Does the Anatomic Distribution of Chronic Pain Influence the Effectiveness of Fixed-Site High-Frequency Transcutaneous Electrical Nerve Stimulation?

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INTRODUCTION

The prevalence of chronic pain among adults in the U.S. is 30%, at an annual economic cost of $600 billion. Prescription opioids are frequently used for chronic pain despite concerns about adverse events. There is a need for nonpharmacological treatments for chronic pain.

Most individuals with chronic pain have multi-site pain. Prior studies demonstrated correlations among pain sites, suggesting chronic pain is anatomically structured.

Transcutaneous electrical nerve stimulation (TENS) is the delivery of electric current across the intact surface of the skin to activate sensory nerve fibers, primarily for pain relief. As an emerging form of TENS, fixed-site high-frequency TENS (FS-TENS) is believed to produce widespread analgesia by decreasing central sensitization and enhancing descending inhibition.

The objective of this study was to determine if the distribution of pain sites influences FS-TENS effectiveness.

METHODS

Study Design and Subject Selection. This retrospective, observational study evaluated users of a FS-TENS device to treat chronic pain over a 10-week period (Quell®, NeuroMetrix, Waltham, MA). The device is worn on the upper calf and semi-continuously stimulates sensory nerves to provide pain relief. The device and a companion smartphone app collects demographics, painful health conditions, pain sites, weather sensitivity, pain intensity and interference with sleep, activity and mood (11-point numerical rating scale) and monitors. utilization. All data are stored in a cloud database and a snapshot of the database was taken on August 5th 2018.

Inclusion criteria were users 1) providing demographic/clinical information, 2) having pain characteristics indicative of chronic pain, 3) reporting pain intensity and interference ratings at baseline and 10 week of FS-TENS use, and 4) consenting to use of anonymized data for research. The primary study outcome was the baseline to 10-week change in composite pain (average of pain intensity and interference with sleep, activity and mood).

Data Analysis. Exploratory factor analysis was used to identify pain site patterns. Factors were determined by principle factors method with orthogonal varimax rotation. Multivariate linear regression was used to determine independent predictors of the outcome. All analyses were performed with STATA Version 15.1 (StataCorp, College Station, TX, USA).

Table 1. Baseline Population Characteristics (N=5021)

Variable	Mean	StDev
Age (years)	55.2	14.3
Female Gender	55%	
Body Mass Index (kg/m^2)	30.4	7.1
No. Painful Conditions	3.7	2.2
No. Pain Sites	4.7	2.5
Duration > 10 Yrs	35%	
Daily Pain	95%	
All Day Pain	50%	
Weather Sensitivity	57%	
Baseline Pain (11-point NRS)		
Composite Pain	6.2	2.1
Pain Intensity	6.3	1.9
Sleep Interference	5.2	3.0
Activity Interference	6.7	2.5
Mood Interference	6.4	2.7

StDev: standard deviation.
Composite Pain: average of pain intensity and sleep, activity and mood interference.

Table 2. Prevalence of Painful Health Conditions (N=5021)

Condition	Prevalence
Arthritis	60.4%
Fibromyalgia	23.8%
Diabetes	14.0%
Restless Leg Syndrome	19.4%
Complex Regional Pain Syndrome	14.6%
Shingles	4.4%
Multiple Sclerosis	2.1%
Herniated Disc	31.0%
Spinal Stenosis	27.1%
Previous Back Injury	42.9%
Previous Neck Injury	25.2%
Previous Arm/Hand Injury	21.7%
Previous Foot/Leg Injury	22.1%
Cancer	4.9%
Headache/Migraine	26.3%

Users may have specified more than 1 condition.

