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The Effect of Ting Point (Tendinomuscular Meridians) Electroacupuncture on Thermal Pain: A Model for Studying the Neuronal Mechanism of Acupuncture Analgesia

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ABSTRACT

Objective: The aim of this study was to characterize the role of Ting points (TP) in acute pain management and its potential use in functional imaging studies by quantitatively assessing: (1) the change in peripheral thermal thresholds before and after the electroacupuncture (EA); and (2) the corresponding behavioral feedback of thermal pain stimulation and the *de qi* sensation of EA.

Design: The study design was prospective.

Settings/location: Healthy subjects were recruited for the study at the University of California, San Diego Medical Center.

Subjects/interventions: Thirteen (13) healthy subjects were studied. Baseline thermal thresholds (cold and warm sensations and cold and hot pain) were measured at premarked testing sites along the medial aspects of bilateral lower extremities. Five (5) seconds of hot pain (HP) was delivered to the testing sites and the corresponding pain visual analog scale (VAS) scores were recorded. Thirty (30) seconds of EA was delivered via the SP1 and LR1 on the left lower extremities at 5 Hz via a 6-V square-wave stimulator.

Outcome measures: The VAS scores of the HP and *de qi* sensation (tingling) during the EA were recorded. The thermal thresholds and VAS scores for the HP and *de qi* were obtained immediately and both 30 and 60 minutes after the EA. Adaptation testing was also carried out to assess the change in thermal thresholds and the VAS scores of HP without EA.

Results: The warm thresholds of bilateral medial calves significantly increased ($p < 0.01$) after 30 seconds of EA stimulation. The HP VAS score reduced significantly at the ipsilateral calf during EA in comparison to preacupuncture and postacupuncture ($p < 0.01$) measurements. No significant change in thermal thresholds was noted in the adaptation paradigm.

Conclusions: EA at the TP has an inhibitory effect on the C-fiber afferents. The analgesic benefit observed is most likely A-δ afferent mediated. Further correlation studies in functional imaging may provide defining data for the observed analgesic mechanism.

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INTRODUCTION

Despite recent favorable clinical outcome data that support the use of acupuncture in treating several chronic pain conditions, the exact analgesic mechanisms of acupuncture in acute pain management are still largely unknown.[1–5] Recent developments in functional imaging technology provide a useful tool for investigating the neuronal mechanism of acupuncture analgesia.[6–12] However, given the inconsistency of stimulation parameters used in manual acupuncture and the long duration of the study paradigm (≥10 minutes), a duration too long for most functional magnetic resonance imaging (fMRI) study design requirements because of the potential signal drop-off and head movement problems, an alternative model is needed to study the central dynamic mechanism of acupuncture in treating acute pain.

Empirically, textbooks describe the use of Tendinomuscular Meridians (TMM) as the initial means of intervention for acute pain.[13] In a pilot study using the traditional TMM treatment protocol, it was demonstrated that manual acupuncture (MA) stimulation at the TMM in the lower extremity generated a change in peripheral thermal sensory threshold at the bilateral medial calf with a potential central effect at the anterior cingulated gyrus as demonstrated in functional magnetic resonance imaging (fMRI).[14] However, to further the understanding of this unique treatment protocol, the specific function of the different needle groups used in the TMM treatment protocol and their corresponding peripheral and central mechanisms require a thorough systematic investigation.

This study intended to characterize specifically the role of the Ting point (TP) in the TMM treatment paradigm. Electroacupuncture (EA) was used in lieu of MA in the current study to provide a consistent means-of-stimulation parameter, as previously it has been shown that different methods of MA may result in different functional imaging results and clinical responses.[8] The objective was to investigate specifically the extent and duration of analgesic effect of short-duration, low-frequency, and high-intensity EA at the TP of the lower extremities and its potential use in fMRI studies of acupuncture by: (1) assessing the change in peripheral thermal thresholds before and after the EA; and (2) studying the corresponding behavioral feedback of thermal pain stimulation and the *de qi* sensation of EA.

