Analysis of Efficacy of Transcutaneous Electrical Nerve Stimulation on Acupoints for Current Perception Threshold: Effects of Stimulation Frequencies and Treatment Duration

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Abstract
We determined current perception thresholds (CPT) for arm and mental foramen areas for quantitative evaluations of the effectiveness of transcutaneous electrical nerve stimulation (TENS) treatment at acupoints. This study of the relationship between frequency and time of stimulation had demonstrated TENS–induced sensory inhibition. Eleven subjects (6 male and 5 female) volunteered to be administered TENS for sessions of varying duration (5 minutes, 10 minutes, 15 minutes) and stimulation frequencies (2 Hz and 100 Hz) at the Hegu (LI4) acupoint. We assessed CPTs for the left arm and mental foramen areas before and after TENS at the Hegu (LI4) acupoint of the left hand. Neurometer CPT was used to evaluate perception thresholds at the homolateral mental foramen and arm. The application of low-frequency and high-frequency TENS on the Hegu (LI4) and Quchi (LI11) acupoints raised the perception threshold of the left mental foramen. We assessed the relationship between these effects and TENS stimulation frequencies and treatment duration. We found that applying TENS to the Hegu (LI4) and Quchi (LI11) acupoints increased CPT values in the mental foramen area. Low–frequency TENS inhibited slow pain response, while high–frequency TENS inhibited both fast and slow pain response. The effects of TENS showed greater frequency dependence than time dependence.

Keywords:
TENS, CPT, Hegu, Neurometer

Introduction
Transcutaneous electrical nerve stimulation (TENS) is a safe, non-invasive mode of nerve stimulation intended to reduce pain, both acute and chronic. The first modern, patient–wearable TENS was patented in the United States in 1974 (1). The effectiveness of TENS in pain relief vs. that of opioid analgesic medications remains controversial (2–5).

Despite controversy as to the effectiveness of TENS in treating chronic pain, a number of systematic reviews or meta–analyses have confirmed its effectiveness in treating postoperative pain and osteoarthritic and chronic musculoskeletal pain (6).

Based on various studies of acupoint stimulation whose purpose is analgesia, the Hegu (LI4) acupoint is widely used to control dental pain (7, 8) and masticatory muscle pain (9).

The Neurometer CPT was selected as the qualifying examination method for its inter–rater reliability and capacity for non–injurious examination. Three different frequencies target the Aβ, Aδ, and C fibers, respectively (Kamins et al. 1986, Masson and Boulton). Electrical stimulus clearly indicates that low frequencies are likely to affect all fiber classes. Based on the threshold current required to evoke a response, reports indicate that acupuncture at peripheral nerves selectively affects response to stimulus at 5 Hz, 250 Hz, and 2,000 Hz. Electrodiagnostic tests performed with a Neurometer CPT device (Neurometer NS–3000, Neurotron Inc, Baltimore, MD)
Methods

Participants

This study was approved by the Human Ethics Committee at the Nihon University School of Dentistry at Masuda, Japan (EC-06-06). We enrolled healthy ASA I volunteers in the study. All participants received institutional approval and informed consent from all participants. We exceeded the minimum recruitment of 15 participants. We also analyzed the roles of neurogenic disease, open skin lesions, or skin discoloration having a history of trauma involving the internal abdominal wall or Queti (L11) acupuncture. We confirmed that all participants understood the acupuncture procedure required for this study.

Abbiatations

CPT: current perception threshold;
TENS: transcutaneous electrical nerve stimulation;
L1 and L11: acupuncture points located at the midpoint between the lateral end of the transverse cubital crease and the lateral epicondyle of the humerus. We chose the Queti (L11) acupuncture point along the Yangming (LI1) meridian, which is also located along the Yangming (LI1) meridian, between the lateral end of the transverse cubital crease and the lateral epicondyle of the humerus. Based on the above, we postulated the acupuncture points corresponding to the non-nerve area.

