Effect of acupuncture on perception threshold: a randomised controlled trial

Shuang Wu,1 Hidenori Yamaguchi,2 Koh Shibutani2

ABSTRACT
Objective To determine the current perception thresholds (CPTs) for arm and mental foramen areas to enable a quantitative evaluation of the effectiveness of acupuncture treatment.

Methods Ninety-eight volunteers enrolled as participants and were randomly assigned to one of three groups: an acupuncture group (34 subjects); a sham acupuncture group (32 subjects) and a waiting group (32 subjects). CPTs for the arm and mental foramen areas were determined before and after acupuncture in a subgroup of 13 participants in the acupuncture group.

Results Acupuncture at LI4 increased the perception thresholds of the left mental foramen in the acupuncture group significantly \((p<0.01)\). The increases were significantly greater than in the control group for all frequencies, and significantly greater than sham acupuncture for 250 Hz and 5 Hz. In the subgroup, only the CPTs at 5 Hz increased significantly for the contralateral mental foramen.

Conclusions Acupuncture at LI4 increases the perception threshold in the mandibular area, but not in the arm. This finding is probably related to the analgesic effect of acupuncture.

INTRODUCTION
Practised in China and other Asian countries for more than 4000 years, acupuncture has considerable potential for pain control. Of the acupuncture points used to induce analgesia, LI4 Hegu has been widely used to control dental pain12 and masticatory muscle pain.3

Despite growing clinical acceptance of acupuncture as a method for alleviating pain of varying causes—notably, musculoskeletal and chronic pain,4 debate continues about its efficacy.56 The consensus appears to be that poor objective data and problems with quantitative methods and measures in many of the acupuncture studies to date preclude any definitive conclusions. For this trial, we used an objective assessment measurement in place of the more commonly used symptom scales (eg, Visual Analogue Scale).

The Neurometer current perception threshold (CPTs) was selected as the objective assessment method owing to its inter-rater reliability and capacity for non-traumatic examination. The three different frequencies targeted were \(A\beta\), \(A\delta\) and \(C\) fibres, respectively.78 Clearly, the use of electrical stimulus means that low frequencies will probably affect all fibre classes. Based on the threshold current required to evoke a response, it has been shown that acupuncture of peripheral nerves selectively affects the response to stimulus at 5 Hz, 250 Hz and 2000 Hz. Electrodiagnostic tests performed with a Neurometer CPT device (Neurometer NS-3000, Neurotron Inc, Baltimore, Maryland, USA) allowed direct quantitative measurements of peripheral sensory nerve function. This automated electrodiagnostic procedure is painless.

Based on the above, we postulated that acupuncture at LI4 might increase the CPT, and that an increase in CPT would be seen in the mandibular area. We also analysed the functions of three types of sensory nerves related to acupuncture-induced analgesia (LI4).

METHODS
This study was approved by the human ethics committee at Nihon University School of Dentistry at Matsudo, Japan (EC-08-008). After obtaining institutional approval and informed consent from all participants, we enrolled healthy (ASA I) volunteers in the study, excluding all candidates with any history of trauma to the inferior alveolar nerve or brachial plexus nerves, neurological disease, open skin lesions or skin disorders over the brachial plexus nerves, neurological disease, open skin lesions or skin disorders over the left mental foramen or LI11 Quchi acupuncture point. We confirmed that all volunteers understood and were able to complete the examination procedure for this study.

In the primary phase, 70 volunteers were randomly assigned to one of three groups: an acupuncture group (34 subjects, 17 male); a sham acupuncture group (18 subjects, 16 male) and a waiting control group (18 subjects, 11 male). In order to balance the sex ratio, another 28 volunteers (five male, 23 female) were recruited and randomly assigned...
to either the sham acupuncture group or waiting control group. In total, 98 volunteers were randomly assigned to one of three groups: an acupuncture group (34 subjects, 17 male); a sham acupuncture group (32 subjects, 16 male) and a waiting control group (32 subjects, 16 male).

LI4 is located on the dorsum of the hand, between the first and second metacarpal bones, at the midpoint of the second metacarpal bone, close to its radial border. This point can also be identified by asking a volunteer to adduct the thumb and the index finger; the point is located at the highest point of the first and second metacarpal muscles.9

When the elbow is flexed, LI11 is located at the midpoint between the lateral end of the transverse cubical crease and the lateral epicondyile of the humerus. We chose to use LI11 as the ipsilateral control measurement site, representing a non-mandibular location.

