Dose-Response of Surface Neurostimulation in Chronic Pain

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INTRODUCTION

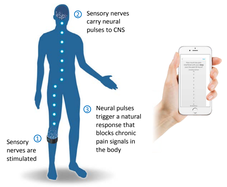
About 100 million people in the U.S. have chronic pain. In addition to the direct experience of pain, people with chronic pain have significant physical and psychological morbidity through its interference with quality of life including sleep, activity and mood. As a result, there is an urgent need for additional therapeutic options. Surface neurostimulation in the form of wearable devices is available as a non-pharmacological option for managing chronic pain.

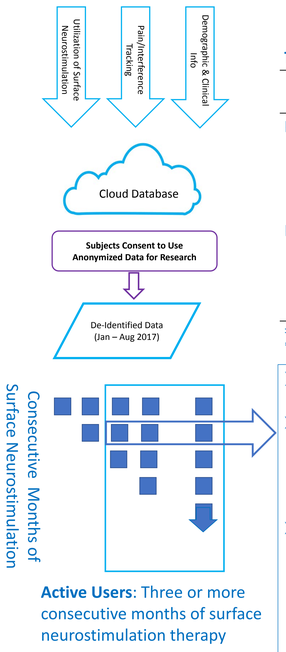
This cross-sectional study evaluated the dose-response of a surface neurostimulator in users with chronic pain.

METHODS

Study Design and Subject Selection. De-identified data were collected from users of a wearable device to treat chronic pain (Quell®, NeuroMetrix, Waltham, MA) during an 8-month period (1/2017-8/2017). The device semi-continuously stimulates sensory nerves at the upper calf and monitors utilization and biometric parameters. A companion smartphone app collects this data as well as demographics, painful health conditions, pain sites, pain intensity and interference with sleep, activity and mood on an 11-point NRS. Active users were those using the device for ≥3 consecutive calendar months (first period used). Inclusion criteria were active users providing demographic/clinical information and consenting to use of anonymized data for research.

Data Analysis. The cross-sectional analysis was conducted on the second month. Typical pain intensity and pain interference were defined as the median value logged during the assessment month. Users were stratified according to days of use (irrespective of amount of use) within the assessment month (low 1-15, intermediate 16-26, high >26). Group differences were evaluated using one-way ANOVA and two-sample t-test. The effect size for high versus low utilization was quantified by Cohen's d. A subset of users in each group also provided baseline pain ratings (prior to any TENS therapy), median of baseline was also calculated. IRB approval was not required because the study was limited to an analysis of anonymized data.





Active Users: Three or more consecutive months of surface neurostimulation therapy

Table 1. Demographic and Clinical Characteristics by Utilization Level

	Surface Neurostimulation Utilization		
	Low	Intermediate	High
Days of Use (within a month)	<16 days	16—26 days	>26 days
User Count: N (%)	1382 (34%)	1237 (30%)	1439 (35%)
Female: N (%)	601 (44%)	521 (42%)	659 (46%)
Age (yrs)*	56 ± 15	57 ± 14	58 ± 13
BMI (kg/m^2)	30 ± 7	30 ± 7	30 ± 7
Pain Duration ≥ 3 Years (%)*	65%	66%	72%
No. Painful Health Conditions*	3.0 ± 2.1	3.0 ± 2.0	3.2 ± 2.2
No. Pain Sites*	4.2 ± 2.6	4.2 ± 2.5	4.4 ± 2.5

* Group means or percentage are statistically different (p<0.01).

Table 2. Pain Intensity and Pain Interference (NRS 0-10) by Utilization Level

	Surface Neurostimulation Utilization		
	Low	Intermediate	High
Pain Intensity (0—10)			
Baseline‡	6.4 (2.0)	6.1 (2.0)	6.2 (2.0)
Typical*	6.0 (2.2)	5.5 (2.2)	5.1 (2.2)
Maximum	6.7 (2.2)	6.6 (2.2)	6.5 (2.2)
Pain Interference with			
Sleep*	4.9 (2.9)	4.4 (2.7)	3.8 (2.7)
Activity*	5.8 (2.6)	5.3 (2.5)	4.7 (2.5)
Mood*	5.5 (2.8)	4.9 (2.8)	4.3 (2.7)

‡ Only a subset of users in each group provided baseline pain intensity ratings. No statistically significant difference.
* Group means or percentage are statistically different (p<0.01).

- **Cross-sectional analysis** on the second month data (N=4058)
  - Stratified to 3 groups based on surface neurostimulation utilization (days of use)
- **No differences between groups**
  - Gender distribution
  - Body Mass Index (BMI)
  - Baseline Pain Intensity Rating
  - Maximum pain intensity
- **Subjects in high utilization group** (utilized 27 days or more in a month)
  - Slightly older
  - Longer pain duration
  - Higher painful health condition count
  - More pain sites
  - Lower typical pain intensity
  - Lower pain interference with sleep, activity, and mood

RESULTS

Demographic and Clinical Characteristics (Table 1). A total of 4058 users met the inclusion criteria (low N=1382, intermediate N=1237, high N=1439). No group differences were found for gender, BMI, or stimulation intensity. Small statistically significant differences were found for age, pain duration, number of painful health conditions and number of pain sites.

Baseline, Typical, and Maximum Pain Intensity (Table 2). Statistically and clinically significant differences were found for typical pain intensity and all three pain interference domains. Typical pain intensity was highest (6.0±2.2) for low utilization group and lowest (5.1±2.2) for high utilization group (one-way ANOVA p<0.0001, pairwise group differences all significant at p<0.001) and Cohen's was 0.46. Baseline and maximum pain intensities were similar for all three groups and had no statistically significant difference between groups (p>0.25).

Typical Pain Interference (Table 2). Pain interference with sleep was highest for low utilization and lowest for high utilization group (one-way ANOVA p<0.0001, pairwise group differences all significant at p<0.001) and Cohen's d was 0.40. Pain interference with activity was 5.8±2.6 (for low utilization) and 4.7±2.5 (for high utilization) (one-way ANOVA p<0.0001, pairwise group differences all significant at p<0.001) and Cohen's d was 0.44. Pain interference with mood was highest (5.5±2.8) for low utilization, and lowest (4.3±2.7) for high utilization group (one-way ANOVA p<0.0001, pairwise group differences all significant at p<0.001) and Cohen's d was 0.43.

CONCLUSIONS

High versus low device utilization (based on days of use) was associated with about a 1-point pain intensity and pain interference difference and moderate effect size in a large heterogeneous population of chronic pain subjects using surface neurostimulation. This result suggests the possibility of a dose-response relationship between utilization and reduction in pain intensity and pain interference with sleep, activity and mood. Optimal reduction in pain interference is most likely achieved with daily device use.

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