Acupuncture Modulates Facial Warm Sensory Thresholds

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Aims: *To assess the effects of four- and six-point acupuncture on facial sensory detection thresholds to thermal and electrical stimuli.* ***Methods:*** *Ten healthy volunteers underwent four-point acupuncture at ST6 and LI4 bilaterally for 15 minutes. A further 10 subjects underwent six-point acupuncture by adding needling at ST2 bilaterally. Sensory testing to thermal and electrical stimuli applied to mental and infraorbital nerve dermatomes was performed at baseline, 10 minutes, 1 hour, and 1 day after needling.* ***Results:*** *In the mental and infraorbital nerve dermatomes, six-point acupuncture significantly increased warm threshold by a peak mean of 1.1°C to 1.4°C (repeated measures ANOVA* $P = .001$*) and this effect was significant at all time points relative to baseline (*$P < .05$*). No significant effects were observed by the four-point acupuncture on warm thresholds, and neither four- nor six-point acupuncture significantly altered electrical detection thresholds.* ***Conclusion:*** *A dose effect, related to the number of points employed, may be present when employing acupuncture.* J OROFAC PAIN 2011;25:32–38

Key words: Aβ-fibers, C-fibers, electrical thresholds, warm thresholds

The use of complementary and alternative medicine (CAM) by patients has become frequent; a staggering 29.8 million Americans resorted to these modalities in 2006 to resolve pain-related issues such as back, neck joint-pains, or headaches.[1] Amongst CAM therapies, acupuncture has become increasingly popular with an estimated 3.1 million Americans using acupuncture for various health problems during 2006.[1] It is also becoming increasingly common for orofacial pain patients to resort to CAM, including acupuncture, to manage their pain.[2–4]

Classical Chinese medicine theory underlying acupuncture therapy is based on the premise that there are patterns of energy that flow through the body known as Qi that are essential for health. Qi flows through meridians along which acupuncture points are located. Disruptions of this energy flow, believed to be responsible for the onset of disease, are corrected by acupuncture stimulation.

Recent years have witnessed a flurry of activity attempting to explain, using modern scientific methodology, the mechanisms by which acupuncture modulates physiological conditions. However, in general, these mechanisms remain unknown. In pain research, acupuncture seems to be clinically efficient for chronic pain[5] and is extremely safe.[6] In systematic reviews, it was concluded that acupuncture might be an effective short-term therapy for masticatory muscle myofascial pain[7–9] and can alleviate acute dental pain.[10] Acupuncture may also be effective for idiopathic headache,[11] abortive treatment of migraine,[12] tension-type headache, and chronic daily headache.[13–15]

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The introduction of the "gate control theory"[16] lent theoretical support for possible pain control by means of an external stimulus applied to the body, such as acupuncture. Later investigations have demonstrated that the nervous system, neurotransmitters, and endogenous substances respond to needling stimulation.[17] It has been established that acupuncture analgesia is partly mediated by opioid peptides produced in the periaqueductal grey and can be reversed by naloxone, an opioid antagonist.[18] The periaqueductal grey and other supraspinal sites of the descending pain modulatory system exert powerful inhibitory effects on the response at the spinal level[19] and trigeminal brainstem complex.[20–22] Non-opioid based mechanisms have also been stipulated.[23] Additional studies have shown that cellular and molecular mechanisms initiated in the local tissue surrounding the acupuncture needle may play a more significant role in the therapeutic effects than previously realized.[24,25] Thus, it has been proposed that acupuncture initiates a mechanotransduction response that propagates through the tissue both spatially and temporally via a series of events induced by the mechanical stimulus of needle manipulation. This is proposed to lead to locally mediated cellular responses and the alteration of local protein and extracellular matrix synthesis. The theory, mechanism, and practice of acupuncture in headache have been extensively reviewed by Zhao et al.[26]

Although there is some experimental evidence supporting the analgesic effect of acupuncture in the trigeminocervical complex,[27,28] its exact mechanisms remain unclear. The present study investigated the effects of two different acupuncture interventions, using four and six needles (as a parallel to dose effect), on facial thermal and electrical thresholds. Traditional acupuncture, with no supplementary electrical stimulation, was used.

Materials and Methods

Subjects

Male or female subjects between the ages of 18 and 50 with no known systemic disease, immune dysfunction, or coagulation disorders were eligible. Exclusion factors included pregnancy, a history of recent (6 weeks) infectious disease (cold, urinary tract infection, upper respiratory infection), prior use of prescription or over-the-counter medications within 4 weeks of study entry, and prior acupuncture therapy. Any subject with signs of skin irritation, scarring, or infection at the proposed acupuncture site was excluded.