All the volunteers were Asian, and most had experience with acupuncture. A disposable needle was inserted at LI4, using a guide tube (acupuncture group). To reduce subjectivity in the acupuncture evaluations, we used a sham needle for the control group. We placed the sham needle at a point 1.0 cm from LI4, so that it just pierced the skin (sham acupuncture group). The waiting control group received no treatment; those in the group were simply asked to wait for 5 min after the start of the procedure.

The Neurometer CPT sensory nerve conduction threshold electrodagnostic examination uses a standardised, automated procedure to generate objective, quantitative measurements of sensory nerve fibre conduction and functional integrity. A biphasic sinusoid alternating current waveform is generated at frequencies of 2000, 250 and 5 Hz.10 Each sensory fibre type responds to a specific frequency of electrical stimulus: 2000 Hz stimulates the Aβ fibres, 250 Hz the Aδ fibres and 5 Hz the C fibres.11 In our study, in a test procedure similar to audiometric testing, the operator slowly increased the stimulus until volunteers consistently reported detecting the stimulus. Differences between the function of the sensory nerve bundles before and after acupuncture were recorded for later analysis.

All testing was done in a quiet, comfortable location. The participants sat in a comfortable chair and relaxed. A gold-plated electrode was positioned at the left LI11, considered not neurologically linked to the mandibular area. Another gold-plated electrode was positioned over the left mental foramen, in a standardised anatomical location for each volunteer. The electrode was placed at the intersection of a vertical line connecting the commissure of the lip to the inferior border of the mandible, divided in half by a lateral line. A small amount of hypoallergenic electroconductive gel was applied to the gold-plated electrode before placement, and the electrode was held in place with non-conductive tape (Softape; Neurotron, Inc) during the procedure.

All volunteers were measured first at the left LI11, then at the left mental foramen. Each test lasted about 10 min for each area. A disposable acupuncture needle (length 40 mm, diameter 0.18 mm, SEIRIN Co, Japan) was then inserted to a depth of 8–12 mm perpendicular to LI4, a procedure that generally produced local soreness, sensations of distension and numbness radiating to the fingertips (de qi). Almost all volunteers in the acupuncture group achieved the sensation. We did not add any needle manipulation for those who did not feel de qi; we did not stimulate the needle again. After 5 min, we removed the needle and measured the CPT again by the same procedure. For further exploration, in the acupuncture group, we randomly selected 13 volunteers (seven male), and measured CPTs of the left and right mental foramen both before and after acupuncture at LI4 of the left hand. All acupuncture procedures were performed by the same operator.

In the other groups, CPTs were measured again after 5 min of sham acupuncture or rest.

**Data analysis**

All data are expressed as number or mean±SD. An analysis of variance (ANOVA) was performed to examine age and weight, and gender was compared using the χ² test. Age, weight and CPTs among the three groups were compared using one-way ANOVA. If the ANOVA identified significant differences, Tukey’s multiple comparison test was used. Any changes in CPTs were analysed with the paired t test, with p<0.05 considered statistically significant. Statistical analyses were performed using a statistical package (SPSS 19.0 IBM for Windows).

**RESULTS**

Table 1 shows a comparison of the demographic data for the three groups. There were no significant differences in gender, age, body height or body weight.

In the acupuncture group, the CPT values (recorded as output intensity, where 1=0.01 mA) of the left mental foramen changed from 110±57.1 (mean±SD) to 119.2±44.1, from 33.4±23.1 to 42.3±29.4 and from 19.6±15.4 to 26.2±16.3 at 2000 Hz, 250 Hz and 5 Hz, respectively. All increases were significant, (p<0.01). There were no significant changes in the waiting control group and sham acupuncture group. (figure 1).

In all groups, there were no significant changes between CPT values of the left arm before and after testing (figure 2).