Table 3. Multivariable Regression Model of Percentage Improvement in Composite Pain (N=1428)

Variable	B	SE	t-value
Age (years)	-0.31	0.12	-2.57**
Female Gender	1.45	3.23	0.45
Body Mass Index (kg/m^2)	-0.06	0.21	-0.26
No. Painful Conditions	1.71	0.80	2.14**
Pain Duration > 10 years	-2.56	3.34	-0.77
Daily Pain	-2.18	9.34	-0.23
All Day Pain	4.17	3.28	1.27
Weather Sensitivity	4.28	3.48	1.23
Baseline Composite Pain (11-point NRS)	-11.79	0.82	-14.36**
Total Therapy (hours)	0.01	0.01	0.82
Adherence (%)	-0.51	0.10	-5.26**
Stimulation Intensity (dB)	-0.06	0.30	-0.20
Stimulation Intensity CoV (%)	31	13	2.28**
Factors (range)			
Upper Body Pain (-1.0, 1.8)	-0.32	2.22	-0.14
Extremity Pain (-1.4, 1.4)	4.88	2.65	1.84*
Hip/Low-back Pain (-1.4, 1.0)	-1.63	3.13	-0.52

Adherence: % of days with at least 30 minutes of stimulation.
Stimulation Intensity: ratio of therapeutic stimulation to sensation threshold expressed in decibels.
B: non-standardized coefficient. Negative value indicates that variable enhances FS-TENS effectiveness.
SE: standard error.
* p<0.1, ** p<0.05.

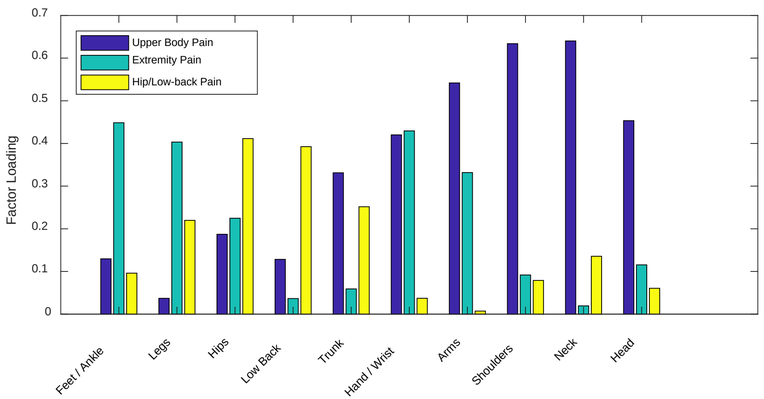

Figure 1. Factor loading of the three retained factors. First factor (Upper Body Pain, 56% of total variance) loads primarily on pain sites of neck, shoulders, arms, head, and hand/wrist. Second factor (Extremity Pain, 25% of total variance) loads primarily on pain sites of feet/ankle, hand/wrist, legs, and arms. Third factor (Hip/Low-back Pain, 16% of total variance) loads primarily on hips and low-back pain sites.

RESULTS

Factor Analysis. Factor analysis was performed on data from 5021 users who provided demographics and baseline pain conditions. Their demographic and baseline pain characteristics are summarized in **Table 1**. Top 5 painful health conditions are arthritis, previous back injury, spinal stenosis, previous neck injury, and fibromyalgia (**Table 2**). Three factors were retained that represented upper-body, extremity and hip/low-back pain (**Figure 1**). Uniqueness (i.e., variance not shared with other variables in the overall factor model) ranges from 57% for neck pain to 83% for low back pain.

Independent Predictors of Primary Outcome (Table 3). 1428 users provided pain ratings at baseline and 10 weeks. The median decrease of their composite pain was 8% (inter-quartile range (IQR) of changes: -36% – 14%). In a subset of adherent users (N=770, defined as those using device on 80% or more days in the 10 week period), median composite pain decrease was 14% (IQR: -43% – 9%). The area under the ROC curve was 0.76 (95% confidence interval: 0.72 – 0.79). Changes in composite pain were not influenced by upper-body or hip/low-back pain, however extremity pain attenuated FS-TENS effectiveness (p<0.1).

CONCLUSIONS

Among FS-TENS users with chronic and multi-site pain, more than half of adherent users reported at least 14% reduction in composite pain in a 10 week study period. The results suggest that FS-TENS analgesia may be widespread in nature.

Extremity pain but not upper body or hip/low back pain was found to attenuate FS-TENS effectiveness, suggesting that certain anatomic pain distributions may be more or less responsive to FS-TENS.

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