Subjects were 20 healthy volunteers aged between 20 to 29 years, recruited from the students at the Hebrew University, mostly preclinical medical and dental students. The young age of the study group reflects that they were recruited from a student body. The subjects were unaware of the specific objective of the study. All of the subjects were nonsmokers. Following application, subjects were interviewed and enrolled by two of the authors together (SZ, EE). All subjects underwent baseline sensory testing in the infraorbital and mental dermatomes of the trigeminal maxillary and mandibular nerves respectively. The institute's ethical committee approved the methodology, and all participants consented.

Subjects were subsequently randomly assigned to two groups:

- *Group 1:* 10 subjects (six males, four females, mean age 24.5) underwent acupuncture at ST6 and LI4 bilaterally (four points).
- *Group 2:* 10 subjects (five males, five females, mean age 23.0) underwent acupuncture at ST2, ST6, and LI4 bilaterally (six points).

A design utilizing independent groups rather than a crossover design was chosen to cancel the effects of the first visit on the subsequent results during the second intervention.

Choice of Acupuncture Points

The choice of acupuncture points is often solely based on accepted and recommended combinations for the painful area treated and combine regional accupoints with distant "distal" points. Additionally, in pain patients, the introduction of needles into locally tender areas (*ashi* points), not necessarily on meridians, is accepted practice. However, individual operators have their own "favorite" points, and this no doubt affected the choice of points in the current study. Thus, there is a large combination of points that may be used for similar conditions. The variety of protocols used for research for masticatory muscle myofascial pain has been reviewed in La Touche et al.[9] Included are regional meridian points (eg, ST2, ST6 in headache/orofacial pain) and distal points that are anatomically removed from the painful site but are efficient "analgesics" (eg, LI4 in headache/orofacial pain).

In acupuncture for the treatment of pain, it is common to stimulate the LI4 point located roughly in the center of the web between the thumb and the palm of the patient's hands (*hegu* points). LI4 is considered one of the most important analgesic points and very effective for the face and head.[29,30] LI4 that was chosen for this experiment has been previously employed for craniofacial muscle pain.[31–33] ST6 has been successfully combined with LI4 in the treatment of

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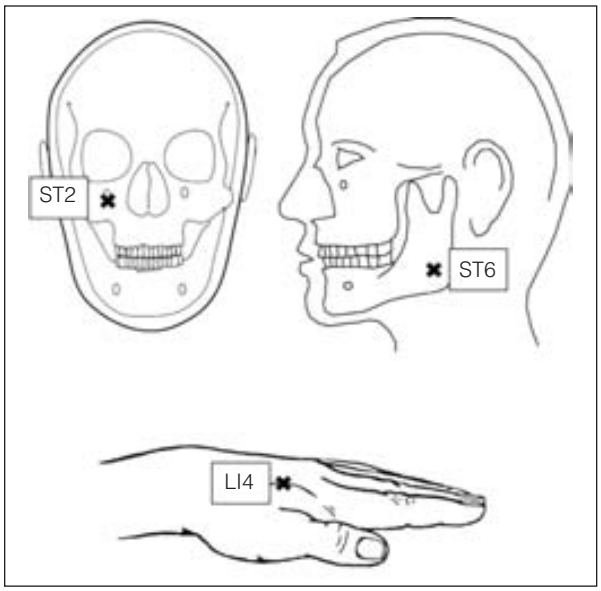

Fig 1 Diagrammatic representation of the anatomical locations of needle insertion.[30] ST6: Anterior and superior to the lower angle of the mandible where the masseter muscle attaches, at the prominence of the muscle when the teeth are clenched. ST2: The point is directly below the pupil of the eye, approximately in the depression at the infraorbital foramen. LI4: On the dorsum of the hand, between the thumb and first (index) finger, at the highest point of the adductor pollicis muscle when the thumb and index finger are adducted.

muscle pain,[31] and ST2 is indicated in the treatment of facial pain[29,30] and is frequently employed in the authors' facial pain clinic. Additionally, ST2 is in the infraorbital nerve (ION) dermatome, and ST6 is located in the mental nerve (MN) dermatome[29,30]; both of these sites underwent quantitative sensory testing (QST) and were therefore highly relevant for the detection of the local effects of acupuncture needles that were placed in these areas. Thus the points chosen for the experiment were LI4 and ST6 for the first group and LI4, ST2, and ST6 for the second group (see Fig 1 for anatomical locations).