A pair of disposable rubber electrodes pads was placed on the skin (Lapar-A Japan). The current output was individually varied, with intensity at the median strength of 15 mA for 10 minutes. We placed a 12 mm in diameter at the left Hegu (L4) acupuncture point on the skin. The 2006, 200, 20, and 5 Hz (1) each sensory fiber type responses to a specific frequency of electrical stimuli was recorded. A 2 Hz frequency was generated at a standardized amplitude of 0.5 V. The current intensity was 2 mA for 10 minutes, 15 minutes, and 15 minutes, respectively. At least one intervenor week separated the TENS treatment sessions. The neurometer CPT: NCT (Neuronet Diagnostic Equipment) was used to measure the sensory nerve fiber conduction velocity. A bilateral sinusoid alternating current was used to detect the sensory nerve fiber conduction velocity. A bilateral sinusoid alternating current was used to detect the sensory nerve fiber conduction velocity. A bilateral sinusoid alternating current was used to detect the sensory nerve fiber conduction velocity. A bilateral sinusoid alternating current was used to detect the sensory nerve fiber conduction velocity.
All volunteers were assessed in advance at the left Quochi (LI11) acupoint, a reflection-free area, followed by the left mental foramen, a reflection area. All results were recorded.

Each test lasted approximately 10 minutes per area. We placed a pair of round disposable rubber electrode pads at the left Hegu (LI4) and Quochi (LI11) acupoints. The operator slowly increased the current output until the volunteer reported mild sensations. After recording the power eliciting this response, the operator continued to increase current output slowly until the volunteer reported the sensation to be intolerable. We established the median power value as the treatment power. After treatment, we disposed of the electrode pads and measured CPT once again by the same procedure. All treatment procedures were performed by the same operator.

**Assessment**

We used CPT as the primary index of TENS efficacy. In the study, in a test procedure similar to audiometric testing, the operator slowly increased the stimulus until volunteers consistently reported detecting the stimulus. We recorded differences in the function of sensory nerve bundles from pre-TENS to post-TENS for later analysis.

**Statistical analysis**

All data were expressed as number or mean ± SD. We compared CPTs using one-way analysis of variance (ANOVA). If the analysis of variance identified significant differences, we applied Tukey’s multiple comparison test. We analyzed any changes in CPTs with the paired t-test, with P<0.05 defined as statistically significant. We performed multiple linear regression analysis to evaluate the relationship between sensory change and the TENS stimulation factor. All statistical analyses were performed using the SPSS 19.0 statistical package for Windows.

**Results**

Our study enrolled eleven volunteers (6 male and 5 female). The mean age was 31.2±7.1 years. The mean height was 163.4±9.6 cm, and mean body weight was 58.9±9.5 cm. There were no differences between 2 Hz group and 100 Hz group.

Table 1 compares CPT before and after TENS for the left arm. In all groups for 2 Hz and 100 Hz of TENS, we observed no significant change in CPT values for the left arm before and after treatment. In the 2 Hz TENS groups for the left mental foramen, at 5 Hz, the CPT values (recorded as output intensity, where 1=0.01 mA) changed from 16.1±12.7 (mean±SD) to 21.2±13.4 in the 5 minute group; from 20.2±15.8 to 24.9±15.5 in the 10 minute group; and from 15.6±13.1 to 22.9±12.4 in the 15 minute group. All these increases were significant (p<0.05). At 250 Hz, the CPT value ranged from 26.5±17.4 to 28.6±16.0 in the 15 minute group in a statistically significant manner (Fig. 1).

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**Table 1.** Compare the current perception threshold (CPT) before and after TENS in left arm.

<table>
<thead>
<tr>
<th>TENS</th>
<th>CPT (Hz)</th>
<th>5 min group</th>
<th>10 min group</th>
<th>15 min group</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Before</td>
<td>After</td>
<td>P value</td>
</tr>
<tr>
<td>2,000 Hz</td>
<td>64.7±17.5</td>
<td>64.4±20.6</td>
<td>0.884</td>
<td>53.8±17.7</td>
</tr>
<tr>
<td>2 Hz</td>
<td>20.6±6.2</td>
<td>20.3±5.8</td>
<td>0.799</td>
<td>18.1±5.1</td>
</tr>
<tr>
<td>5 Hz</td>
<td>11.7±11.5</td>
<td>12.1±10.0</td>
<td>0.617</td>
<td>13.6±6.6</td>
</tr>
<tr>
<td>100 Hz</td>
<td>62.9±9.8</td>
<td>63.6±10.3</td>
<td>0.495</td>
<td>57.5±13.9</td>
</tr>
<tr>
<td>250 Hz</td>
<td>21.0±2.2</td>
<td>21.0±2.3</td>
<td>1.000</td>
<td>20.0±3.7</td>
</tr>
<tr>
<td>5 Hz</td>
<td>17.3±4.0</td>
<td>18.0±4.6</td>
<td>0.639</td>
<td>14.4±5.1</td>
</tr>
</tbody>
</table>

N=11 Data were mean±SD
Values are output intensity (1=0.01 mA)
For 100 Hz TENS groups in the left mental foramen, at 5 Hz and 250 Hz, CPT values changed significantly (p<0.05) at treatment durations of 5, 10, and 15 minutes. However, at 2 Hz and 100 Hz, no significant changes occurred at 2,000 Hz of the CPT values at any time (Fig. 2).