MATERIALS AND METHODS

With institutional review board (IRB) approval, healthy subjects were recruited for the study based on the following inclusion and exclusion criteria shown in Table 1.

EA paradigm

First, the subject was asked to lie comfortably on a patient bed. A drape screen was then placed to block the subject's view from the sites of testing. The locations of measurements at the calf and thigh areas along the Spleen (SP) and Liver (LR) TMM were marked with a surgical marking pen. The four corners of the measuring probe were carefully marked between the intended *cun* spaces (i.e., distance of acupuncture point from specific anatomical landmark, discussed later) for all measurements taken in the study. Equivalent mirror anatomical landmarks were marked on both legs. The locations of the acupuncture needle placement were also marked at the SP1 and LR1 TP at the left lower extremities with the assistance of an acupuncture point finder. The locations of the paired grounding electrodes for the TP were marked in adjacent locations, at least 2 cm away, where the electroconductivity was undetectable with the sensitivity level of the point finder set at 3. Two 1.5 cm × 1.5 cm cardiac electrodes were placed over the two grounding areas. Baseline nonnoxious thermal thresholds (cold and warm sensations) and noxious thermal thresholds (cold and hot pain) were measured along the premarked testing sites using a Peltier Thermal Analyzer (Medoc Advanced Medical Systems, Durham NC) (Fig. 1A,B).

The visual analog scale (VAS) scores of the hot point (HP) obtained after 5 seconds of hot pain stimulation at the pre-acupuncture treatment HP threshold were applied at the four testing sites. After the baseline measurement and optimal needle placement locations were confirmed with the point finder, acupuncture needles were placed at the following sites of the subject's left lower extremity:

1. SP1 (Yinbai)—on the dorsal aspect of the big toe, at the junction of lines drawn along the medial border of the nail and the base of the nail, approximately 0.1 *cun* from the corner of the nail.

TABLE 1. RECRUITMENT OF SUBJECTS

Inclusion criteria	*Exclusion criteria*
Age 18–80 years	History of psychologic illness
Male or female	History of claustrophobia
No acupuncture treatment for the past 2 weeks	Lack of ability to understand experimental protocol and to communicate adequately in English
No analgesics for the past 2 weeks	Pregnancy
Absence of neuropathic pain states	Pending litigation
	History of head trauma
	History of trauma or surgery to lower extremities and pelvic area

A

B

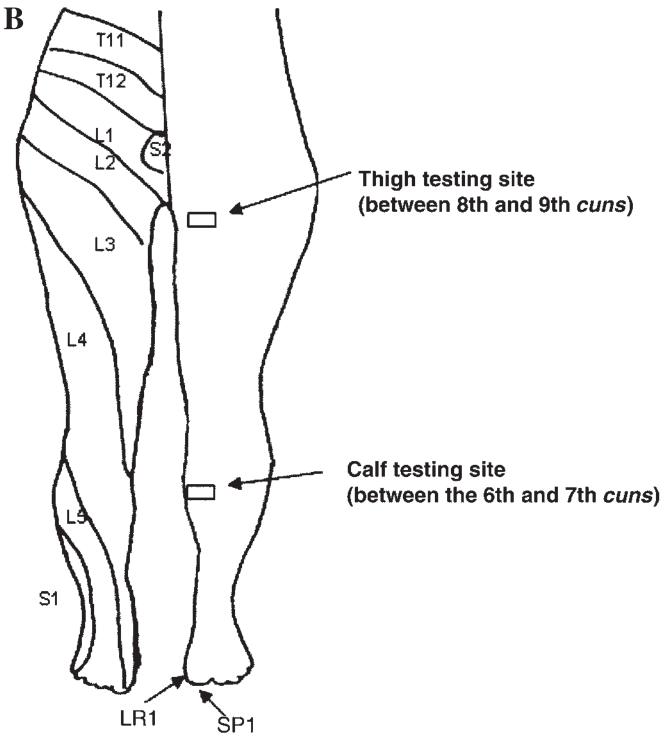

FIG. 1A. Thermal sensory measurement via a Peltier Thermal Analyzer (Medoc Advanced Medical Systems, Durham, NC). **B.** Locations of the testing sites and the corresponding dermatomes.