The changes between CPTs values before and after testing are shown in table 2. No changes in CPT values for the left arm were seen either between or within groups. However, changes in CPTs for the left mental foramen

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Waiting control group (n=32)</th>
<th>Acupuncture group (n=34)</th>
<th>Sham acupuncture group (n=32)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>27.9±5.3</td>
<td>31.2±6.4</td>
<td>28.7±6.5</td>
</tr>
<tr>
<td>Gender (M/F)</td>
<td>16/16</td>
<td>17/17</td>
<td>16/16</td>
</tr>
<tr>
<td>Body height (cm)</td>
<td>167.2±9.6</td>
<td>168.1±9.9</td>
<td>166.7±9.4</td>
</tr>
<tr>
<td>Body weight (kg)</td>
<td>60.4±12.1</td>
<td>64.4±13.6</td>
<td>63.2±13.6</td>
</tr>
</tbody>
</table>

Results are shown as mean±SD

No p values were significant.
were significantly different between the acupuncture group and waiting control group at 2000 Hz, 250 Hz and 5 Hz; significant differences were also seen in CPTs between the acupuncture group and the sham acupuncture group at 250 Hz and 5 Hz, though not at 2000 Hz.

There were significant differences in CPT values for the right mental foramen before and after acupuncture at 5 Hz (p<0.05) (table 3).

**DISCUSSION**

The CPT is a reliable non-invasive measure for quantifying sensory function in the mental foramen area.\(^\text{12}\) The Neurometer can be used for the evaluation and localisation of functionality of the third division of the trigeminal nerve (V3),\(^\text{13}\) the mandibular nerve, which carries sensory information from the mandibular area. CPT changes suggest changes in the sensory function of the nerve.

We found statistically significant changes between CPT values before and after acupuncture at the left mental foramen. The range of values for CPT seen in this study was consistent with that reported in earlier studies using other test sites and the Bofors pulp tester,\(^\text{14}\) Visual Analogue Scale,\(^\text{3}\) potassium iontophoresis,\(^\text{15}\) and so forth. In sum, we detected differences in CPT values at the left mental foramen in response to electrical stimuli before and after acupuncture.

Some articles have discussed the analgesic effects induced at different intensities at homotopic and heterotopic acupuncture points,\(^\text{16}\) suggesting that acupuncture at low intensities may produce homotopic analgesic effects and reflex suppression. The specific function of an acupuncture point is determined by the anatomical relationship between the focus and the segmental location of the acupuncture point. Some research points to a link between analgesic effects and spinal segments. Although the left elbow and LI4 both correspond to the brachial plexus, and are both on the Large Intestine Meridian (Te no Yomeidachokei), CPT values for the arm showed no statistically significant changes after acupuncture. This suggests a special relationship between LI4 and the mandibular area. This is consistent with the various meridians and acupuncture points in traditional Chinese medical theory.

**Table 2** Changes in CPT. Values are output intensity (1=0.01 mA)

<table>
<thead>
<tr>
<th>Region</th>
<th>CPT (Hz)</th>
<th>Waiting control group (n=32)</th>
<th>Acupuncture group (n=34)</th>
<th>Sham acupuncture group (n=32)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Left arm</td>
<td>2000</td>
<td>0.4±6.4</td>
<td>–0.6±8.4</td>
<td>0.4±9.9</td>
</tr>
<tr>
<td></td>
<td>250</td>
<td>0.3±3.2</td>
<td>0.0±4.4</td>
<td>–0.4±3.5</td>
</tr>
<tr>
<td></td>
<td>5</td>
<td>–0.2±3.0</td>
<td>0.0±5.5</td>
<td>0.1±5.7</td>
</tr>
<tr>
<td>Left mental foramen</td>
<td>2000</td>
<td>0.3±11.5</td>
<td>8.8±18.7*</td>
<td>2.8±10.7</td>
</tr>
<tr>
<td></td>
<td>250</td>
<td>0.7±4.6</td>
<td>9.6±14.5†‡</td>
<td>0.2±8.2</td>
</tr>
<tr>
<td></td>
<td>5</td>
<td>0.4±4.2</td>
<td>6.8±8.4†‡</td>
<td>0.4±6.1</td>
</tr>
</tbody>
</table>

Results are shown as mean±SD.

* p<0.05 compared with the waiting control group.
† p<0.01 compared with the waiting control group.
‡ p<0.01 compared with the sham acupuncture group.