Table 2 shows the changes from pre-to post-testing in CPT values. We observed no differences either between or within groups with regard to changes in the mental foramen at CPT values of 2,000 Hz, 250 Hz, or 5 Hz for 2 Hz TENS or for at CPT values of 2,000 Hz or 250 Hz for 100 Hz TENS. However, for 100 Hz TENS, we observed significant differences between the 5 minute group and 15 minute group at 5 Hz (p<0.05).

Table 3 shows the major TENS factors based on multiple linear regression analysis.
Table 2. Changes in current perception threshold (CPT) of left mental foramen area

<table>
<thead>
<tr>
<th>Frequency of TENS stimulate</th>
<th>Frequency of CPT</th>
<th>Time length of TENS stimulate</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>5 min stimulate group (n=11)</td>
<td>10 min stimulate group (n=11)</td>
</tr>
<tr>
<td>2 Hz</td>
<td>2.4±15.1</td>
<td>0.4±8.2</td>
</tr>
<tr>
<td>250 Hz</td>
<td>3.6±5.5</td>
<td>1.7±5.5</td>
</tr>
<tr>
<td>5 Hz</td>
<td>5.1±4.5</td>
<td>4.7±6.3</td>
</tr>
<tr>
<td>2,000 Hz</td>
<td>8.9±18.6</td>
<td>-3.2±7.8</td>
</tr>
<tr>
<td>100 Hz</td>
<td>6.9±7.4</td>
<td>5.8±4.9</td>
</tr>
<tr>
<td>250 Hz</td>
<td>7.6±2.2*</td>
<td>8.4±3.7</td>
</tr>
</tbody>
</table>

Data were mean±SD
Values are output intensity (1=0.01 mA)
*: p=0.016 Compared with 15 min stimulate group

Table 3. Multiple linear regression analysis for main factors of TENS

<table>
<thead>
<tr>
<th>β (Standardized Coefficients)</th>
<th>t</th>
<th>Sig.</th>
</tr>
</thead>
<tbody>
<tr>
<td>(Constant)</td>
<td>1.534</td>
<td>.127</td>
</tr>
<tr>
<td>x1 : Frequency</td>
<td>.360</td>
<td>.433</td>
</tr>
<tr>
<td>x2 : Time</td>
<td>.134</td>
<td>.648</td>
</tr>
</tbody>
</table>

r²=0.148
Dependent Variable: y=Change of CPT at 250 Hz and 5 Hz between before and after TENS stimulate

Discussion

The Hegu (LI4) acupoint is widely used to control dental pain (7, 8) and masticatory muscle pain (9). In 1997, the NIH approved acupuncture as a treatment for dental pain (13). Treatment applied to the Quchi (LI11) acupoint, combined with treatment at the Hegu (LI4) acupoint, is capable of treating conditions affecting the head, face, ears, eyes, mouth, and nose. In our research, we used TENS to stimulate these two acupoints. TENS is used in dentistry, generally by placing the electrode pads on areas affected by pain and trigger points (14). Applying TENS to an acupoint will produce acupuncture-like effects. Based on our hypothesis that applying TENS at the Hegu (LI4) and Quchi (LI11) acupoints affects sensitivity in the mandibular area, we substituted the TENS location on trigger points. The results support this assumption.

In a previous study, we demonstrated that acupuncture stimulation at the Hegu (LI4) acupoint increased the CPT for the mental foramen area (15). The current perception threshold (CPT) proved to be a reliable, non-invasive measure for quantifying sensory function in the mental foramen area (16). The Neuometer can be useful in evaluating and localizing the functionality of the third division of the trigeminal nerve (V3) (17). The mandibular nerve (V3) carries sensory information from the mandibular area. Accordingly, the CPT of the mental foramen area may help evaluate sensory function in the mandibular area. Changes in CPT values suggest changes in nerve sensory function. Following treatment, applying TENS to the Hegu (LI4) and Quchi (LI11) acupoints increased the CPT for the mental foramen area, suggesting reduced sensitivity in the mandibular area. Our previous study reached similar conclusions.

