# Effectiveness of Fixed-Site High-Frequency Transcutaneous Electrical Nerve Stimulation among Individuals with Chronic Pain and Abnormal Sleep

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## PURPOSE

Most people with chronic pain complain of disturbed sleep and daytime lethargy. Polysomnography studies show that chronic pain patients have shorter sleep duration, less REM sleep, lower sleep efficiency and greater numbers of periodic leg movements compared to healthy controls.

Prescription pain medications are frequently used to treat chronic pain despite concerns about adverse effects and addiction. Transcutaneous electrical nerve stimulation (TENS) is a non-invasive treatment for chronic pain without significant side effects. Fixed-site high-frequency TENS (FS-TENS) is an emerging form of TENS in which the stimulator is designed for a predetermined location rather than for co-localization with the patient's pain. A single target site enables design of small wearable devices that may be used nearly continuously, including while sleeping.

The objective of this study was to evaluate whether sleep abnormalities moderate the effectiveness of FS-TENS. To address this question, we compared pain outcomes in a large, real-world population of FS-TENS users stratified by objective sleep measurements.

## METHODS

**Study Design and Inclusion Criteria.** This retrospective, observational study evaluated users of a FS-TENS device to treat chronic pain (Quell®, NeuroMetrix, Waltham, MA) over a 10-week period. In addition to providing neurostimulation, the device and a companion smartphone app collected utilization data, demographics, self-reported pain characteristics, pain ratings, and objective sleep data using actigraphy techniques. The pain ratings included pain intensity and pain interference with activity, sleep and mood on an 11-point numerical rating scale. Device users were included if they provided demographic data and pain characteristics indicative of chronic pain (i.e., daily/weekly pain with duration >3 months), baseline pain ratings, and wore their device at least 3 nights during weeks 1-2. The subset of users with 10-week follow-up pain rating were used for evaluation of pain outcomes.

**Group Allocation and Primary Outcome**. The sleep measurements included time in bed (TIB in minutes), total sleep time (TST, time within TIB spent sleeping), sleep latency (SL, time from going to bed to falling asleep), sleep efficiency (SE = TST/TIB), and the periodic leg movement index (PLMI, number of periodic leg movements per hour of sleep). The sleep assessment was based on the median of nights during weeks 1-2 of the study period. Participants were allocated to an impaired sleep (IS) group if TST < 360 or to an acceptable sleep (AS) group if TST ≥ 360. The primary study outcome was the baseline to 10-week change in pain ratings. Composite pain is defined as the average of pain intensity and the three pain interference values. Differences between groups or between baseline and follow-up composite pain were evaluated by the Wilcoxon rank-sum test. Differences among proportions were evaluated by the Pearson chi-square test.


**Table 1. Demographic and Pain Characteristics**

| | IS Group (N=471) | AS Group (N=1563) |
|---|---|---|
| Demographics | | |
| Female: (%)* | 52.5% | 60.2% |
| Age: (yrs)* | 55.1 ± 12.4 | 52.7 ± 14.4 |
| BMI: (kg/m²)* | 31.7 ± 8.2 | 30.2 ± 6.7 |
| Self-Reported Health Conditions (only those with group difference) | | |
| Diabetes* | 20.0% | 11.0% |
| Foot Pain* | 58.8% | 51.9% |
| Pain Duration > 10yrs* | 42.1% | 36.0% |
| Baseline Pain Ratings | | |
| Pain Intensity | 6.5 ± 2.0 | 6.3 ± 1.9 |
| Interference w/Sleep* | 5.9 ± 2.9 | 5.4 ± 2.9 |
| Interference w/Activity* | 7.1 ± 2.4 | 6.7 ± 2.4 |
| Interference w/Mood | 6.6 ± 2.7 | 6.5 ± 2.6 |
| Composite Pain* | 6.5 ± 2.0 | 6.3 ± 2.0 |
| Objective Sleep Measures | | |
| Time in Bed (min)* | 371 ± 46 | 497 ± 62 |
| Total Sleep Time (min)* | 313 ± 31 | 444 ± 56 |
| Sleep Latency (min)* | 33 ± 31 | 26 ± 26 |
| Sleep Efficiency (%)* | 85.0 ± 7.3 | 89.4 ± 5.0 |
| PLM Index* | 10.6 ± 12.8 | 6.7 ± 8.0 |

Mean and standard deviation are shown. * indicate group mean is different (p<0.05).