2. LR1(Big Mound).—on the dorsal aspect of the big toe, at the junction of lines drawn between the lateral border of the nail and the base of the nail, approximately 0.1 *cun* from the corner of the nail.[15]

The subject was then asked to rate the degree of *de qi* sensation on a linear VAS scale immediately after the needle placements. The acupuncture needles and the grounding electrodes were then attached to an EA stimulator via two pairs of alligator clips. Thirty (30) seconds of EA stimulation with a square-wave form was then delivered to the subject. At the last 10 seconds of EA, 5 seconds of HP stimulation with the preacupuncture treatment HP threshold was delivered to the left calf testing site via the Peltier probe. The subject was again asked to rate, on two separate linear VAS sheets, the degree of *de qi* sensation at the beginning of the EA stimulation and also the intensity of HP that was delivered at the end of the stimulation. Immediately after that, the baseline thermal sensory thresholds and HP VAS scores were repeated at the testing sites. These measurements were also repeated at 30 minutes and 60 minutes to assess the temporal effects of the stimulation.

Adaptation paradigm

To assess the potential effect of repeated thermal sensory measurements and HP simulations, the subjects tested in the EA paradigm were asked to return at least 2 weeks later for the adaptation testing, in which baseline thermal sensory thresholds and HP VAS score measurements were carried out at the same testing locations with the initial baseline measurements, followed by repeated measurements at 30- and 60-minute intervals. However, no acupuncture needles were placed this time.

Acupuncture

One-inch-long, 36-G, gold-plated sterile acupuncture needles were used for the study because of their fMRI compatibility. An acupuncturist who was a medical doctor with 5 years of post–UCLA University of California at Los Angeles acupuncture training practice experience performed all needle insertions in all subjects. The needles were premarked sterilely with a surgical marking pen so that the depth of needle placement was between 0.5 and 1 cm. The stimulation of the acupuncture points (Fig. 2) was provided at a constant frequency of 5 Hz with a pulse width of 300 microseconds at the amplitude of 8 (maximum 10) via a 6-

FIG. 2. Electroacupuncture at the Ting points (SP1 and LR1).

volt ES-160 (Electro-Therapeutic Devices Inc., Markham, Ontario, Canada) clinical acupuncture stimulation device, which carries a digital display of the stimulation paradigm.

Cun *measurement and testing sites*

Testing sites were chosen along the SP and LR meridians at the medial aspect of the thighs and calves. In classical acupuncture literature, the distance of an acupuncture point from a certain anatomical landmark was measured by a unit called a *cun*. The number of *cun* between different parts of anatomical landmarks is well established in acupuncture literature. Given the difference in body lengths and sizes of the subject and for consistency in the study, an elastic ribbon that was about the size of a 0.5-inch-wide ruler with units marked was used to indicate the correct number of divisions (*cun*) for that body region, and the sites of testing and stimulation were marked. At the medial thigh, the site of study was between the 8th and 9th *cun* measuring from the midline of the superior border of the pubic symphysis to the medial epicondyle of femur (a total of 18 *cun*). At the medial calf, the measurement was between the 6th and 7th *cun* measuring from the medial condyle of the medial malleolus (a total of 13 *cun*).

Needle placement location

Anatomical landmarks were first used to mark the approximate locations of acupuncture needle placement, and the exact location of the needle placement was further confirmed by measuring the electroconductivity of the needle placement site. A clinical acupuncture electroconductivity measuring device (Point Finder, Hong Kong, China) with a preset clinical acceptable sensitivity level of 3 of a maximum of 10 was used for locating the exact location of the acupuncture needle placement. The locations were then marked with a surgical marking pen.