A widespread difficulty is that the extent of the pain experienced by patients depends on numerous factors. For example, gender, ethnicity, and psychological state all influence pain perception (18). Although the significant individual differences about CPT also existed, the CPT reflected the trend of sensitivity objectively. Long-duration and alternating-frequency TENS is generally chosen for clinical applications and therapeutic purposes. To identify a more effective way to discuss the effectiveness and
selectivity of TENS at the Hegu (LI4) acupoint in modifying sensory function in the mandibular area and to identify the effects of stimulation frequency and treatment duration, we designed a study to evaluate the relative effectiveness of different stimulation frequencies and treatment durations.

One previous study indicates that applying low-frequency (2 Hz) TENS to the hand and leg markedly increases immunoreactive Met–enkephalin–Arg–Phe, whereas high-frequency (100 Hz) TENS produces a 49% increase in immunoreactive dynorphin A after the application of TENS for 30 minutes (19). Researchers widely accept the explanation that TENS analgesia is mediated by endogenous opioids, and much subsequent research has focused on this mechanism. However, in our research, we observed no significant statistical differences from pre-to post-TENS in CPT values for the arm. We also found no evidence to suggest a central analgesic effect. Nonetheless, we were unable to rule out a molecule signaling mechanism. Variations from individual to individual and differences in acupuncture methods may account for the differences in results.

In the high-frequency (100 Hz) TENS group, for the left mental foramen, CPT at 5 Hz and 250 Hz increased significantly (p<0.05) in all three durations groups (5 minutes, 10 minutes, and 15 minutes). In the low-frequency (2 Hz) TENS group, for the left mental foramen, CPT at 5 Hz increased significantly (p<0.05) in all three duration groups. This indicates that even after brief stimulation, applying low-frequency (2 Hz) TENS and high-frequency (100 Hz) TENS to the Hegu (LI4) and Quchi (LI11) acupoints may increase the perception threshold of the left mental foramen. Low-frequency (2 Hz) TENS inhibited slow/second pain response; high-frequency TENS (100 Hz) resulted in a broader inhibition of pain response, inhibiting both fast/first pain response and slow/second pain response. This result in particular suggests that the effectiveness of TENS is related to the stimulation frequency. In another study, high frequency stimulation relieved pain in 7 of 12 patients with severe chronic pain, while low frequency stimulation relieved pain in just 1 of 12 patients (20). In accordance with gate control theory (21), 100 Hz TENS applied for 5–15 minutes stimulates large diameter afferent fibers, reducing the transmission of pain signals.

In the low–frequency (2 Hz) TENS group, for the left mental foramen, the CPT at 250 Hz increased significantly in the 15 minute group (p<0.05). In the high–frequency (100 Hz) TENS group, for the left mental foramen, the increase in CPT at 5 Hz grew more pronounced over time. We saw significant differences between the 5 minute group and the 15 minute group (p<0.05). With both the broader effects of low–frequency TENS and greater efficacy of high–frequency TENS, the duration of the stimulation affects the effectiveness of TENS.

The TENS stimulation frequency and treatment duration both affected TENS effectiveness. We compared the importance of these two factors via multiple linear regression analysis. The results indicate that frequency is the major influencing factor (p<0.001, β=0.36). The effectiveness of TENS is more frequency–dependent than time–dependent. This result indicates the appropriate frequency is superior to simply prolonging the duration of TENS treatment.

**Conclusion**

We found that applying TENS to the Hegu (LI4) and Quchi (LI11) acupoints in our study subjects increased CPT values in the mandibular area. These findings have potential implications for our understanding of perception threshold and for pain relief therapy. Applying TENS appears to work as effectively as applying TENS to trigger points. Low–frequency stimulation inhibited slow pain response, while high–frequency TENS inhibited both fast and slow pain response, with inhibition increasing over time. Lastly, the effectiveness of TENS is more frequency–dependent than time–dependent.

**References**

1. D.MD, inventor Medtronic, Inc. (Minneapolis, MN), assignee. TRANSCUTANEOUS STIMULATOR AND STIMULATION METHOD. United States pat-