**Table 2. Change in Pain Rating over 10 Week Study Period**

| | IS Group (N=178) | AS Group (N=577) | Group Diff. p-value |
|---|---|---|---|
| Pain Intensity | -0.43 ± 2.40 | -0.46 ± 2.42 | 0.868 |
| Interference w/Sleep | -0.60 ± 3.17 | -0.42 ± 2.89 | 0.466 |
| Interference w/Activity | -1.25 ± 2.84 | -1.05 ± 2.75 | 0.398 |
| Interference w/Mood | -1.01 ± 2.82 | -1.14 ± 2.87 | 0.590 |
| Composite Pain | -0.82 ± 2.34 | -0.77 ± 2.30 | 0.782 |

All changes are significant (p<0.001). Differences between groups are not significant.

## RESULTS

**Table 1** shows device users' demographics and pain characteristics. The inclusion criteria were met by 2034 device users; 471 (23%) in the IS group and 1563 (77%) in the AS group. The IS group was older (p=0.003), less likely to be female (p=0.004), had higher BMI (p=0.001), had longer pain duration (p=0.027), and was more likely to have foot pain and diabetes. The IS group had higher pain interference with sleep (p=0.001) and activity (p=0.006) at baseline. The IS group was also less active than the AS group during the first two weeks (316±217 steps/hour vs 371±205 steps/hour, p<0.001). Sleep data were estimated from 7±3 (IS) and 8±4 (AS) nights. There were significant differences for all sleep metrics.

Utilization (%days using device) was 73±25 (IS) compared to 75±25 (AS), p=0.287. Weekly therapy was 41±24 hrs/week (IS) compared to 43±24 hrs/week (AS), p=0.230.

**Table 2** shows pain rating changes for a subset of 755 device users who also included a 10-week follow-up pain rating. In a subset of participants with daily FS-TENS use (utilization ≥90%, 48% of IS group and 52% of AS group), composite pain decreased by 1.2±2.5 (IS) and 1.2±2.5 (AS), p=0.421. The combined effect size was 0.52 (95%CI 0.38-0.67).

Although there was no overall difference in pain outcomes between groups, trends were found between IS and AS participants for self-reported fibromyalgia (-0.3±2.2 vs -0.8±2.2, p=0.094), previous arm/hand injury (-0.4±2.1 vs -1.0±2.2, p=0.056) and previous foot/leg injury (-0.1±2.5 vs -0.9±2.1, p=0.001). There were no differences for other high-prevalence health conditions including arthritis, herniated disc, spinal stenosis, previous back injury, previous neck injury and headaches/migraine.

## CONCLUSIONS

One-quarter of real-world FS-TENS users had impaired sleep based on objective measurements. The abnormalities included low TST, low SE and elevated PLM. The primary finding was that FS-TENS effectiveness was generally independent of sleep characteristics. Participants with impaired and acceptable baseline sleep had similar outcomes after 10-weeks of FS-TENS therapy as assessed by pain ratings.

A subset of participants with self-reported fibromyalgia, previous hand/arm injury or previous foot/leg injury and abnormal sleep exhibited trends towards less effective outcomes when compared to participants with acceptable sleep. Patients with fibromyalgia and extremity injuries are susceptible to central sensitization and deficient descending pain inhibition. It is possible that the impact of impaired sleep and pathological alternations in central pain processing combine to render therapeutic interventions that activate descending pain inhibition less effective.

The importance of sleep to chronic pain management and overall health highlights the need for sleep monitoring and treatment personalization. Integration of therapeutic and digital health tools, such as the FS-TENS device used in this study, may be beneficial in achieving this goal.

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