Sleeved acupuncture needles were employed (Seirin J-type no. 5; 0.25 mm diameter, 4-cm length) and were introduced by the same operator using a standard technique that included rotating the needle. The needles were left in place for 15 minutes. A second researcher placed the electrodes and oversaw the sensory testing. Sensory testing for both paradigms was largely operator independent; the patient released the button on a computer mouse the moment he/she felt any sensation at the test site. Repeat sensory testing was performed at 10 minutes (needles still in place), 1 hour, and 24 hours (1 day) following needle introduction.

Sensory Testing

Sites. Sites were tested bilaterally and the mean of these for each site at each time point employed for further analysis. The areas tested were the ION dermatome (directly below the midline of the eye and approximately midway between the upper lip and lower eyelid) and the MN dermatome (below the lower lip, just under the vermilion border, and approximately 0.5 cm lateral to the midline).

Thermal. Sensory detection thresholds for warm stimuli were evaluated by a 5 × 5-mm water-cooled Peltier probe (Medoc TSA 2001) using a staircase paradigm in which stimulus intensity (temperature) was alternately increased on successive trials until a non-noxious sensation was evoked and decreased until no sensation was experienced. After each change in direction, the amount of stimulus change from each trial was reduced by 50%, and the ascending and descending trials were repeated until this increment was reduced to 0.1°C. In this series, the starting temperature was 32°C, and the starting increment was 3.0°C. This is accepted methodology to test C-fiber-evoked responses.[34–36]

In the staircase procedure, a specific stimulus intensity is delivered, and the subject signals whether the stimulus is detected. The response is used to modify the intensity of future stimulation to track a specific subjective level such as sensory threshold.[37] This method usually requires longer examination times; however, the method is easy for the subject and more accurate and reliable.[38]

In the alternative, method of limits, the subject is required to indicate detection of an increasing stimulus or the disappearance of a decreasing stimulus, which is often difficult and confusing.[39] It is, however, a simple and fast method that can be very useful in situations in which the expected abnormalities are obvious and large but needs repetition to validate results. The staircase paradigm was chosen over the method of limits.

Electrical. For electrical non-noxious detection threshold, continuous trains of constant current electrical stimuli were delivered to the skin through 8-mm diameter spherical gold-plated electrodes spaced 20 mm apart. Stimulus frequency was 200 Hz with a 50% duty cycle, and polarity of the electrodes was randomized. Detection thresholds were assessed by an ascending method of limits. Stimulating current was increased slowly until the subject indicated detection. Three detection thresholds were evaluated for each location and the mean calculated and used for data analysis. At these settings, this is an accepted technique to assess A-β fiber-evoked sensations[35,38,40–42] and has been employed in previous clinical publications.[34,35]

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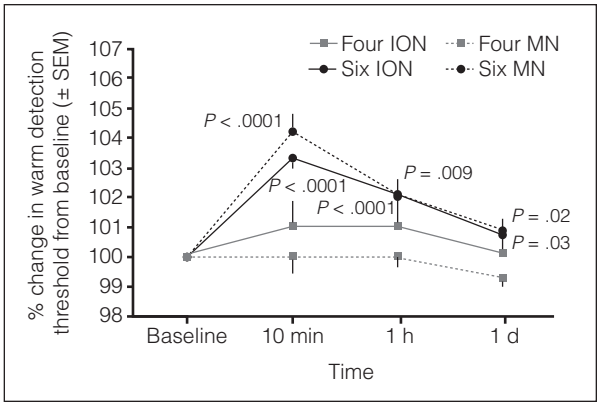

Fig 2 Changes in warm detection thresholds in the ION and MN dermatomes following treatment with four or six acupuncture needles. Results are shown as percentage change from baseline levels. The statistics shown reflect comparisons of values at timepoints relative to baseline. Significant changes were observed at both test sites employing six-point needling, but no significant effect is observed with four needles.

Statistical Analyses

Data was tabulated and analyzed with SPSS for Macintosh (PASW version 18), with alpha for significance set at .05. To adjust for baseline differences between the subjects, all data were converted to changes from baseline value (computed to 100) in percent. A repeated measures analysis of variance (RM-ANOVA) was employed to analyze all the data with the four time points as the repeated dependent variables and the number of needles inserted as the independent variable (between subjects). For each experimental group (four and six needles), an RM-ANOVA was run, and differences between all time points and baseline (within subjects) were analyzed individually by employing SPSS's simple contrast analysis (included in the RM-ANOVA).

Results

All subjects completed the testing protocol. No complications, such as pain or swelling in the acupuncture areas, were reported.