De qi *sensation*

The *de qi* sensations are known qualitatively as having different components of sensations such as dull aching, needle grasping, heaviness, or electricity-like (tingling) in different acupuncture literature.[16–19] The exact clinical correlation of the clinical effect to the different elements of *de qi* sensations is still unknown. However, given that the current study used direct current electricity as a means of stimulation, the subjects were primarily asked to rate their *de qi* sensations, based on the degree of tingling that they felt, on a linear VAS.

Thermal sensory testing

Nonnoxious thermal sensations including cold and warm, and noxious thermal sensations such as cold and hot pain thresholds, were measured by using a Thermal Sensory Analyzer (Medoc Advanced Medical Systems, Minneapolis, MN). This device consisted of a thermode measuring 46 × 29 mm. The temperature of the thermode could either rise or fall (at a rate of 1.2° C/second for cold and warm sensations, and 3°C/sec for cold and warm pain), depending on the sensations that were being tested. The subject signaled the onset of feeling the tested sensation by pressing a switch, which in turn reversed the temperature change and returned the temperature of the thermode to the 32°C baseline. The computer then recorded the temperature of the thermode when the switch was pressed. The average value of testing result would be automatically calculated by the computer and displaced on the screen. This method of peripheral sensory testing has been well established in literature and has been used extensively in pain-related studies.[14,20–22]

Visual analogue scale and behavioral measurement

The VAS is a horizontal linear scale with the length of 100 mm. One end of the scale was marked “No Pain” or “No Tingling” and at the other end of the scale was marked “Worst Pain Imaginable” or “Maximal Degree of Tingling.” These two different sets of marking were used for the HP or *de qi* sensations, respectively.

Data analysis

A Student’s paired *t*-test was used to compare the pretreatment and post-treatment values of the thermal thresholds and VAS scores for hot pain and *de qi* sensations. Comparisons were also made for the thermal thresholds and HP VAS scores between baseline and repeated measurements obtained at the 30- and 60-minute intervals during the adaptation tests.

RESULTS

With IRB approval and informed consent, 13 subjects (eight male and five female) were enrolled in the studies. The median age for the cohort was 30 years, with an age range of 18–45 years.

Thermal thresholds

EA paradigm. The baseline cold and warm sensations and cold and hot pain thresholds were measured along the SP and LR TMM and are shown in Table 2. There is no difference between the bilateral lower extremity baseline thermal thresholds at the corresponding opposite testing sites.

The bilateral medial calf warm thresholds significantly increased ($p < 0.01$) over the baseline warm thresholds immediately at 30 minutes, and at 60 minutes after 30 seconds of EA stimulation (Table 3).

No significant change in the warm threshold was observed in the thighs, and no significant difference was noted

TABLE 2. BASELINE THERMAL THRESHOLDS (°C ± SD) AT THE BILATERAL LOWER EXTREMITIES

Thermal threshold tested (°C)	*Anatomical locations (N = 13)* *Ipsilateral medial calf*	*Contralateral medial calf*	*Ipsilateral medial thigh*	*Contralateral medial thigh*
Cold	26.5 ± 3.3	25.5 ± 3.1	25.9 ± 2.0	25.8 ± 2.0
Warm	39.1 ± 3.6	39.8 ± 3.6	36.8 ± 2.3	36.0 ± 1.4
Hot pain	2.6 ± 6.4	1.8 ± 4.6	2.5 ± 6.3	2.6 ± 6.5
Cold pain	48.0 ± 1.9	48.4 ± 1.7	47.9 ± 1.2	47.7 ± 1.4

SD, standard deviation.

in the baseline thermal thresholds of the bilateral calves and thighs. Likewise, no change in the cold and cold pain thresholds was noted in the bilateral calf and thigh testing sites. There were no significant changes in the hot pain threshold in the contralateral calf and bilateral medial thighs.

