neurostimulation, and also shows a potential mechanism of action of this method. Further work is needed to better understand the mechanism of this neuromodulation method.





* indicates statistical significance
C: Control group
S: Spinal cord injury group
N: Neurostimulation group

References

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3. Wang Y, and Hassouna MM, “Neuromodulation reduces c-fos gene expression in spinalized rats: A double-blind randomized study”, J Urol, Vol. 163, 1966-70, 2000.

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Is this a clinical trial?	**No**
What were the subjects in the study?	**ANIMAL**
Were guidelines for care and use of laboratory animals followed or ethical committee approval obtained?	**Yes**
Name of ethics committee	**University Health Network Animal Care Committee in accordance with the policies established in the Guide to the Care and Use of Experimental Animals prepared by the Canadian Council on Animal Care.**