Thermal

Total Sample Analysis. In the ION dermatome, needling significantly altered the warm threshold over time (RM-ANOVA: F = 7.2, df = 3, P = .003), and these changes were significantly different between the group with four and the group with six needles (P = .04). A similar pattern was observed in the MN dermatome (RM-ANOVA: F = 6.1, df = 3, P = .006), with a significant difference between the group with four and the group with six needles (P = .001). The results are shown in Fig 2.

Warm Threshold: Specific Effects of Six Needles. In the six-needle group, the warm threshold of the ION dermatome changed significantly over time (RM-ANOVA: F = 18.9, df = 3, P = .001), and within subjects, contrasts showed that the warm threshold was higher relative to baseline (10 minutes: P < .0001, 1 hour: P = .009, 1 day: P = .03) at all time points. The peak increase in warm threshold of the ION dermatome occurred at 10 minutes in the six-needle group, approximately 3% higher than at baseline, which represents a rise of about 1.1°C.

Similar effects were observed in the MN dermatome (RM-ANOVA: F = 20.1, df = 3, P = .001) and within subjects, contrasts of all time points relative to baseline were also significant (10 minutes: P < .0001, 1 hour: P < .0001, 1 day: P = .02). In the MN dermatome, peak increase in warm threshold occurred at 10 minutes in the six-needle group, 4.2% higher than at baseline, which represents a rise of about 1.4°C.

Warm Threshold: Specific Effects of Four Needles. Both in the ION and MN dermatomes, there was no significant change in warm thresholds over time in the four-needle group (RM-ANOVA: P = .63, P = .66, respectively). Within subjects, contrasts of all time points relative to baseline were also not significant (P > .05).

Electrical

Total Sample. Both in the ION and MN dermatome, changes in electrical sensory thresholds were not significant over time following needling (RM-ANOVA: F = 1.3, df = 3, P = .32 and F = 2.8, df = 3, P = .07, respectively). Similarly, in both dermatomes, no significant effect was observed between the group with four and the group with six needles (P = .45 and P = .23, respectively). The results are shown in Fig 3.

Electrical Threshold: Specific Effects of Four and Six Needles. When analyzed separately, both the four-needle and six-needle groups showed no significant changes in electrical thresholds over time in the ION dermatome (RM-ANOVA: F = 0.62, df = 3, P = .62 and F = 3.2, df = 3, P = .09, respectively) or in the MN dermatome (RM-ANOVA: F = 1.47, df = 3, P = .3 and F = 1.2, df = 3, P = .36, respectively).

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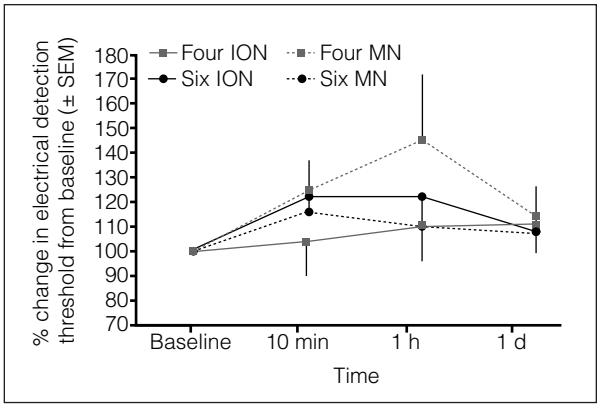

Fig 3 Changes in electrical detection thresholds in the ION and MN dermatomes following treatment with "four" or "six" acupuncture needles. Results are shown as percentage change from baseline levels. No significant effects were observed for both treatment groups at both sites.

Effects of Gender

No effects of gender were observed on the RM-ANOVA model when this was run with the number of needles as a second independent variable. This was true for warm and electrical stimuli in both the ION and MN dermatomes.

Discussion

The major finding of this study was the clear increase in warm detection threshold in the ION and MN dermatomes attained by six-point acupuncture. The effect was statistically significant and clinically translates into a substantial increase of 1.1 to 1.4°C in sensory thresholds. Previous studies on nerve injury patients[34,41,42] have shown that a rise of 1°C is associated with clinical symptomatology. Extrapolating from this, it is legitimate to assume that such a change may be significant in the "analgesic" effects observed in acupuncture. This rise is comparable to that observed in previous studies employing electroacupuncture (2 to 3°C)[43] or electrically stimulated accupoints (1.54°C).[44] One previous study showed no significant differences in cold and hot pain thresholds between sham and real acupuncture,[45] but as the authors themselves suggested, the study was inconclusive. With four-point acupuncture in the present study, the changes in warm detection threshold were mild (usually < 0.5°C) and not statistically significant. The relatively mild response may be due to the fact that electrical supplementation to the needling was not used.