Adaptation paradigm. Nine (9) of 13 subjects who participated in the initial acupuncture treatment paradigm participated in the adaptation testing paradigm. No significant change was noted in thermal thresholds over the baseline values at 30-minute and 60-minute intervals.

Comparison of thermal sensory thresholds. No statistical difference was found between the two settings in the nine subjects who participated in both the acupuncture and adaptation testing paradigms (Table 4). Because the 30-minute and 60-minute thermal thresholds in the acupuncture paradigm were made after EA rather than after the baseline measurement, no interparadigm comparison was made.

Hot pain VAS scores

EA paradigm. A significant hot pain VAS score reduction was noted at the ipsilateral calf during EA in comparison to the preacupuncture and postacupuncture hot pain VAS scores ($p < 0.01$).

Adaptation paradigm. No significant change in the HP VAS score was observed in all four locations measured at the three different time points.

de qi *sensation*. The degree of *de qi* significantly increased during EA and subsided rapidly after EA. The correlation between the degree of *de qi* sensation and the change in HP VAS scores is illustrated in Figure 3.

DISCUSSION

Peripheral thermal sensory thresholds

The results of the current study suggests that low-frequency and high-intensity EA stimulation at the distal end of digits, classically known as the Ting points of the acupuncture meridians, can provide transient analgesic benefit to hot noxious stimulation with corresponding bilateral warm threshold changes in the area of the same or adjacent dermatomes. Points with high electroconductivity were chosen and used to optimize acupuncture efficacy, as EA was used as the means of stimulation in the current study. No thermal sensory threshold and HP VAS scores were assessed immediately after the needle placement because the placement of needles without stimulation in the TP had not resulted in any significant changes in the testing parameters in a previous study.[14] As the adaptation study paradigm showed no statistically significant change in warm and other thermal thresholds tested in the study, the possibility that the observed changes in warm thresholds after the EA were caused by an adaptation process resulting from repeated noxious stimulation or thermal threshold measurements was excluded. In addition, the lack of change in the thermal thresh-

TABLE 3. THE EFFECT OF ELECTROACUPUNCTURE ON WARM THRESHOLDS N = 13

	Ipsilateral warm thresholds (°C)		*Contralateral warm thresholds (°C)*	
	Calf	*Thigh*	*Calf*	*Thigh*
Pre-EA	39.1 ± 3.6	36.8 ± 2.3	39.8 ± 3.6	36.0 ± 1.4
Immediately post-EA	42.3 ± 2.5**	38.0 ± 3.0	42.0 ± 3.3**	37.4 ± 2.4
30 Minutes post-EA	43.2 ± 2.6**	38.1 ± 2.8	42.5 ± 3.1**	37.4 ± 1.8
60 Minutes post-EA	42.4 ± 2.6**	38.4 ± 3.3	42.7 ± 2.4**	38.4 ± 2.4**

EA, electroacupuncture.
**$p < 0.01$.

Table 4. Baseline Thermal Thresholds of the Subjects who Participated in both the EA and the Adaptation Testing Paradigms (N = 9)

	Baseline thermal threshold (°C ± SD)											
	C-IP CAL	*C-Con CAL*	*C-IP TH*	*C-Con TH*	*W-IP CAL*	*W-CON CAL*	*W-IP TH*	*W-CON TH*	*HP-IP CAL*	*HP-CON CAL*	*HP-IP TH*	*HP-CON TH*
Adaptation	28.8 ± 1.7	28.5 ± 1.7	29.2 ± 1.9	28.1 ± 2.4	37.5 ± 3.2	37.5 ± 3.5	35.5 ± 2.6	35.4 ± 2.4	46.7 ± 2.9	46.4 ± 3.0	48.8 ± 4.5	49.4 ± 3.7
EA	27.8 ± 2.0	26.0 ± 2.6	26.8 ± 1.6	26.2 ± 1.8	38.9 ± 3.9	39.5 ± 4.0	36.8 ± 2.4	35.7 ± 1.6	47.9 ± 2.0	48.2 ± 2.0	47.9 ± 1.4	47.5 ± 1.6

EA, electroacupuncture; SD, standard deviation; C, cold threshold; W, warm threshold; HP, hot pain threshold; IP, ipsilateral; CON, contralateral; CAL, calf; TH, thigh.