**DISCUSSION**

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Additionally, it is worth noting that National Institutes of Health and British Medical Association approved acupuncture as treatment for dental pain in 1997 and 2000.17,18

In a neuromagnetic study, Yang et al.19 measured brain magnetic fields evoked by acupuncture at LI4. The results showed that stimulation of LI4 can inhibit maxillofacial pain, pointing to a potential mechanism for inhibiting dental pain via LI4. Cerebral fMRI studies have shown that stimulating the LI4 activates multiple brain areas,20–22 including the bilateral hippocampus, parahippocampal gyrus, amygdala body area, rostral side/caudal side of the cingulate gyrus, prefrontal lobe, occipital lobe and the left infratemporal gyrus. Based on these results, we considered the potential for neural pathway connections between the LI4 and the brain.

The palomental reflex is a primitive reflex consisting of a twitch of the chin muscle elicited by stroking a specific part of the palm. The reflex, which may be present in healthy people of all ages,23 suggests a link between the thenar eminence and the mandible. The results of a morphological study performed by the biotin labelling method, which also examined the expression of c-fos, suggest that the mandibular area is linked directly to the nucleus tractus solitarii (NTS).24 While the LI4 region has no direct mapping to the NTS, messages generated by electroacupuncture at LI4 may reach the NTS.25 An additional study indicated that noxious facial stimuli induced the expression of c-fos in the NTS,26 and electroacupuncture at a facial acupuncture point significantly induced the expression of c-fos in the NTS.27 Taken together, we presume that there may be a pathway between LI4 and facial skin (especially the mandibular area). This pathway is involved in the inhibition of the mandibular sensation following LI4 acupuncture treatment.

CPT values were assessed using a painless transcutaneous electrodiagnostic threshold test of the peripheral nervous system. The frequencies of 2000 Hz, 250 Hz and 5 Hz, respectively, correspond to tactile discrimination and temperature perception (Aβ fibre) and fast/first pain response (Aδ fibre), and slow/second pain response (C fibre). In this study, CPT values of the left mental foramen at 2000 Hz, 250 Hz and 5 Hz, respectively, increased after acupuncture at LI4. Moreover, there was a significant difference between the acupuncture group and waiting control group at 2000 Hz, 250 Hz and 5 Hz, and a significant difference between the acupuncture group and sham acupuncture group at 250 Hz and 5 Hz. This indicated that acupuncture treatment influenced Aβ, Aδ and C fibres.

A major functional feature of acupuncture points might be the site where the polymodal receptors are sensitised. When an acupuncture needle is inserted into these sensitised tissues, the polymodal receptors can provoke stronger responses than those applied to normal tissues.27,28

We measured perception thresholds and not pain thresholds. While our findings cannot be directly applied to analgesia, they are consistent with the evidence that activation of Aβ, Aδ and C fibres by acupuncture can induce analgesic effects.

To compare changes in CPT values for the arm and mandibular area, we acupunctured only the left LI4 and assessed CPT in the left arm and left mental foramen. According to traditional Chinese medicine, however, treatment of maxillofacial region pain requires acupuncture at LI4 bilaterally. We compared the CPT of the left mental foramen (homolateral side) with the right mental foramen (contralateral side) both before and after acupuncture.

CPT values for the right mental foramen did not change significantly at 2000 Hz or 250 Hz, but showed significant increases at 5 Hz. This suggests that acupuncture-induced analgesia may be regulated by slow pain response at the contralateral side. We believe acupuncture at LI4 may induce analgesia by bilaterally increasing CPT at 5 Hz in the mandibular area. The analgesia resulting from acupuncture at the LI4 in the homolateral mandibular area

Figure 2  Current perception threshold values for the left arm for pretesting and post-testing at 2000 Hz (A), 250 Hz (B) and 5 Hz (C). Data are presented as mean and SD.
was comparable or better than that for the contralateral mandibular.

CONCLUSION

In summary, we found that acupuncture at LI4 increased CPT values in the mandibular area among our study subjects. Additionally, unilateral acupuncture performed at LI4 had bilateral effects. Our findings may be relevant to the pain threshold, and thus, possibly, to pain relief.

Competing interests None.

Patient consent Obtained.

Ethics approval This study was approved by the human ethics committee at Nihon University School of Dentistry at Matsudo, Japan. Approval No: EC08-008.

Provenance and peer review Not commissioned; externally peer reviewed.

REFERENCES

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