How are these effects obtained by simple needling? It has been proposed that acupuncture initiates a mechanotransduction response that propagates through the tissue both spatially and temporally via a series of events induced by the mechanical stimulus of needle insertion and manipulation.[46] Affected structures include peripheral nerves, connective tissue fibers, and fibroblasts. Many facial acupuncture points are located along terminal or cutaneous branches of the trigeminal nerve[47] and at the intersection of tissue planes,[48] suggesting that peripheral nerve stimulation and connective tissue effects may be involved. Langevin et al[48] found 80% correspondence between the sites of acupuncture points and the location of intermuscular or intramuscular connective tissue planes in postmortem tissue sections. Based on the anatomical relationship of acupuncture points and meridians to connective tissue planes, they proposed that connective tissue distortion activates connective tissue fibers and fibroblasts that seem to have an important role in the effects of acupuncture. Indeed, based on the gate control theory of pain, it is possible to explain acupuncture's analgesic effect partly by Aβ nerve stimulation.[26] In support are experimental studies showing that acupuncture suppresses c-fos expression and release of substance P in trigeminal nucleus caudalis.[26] These effects may also be explained by acupuncture-induced release of endogenous opioids locally in trigeminal nucleus caudalis and systemically.[26,49] Naloxone, an opioid antagonist, is able to reverse acupuncture analgesia. Most of the studies have employed electroacupuncture, which seems to potentiate the effects of simple needling[50] probably by recruiting Aδ-fiber-induced inhibition of C-fiber-evoked effects.

The graded response (ie, six needles were more effective than four needles) lends credibility to the experimental setup in the present study and suggests a possible "dose-effect" between the number of acupuncture points employed and the changes in thermal sensory thresholds observed. The mechanisms may involve spatial summation of incoming stimuli; this is feasible for the present results, given the effects of the extra needles in the trigeminal zone. Alternatively, there may be increased release of opioids. Similarly, extended electoacupuncture duration or intensity can result in significant changes in sensory or pain thresholds[43,51] and

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reduction of experimental pain.[52] These effects may involve temporal summation and increased release of endogenous opioids. The significant effect observed with six needles seems a generalized effect and not local. Although ST2 was added and is located in the ION dermatome, there was also a significant change in the MN thresholds and not only in the ION dermatome, which would have been expected had the effect of the extra needle been solely local. Distant effects are also the basis for the analgesic effect of LI4.

Clinically, however, one acupuncture point is often enough to demonstrate a significant effect on reported pain.[33,53] This may suggest that the clinical response in acupuncture may not always reflect the physiological changes observed, which is supported by the fact that sham acupuncture often has clinical effects comparable to that of true acupuncture,[26,54] particularly in the long-term management of pain.[5] It would be interesting to correlate changes in sensory thresholds with clinical improvement in the long-term management of chronic pain patients treated with acupuncture. One study on "craniomandibular pain" patients examined the effects of acupuncture on pressure-pain thresholds and clinical outcome at baseline and after 6 months.[55] The acupuncture patients improved more than controls immediately after treatment. At the 6-month follow-up, no significant differences in pressure-pain threshold or clinical dysfunction score were found in the acupuncture group compared with the short-term results. This study needs replication with quantitative sensory testing at more time points.

The results of electrical threshold testing were not statistically significant, and no dose effect was observed. A lack of significant effect of acupuncture on Aβ-related sensory threshold has been previously reported following acupuncture[43] and electrical stimuli of acupuncture points.[44] In the present study, there were large changes in electrical detection thresholds, but they were inconsistent across the sample, leading to large SEMs. Moreover, there was no dose effect observed. The authors have no convincingly plausible explanation for this inconsistent effect: It is possible that electrical testing may inadvertently "include" Aδ nociceptors, and this may explain why some subjects showed increases in electrical thresholds. The methodology employed has been used by the authors previously and has proved a reliable tool to detect changes in Aβ-fiber-evoked thresholds.[34,35,38,56]

No gender effects were observed, but the sample was small, and the authors had no information at what point in the menstrual cycle each female subject was at the time of testing. Indeed, all study conclusions must be interpreted and tempered by the small sample size.

In conclusion, since six needles were significantly more effective than four needles, this suggests a "dose effect" on warm detection thresholds. Although the clinical effects were not tested in this study (ie, effects on pain), it is tempting to extrapolate to the clinical setting that more needles may, at times, be more effective. However, there is a need for studies that correlate improvement in pain-related outcomes with changes in sensory thresholds and the number of needles used.

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