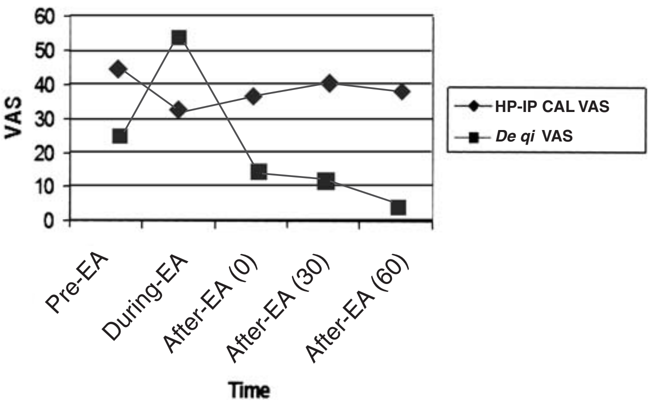

FIG. 3. The Visual analogue Scale (VAS) scores of hot pain (HP) and *de qi* sensations. Analgesic benfit. EA, electroacupuncture; HP, hot pain; HP-IP CAL hot pain threshold on the ipsilateral calf.

olds in the thigh areas that were tested in both the EA and the adaptation testing paradigms further argued against the notion that observed changes in warm thresholds were caused by repeated testing.

Previous nerve block studies have asserted that acupuncture can have a neuronal modulatory effect via segmental and/or suprasegmental mechanisms on noxious peripheral afferent inputs, largely mediated through the myelinated fibers.[23–26] The results of this study provided further support of this assertion. Broadly speaking, high-frequency and low-threshold mechanostimulation is transmitted by the myelinated A-β fibers. Cool and well-localized pain is carried by the smaller myelinated A-δ fiber, whereas warm, hot, and cold pain sensations are largely carried by the unmyelinated C-fiber.[27,28] As classically proposed in the Gate Theory of Melzack and Wall, activation of myelinated fibers can produce inhibitory effects on the transmission of impulses in the small unmyelinated primary afferent fibers via the inhibitory circuits at the superficial laminae of the dorsal horn.[27] Other examples of the neuromodulatory effect of myelinated fiber include the role of A-δ fibers in modulating cold pain sensation, which is mediated via C-fibers.[30] Although it has been postulated in the past that suprasegmental inhibition is mainly mediated through the activation of large myelinated fibers via low-frequency acupuncture stimulation, and that segmental inhibition is mediated by small myelinated fibers via high-frequency acupuncture stimulation, more recent studies suggest that both low- and high-frequency EA stimulation can achieve antihyperalesic effects. This suggests that aside from the stimulation frequency other factors such as the duration and intensity of stimulation, as well as the location of needling, may also play roles in the outcome of analgesic effect.[31,32] Although this mode of inhibition by peripheral afferent inputs can be mediated by different fibers (including A-α, A-β, and C-fibers themselves), previous animal studies with stimulation frequency in the range of 0.2 to 20 Hz have demonstrated that it is the A-δ fibers that provided the most robust means of inhibition to C-fiber–mediated noxious stimuli.[33,34] The change in warm thresholds and the significant reduction in HP VAS scores during acupuncture in this study strongly indicate that the effect of acupuncture has an inhibitory effect on the C-fibers.

