Transcutaneous Electrical Nerve Stimulation Decreases Both Chronic Pain and Periodic Leg Movements – Evidence for Decreased Central Excitation and Enhanced Central Inhibition?

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INTRODUCTION

Periodic leg movements (PLMs) are repetitive movements characterized by rapid partial dorsiflexion of the ankle, extension of the great toe, and partial flexion of the knee and hip that occur during non-REM sleep. Abnormal PLMs occurs in most patients with restless leg syndrome and are associated with an increased risk of hypertension and cardiovascular disease. Elevated PLMs in subjects with chronic pain compared to non-pain controls has been reported. Although the neurologic generator for PLMs is unknown, evidence points to enhanced spinal cord excitability and deficient descending inhibition.

Transcutaneous electrical nerve stimulation (TENS) is a non-invasive treatment for chronic pain without significant side effects. TENS is believed to improve chronic pain by decreasing central sensitization and enhancing descending inhibition through opioidergic pathways.

We hypothesized that subjects experiencing a reduction in chronic pain following 10-weeks of TENS use would also demonstrate a reduction in PLMs.

METHODS

This retrospective, observational study evaluated users of a TENS device (Quell®, NeuroMetrix, Waltham, MA) to treat chronic pain over a 10-week period. The device is always placed on the upper calf (see Figure 1) and is comprised of a one-channel electrical stimulator, a stretchable band to secure the stimulator to the leg, and an electrode array. The electrode array is comprised of 4 hydrogel pads, each approximately 15 cm^2, configured as two 30 cm^2 electrodes. When placed on the upper calf, the electrode array wraps around the leg overlapping sensory dermatomes S2 through L4. These dermatomes are typically targeted when treating foot, leg and low back pain with TENS.

The device and companion app collect utilization data, demographics, pain characteristics, pain ratings, and objective sleep metrics derived from actigraphy that are stored in a cloud database. The pain ratings included pain intensity and pain interference with activity, sleep and mood on an 11-point NRS. The primary study outcome was the baseline to 10-week change in composite pain (mean of pain intensity and the three pain interference values.

Device users were included in the study if they provided demographic data and pain characteristics indicative of chronic pain (i.e., daily/weekly pain with duration >3 months), baseline and 10-week follow-up pain ratings, and wore their device at least 3 nights during weeks 1-2. Participants with baseline PLMI (PLMs/hr of sleep) = 0 were excluded.

Responders were defined as participants reporting a ≥15% reduction (i.e., minimum clinically meaningful change) in composite pain from baseline to 10-weeks. Responders and non-responders were compared by the Wilcoxon rank-sum test.

Table 1. Comparison of demographics and baseline pain characteristics between responders and non-responders.

Characteristic	Responder (N = 304)	Non-Responder (N = 351)	P-value
Female gender: %	61.8	61.3	0.877
Age: mean (SD)	56.5 (13.2)	52.8 (13.3)	<0.001
BMI (kg/m^2): mean (SD)	30.7 (6.8)	31.3 (7.2)	0.257
Duration of pain ≥ 4 yrs: %	74.7	80.9	0.054
No. pain sites: mean (SD)	5.3 (2.5)	5.5 (2.5)	0.258
Lower extremity pain (%)	92.1	93.7	0.416
Low back pain (%)	82.9	84.6	0.551
Extra-segmental pain (%)	80.3	79.2	0.736
No. painful health conditions: mean (SD)	3.1 (1.9)	3.1 (1.9)	0.935
Daily pain: %	98.4	96.9	0.218
All day pain: %	52.6	59.0	0.103
Weather sensitive: %	67.8	71.2	0.337
Baseline pain: mean (SD)			
Pain intensity	6.8 (1.6)	6.6 (1.6)	0.167
Pain interference with sleep	6.1 (2.8)	5.7 (2.7)	0.038
Pain interference with activity	7.1 (2.2)	6.8 (2.2)	0.037
Pain interference with mood	6.9 (2.3)	6.7 (2.4)	0.271

Table 2. Comparison weeks 1-2 actigraphic sleep metrics in responders and non-responders.

Sleep Measure	Responders (N = 304)	Non-Responders (N = 351)	P-value
Time in Bed (min)	467 (77)	470 (79)	0.675
Total Sleep Time (min)	410 (74)	411 (75)	0.998
Sleep Efficiency (%)	87.9 (5.5)	87.5 (5.8)	0.395
Wake After Sleep Onset (min)	29.2 (16.2)	29.6 (15.8)	0.474
PLMI	10.2 (11.7)	8.5 (10.2)	0.342
Position Changes / hr	1.2 (0.9)	1.2. (0.9)	0.765

Table 3. Comparison of TENS adherence parameters in responders and non-responders.

Sleep Measure	Responders (N = 304)	Non-Responders (N = 351)	P-value
Utilization (%)	89.8 (14.7)	84.4 (18.4)	<0.001
Sleep Utilization (%)	63.5 (23.1)	57.6 (25.3)	0.004
Hours / week	58.0 (22.0)	51.3 (22.3)	<0.001
Sensation threshold (mA)	16.1 (13.9)	15.2 (12.9)	0.456
Stimulation intensity (dB)	4.6 (5.7)	4.9 (5.6)	0.858

Figure 1

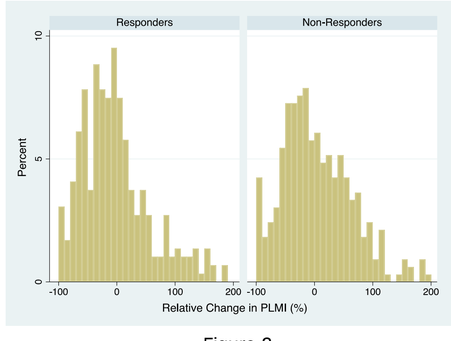

Figure 2

RESULTS

There were 304 responders and 351 non-responders. Table 1 compares baseline demographics and pain characteristics between the two groups. Both groups had long duration, multi-site pain and several painful conditions. Essentially all participants had lower extremity or low back pain, and most had extra-segmental (i.e., segments unrelated to nerve stimulation) pain. There were few statistically significant differences between the groups; responders were older and had greater pain interference with sleep and activity at baseline.

Table 2 compares sleep measures at baseline. There were no statistically significant differences. Table 3 compares TENS adherence parameters in the two groups. The two groups had generally similar adherence, with the responders having slightly higher device use that is likely not clinically meaningful.

The median relative change in PLMI from weeks 1-2 to weeks 9-10, over the entire study population, was -5.0% (95% CI -10.5, 0.0). Figure 2 shows the distribution of PLMI changes stratified by responder status. Responders exhibited a median -9.8% (95% CI -18.2, -3.9) change in PLMI compared to a median 0% (95% CI -8.0, 9.5) change in non-responders (p=0.023). This result was further confirmed by the two-sample Kolmogorov-Smirnov test (p=0.020).

CONCLUSIONS

The key finding from this study is that TENS users who reported at least a minimum clinically important reduction in composite pain, also experienced a statistically significant reduction in PLMI. We hypothesize that TENS reduces both pain and PLMs through an overlapping reduction of central excitation and/or enhancement of central inhibition.

This study also demonstrates that TENS improves both patient reported and objective outcomes, further supporting the clinical utility of this non-invasive chronic pain treatment.

REFERENCES

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