Although high frequency and low mechanostimulation such as stroking are mediated through A-β afferent fibers, the low frequency and high mechanostimulation such as punctuate stimulation with a monofilament is most likely mediated via A-δ afferent fibers.[35,36] Although the lack of change in the cold threshold suggests that a short duration of low-frequency EA has a minimal effect on the A-δ afferent fiber, the tingling sensation that closely resembles a punctuate vibratory sensation is most likely mediated via A-δ afferent fibers. It appears that the analgesic benefit observed is most likely A-δ afferent mediated. In addition, the lack of change in the warm threshold in the thigh area along the TMM suggests that the analgesic effect of TP EA stimulation at low frequency is primarily close to the area of stimulation. This observation may result from a segmental and/or suprasegemental effect. Further correlation studies in fMRI may provide defining data. Limitations of this study are that it is unclear from the current results how the change in frequency and duration or repeated stimulation may affect the analgesic effect of the low-frequency EA at the TP. These issues are being addressed in ongoing studies to correlate further the findings of functional imaging studies.

Clinical implications

The result of the study confirms and provides objective evidence of the analgesic benefit of TMM for acute experimental pain as described in textbooks.[13,37] (Helms 1995; Seem M 1997). The textbook description of the TMM treatment paradigm consists of manual stimulation in both the TP and Gathering points (GP) with local needle placement around the lesions. In the case of lower extremities, the GP is located at CV2, which is anatomically located near the L1 and L2 dermatomes. The current results indicate that the analgesic area in the anatomical or dermatomal area adjacent to the area of stimulation is affected. Accordingly, it may be necessary to place and to stimulate CV2 to achieve a similar benefit at the medial thigh area. Whether the onset and duration of analgesic benefit will lengthen with simultaneous stimulations at the TP and GP is a matter for further investigation. In addition, given the potential involvement of A-β fibers, direct low-frequency EA should be avoided in patients with neuropathic states in which allodynia may occur as a result of the wide dynamic range neurons sprouting into the superficial laminae.[38–40] As a result, activation of the A-β may induce hyperalgesia and worsen pain.

Use of current model for future studies

Variations in point selection, depth of needle placements, and stimulation parameters are some of the major issues in interpreting the outcomes of some of the previous acupuncture studies.[1] The current study uses well-defined anatomical landmarks, eletroconductivity, and marked acupuncture needles to minimize variation in the acupuncture point selection and needle placement. In addition, fixed frequency, wavelength, and intensity of stimulation were used to ensure consistency in the stimulation parameters. On the other hand, this system also allows flexibility in altering the stimulation parameters for comparisons in future studies. Furthermore, the locations of the thermal threshold and noxious stimulation were marked in locations that are equal in anatomical proportions among subjects.

Unlike previous studies, the current study used individually predetermined HP thresholds as the means of noxious thermal pain stimulation. As individual hot pain thresholds may vary, the predetermined HP threshold noxious stimulation provides a more individually specific HP stimulation than fixed temperature stimulation. The information regarding reliability and reproducibility that was obtained from the peripheral thermal sensory measurements, and the behavioral feedback from noxious stimulation and EA *de qi* sensation, are important in generating and interpreting fMRI central dynamic localizing data. The resulting transient analgesic benefit during the short duration of EA stimulation provides a unique advantage for the repeated stimulus paradigms needed in fMRI studies.

CONCLUSIONS

In this study the role of TP in the classic TMM treatment paradigm for acute thermal pain was further characterized, and evidence was provided for the neuromodulatory functions of acupuncture. The use of quantitative peripheral sensory testing and behavioral feedback assessment provided additional information for understanding the neuronal mechanisms of acupuncture analgesia regarding the location, frequency, and duration of stimulation. With controllable EA parameters and subject threshold-dependent noxious stimulation, the data obtained from the current model and the corresponding findings in fMRI studies may provide further insight into the complex neuromodulatory mechanisms of acupuncture.

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