

Two styles of acupuncture for treating painful diabetic neuropathy – a pilot randomised control trial

Andrew C Ahn, Taher Bennani, Roy Freeman, Osama Hamdy, Ted J Kaptchuk

Summary

In a pilot study, we evaluated the clinical and mechanistic effects of two styles of acupuncture, Traditional Chinese Medicine (TCM) and Japanese acupuncture, for the treatment of painful diabetic neuropathy. Out of seven patients enrolled, three received Traditional Chinese acupuncture while four received Japanese style acupuncture. Treatments were delivered once a week for 10 weeks. Acupuncturists were permitted to select the needle interventions. Substantial differences in diagnostic techniques, choice of acupuncture points, and needle manipulation were observed between TCM and Japanese acupuncturists. Clinically, patients allocated to Japanese acupuncture reported decreased neuropathy-associated pain according to the daily pain severity score, while the group allocated to the TCM acupuncture reported minimal effects. Both acupuncture styles, however, lowered pain according to the McGill Short Form Pain Score. The TCM style improved nerve sensation according to quantitative sensory testing while the Japanese style had a more equivocal effect. No evident changes were observed in glucose control or heart rate variability in either group.

Keywords

Acupuncture, diabetic neuropathy, Japanese acupuncture, Traditional Chinese Medicine.

Introduction

Diabetic neuropathy, generally considered to be the most symptomatically distressing complication of diabetes, affects more than 30% of people with diabetes.¹ Unfortunately, no consistently effective treatment for diabetic neuropathy is available and patients and providers are forced to struggle with medications that provide only partial relief.² Several small studies suggest that acupuncture may provide the needed assistance for pain reduction. Human case series have demonstrated substantial symptom reduction without added side effects.^{3,4} Animal models have suggested the anaesthetic and nerve-regenerative capacities of acupuncture.^{5,6} While these preliminary data offer promise, they are insufficient to provide compelling evidence to adopt acupuncture as a therapy for diabetic neuropathy.

Proper evaluation of acupuncture for diabetic neuropathy is complicated by two important factors. First, diabetic neuropathy is a complex disease with multiple pathophysiological causes and variable

clinical presentations.⁷ It can present with pain or loss of sensation or both. Second, acupuncture styles are numerous and varied. One style may employ an entirely different technique when compared with another style. Unless the important details are made clear from the start, the amalgamation of these two complex factors when evaluating acupuncture for diabetic neuropathy can yield inconsistent results. Relevant factors such as type of acupuncture, physiologic effects, and appropriateness of clinical outcome measures should be thoroughly appraised.

The study of acupuncture for diabetic neuropathy may be complex but may also offer an opportunity to evaluate the varied effects of acupuncture based on style and clinical outcome. This pilot study has two primary aims: (1) to assess the feasibility of studying two acupuncture styles, Traditional Chinese Medicine and Japanese Kiiko-Matsumoto style acupuncture, for treatment of painful diabetic neuropathy, and (2) to obtain preliminary data for the clinical and mechanistic effects of acupuncture on diabetic

Andrew C Ahn
instructor in medicine
Harvard Medical School
and
Beth Israel Deaconess
Medical Center, Boston
MA

Taher Bennani
clinical researcher
Joslin Diabetes Center
Boston, MA

Roy Freeman
professor
Beth Israel Deaconess
Medical Center, Boston
MA

Osama Hamdy
instructor in medicine
Joslin Diabetes Center
Boston, MA

Ted J Kaptchuk
associate professor
Harvard Medical
School, Boston, MA

Correspondence:
Andrew C Ahn

aahn@hms.harvard.edu

neuropathy. We hypothesise that TCM and Kiiko-style Japanese acupuncture have different clinical and mechanistic effects on diabetic neuropathy.

Methods

Patients were recruited from primary care and speciality diabetes clinics at Beth Israel Deaconess Medical Center and Joslin Diabetes Center in Boston, Massachusetts from August to November 2004. Paper flyers and pamphlets were regularly placed in strategic areas around the clinic sites. Physicians were also requested to refer any eligible patient with diabetic neuropathy.

Patients were considered eligible if they were over the age of 18 years, had type I or type II diabetes, had experienced pain or tingling in both lower extremities for more than six months, scored more than 40 out of 100 on the visual analogue scale of the short-form McGill Pain Questionnaire (SF-MPQ), had a score greater than two on the Michigan Neuropathy Screening Instrument (MNSI), and were acupuncture naïve. Patients were excluded if they were pregnant, or if they had evidence of lower extremity vascular insufficiency or claudication, neuropathy from other causes, a history of amputations other than the toes, if they reported use of any investigational drugs within the previous six months, or if they reported changes in pain medications two months before enrolment.

Prior to acupuncture treatments, study participants completed a two week run-in period requiring completion of diaries on pain severity, sleep interference, glucose control, and usage of medications. Information was recorded four times a day, coinciding with times when blood glucose levels might be checked: before each meal and before bedtime. The run-in period ensured that participants were compliant with the diaries and demonstrated sufficient pain attributed to diabetic neuropathy. Individuals who reported more than four observations of pain greater than four (on the 11-point Likert scale) within a week were retained in the study. For qualifying participants, the information acquired during the run-in period was used for baseline information.

Participants were randomised to two styles of acupuncture: Japanese style (Kiiko-Matsumoto's Form) and Traditional Chinese Medicine style. Kiiko-Matsumoto form of Japanese acupuncture was

chosen because of its popularity in the New England area and the availability of classes and textbooks detailing its principles and techniques.⁸⁻¹¹ For simplicity, this style of Japanese acupuncture will herein be referred to simply as Japanese acupuncture with the caveat that Kiiko-style is one of many Japanese styles. Acupuncture treatments were performed at the Harvard-Thorndike General Clinical Research Center at Beth Israel Deaconess Medical Center. Treatments were delivered weekly for a total of 10 treatments. The treatment length and intervals were determined after consulting the acupuncturists. Following a pragmatic treatment protocol, acupuncturists were permitted to treat patients as if the patients were being seen in a normal clinical setting. However, massage, herbal prescriptions (or any other medical prescription), moxa, cupping, and lifestyle modifying therapies were not allowed. During the study period, study participants were advised not to change their pain medications, although changes in acetaminophen use were allowed with a maximum dose of 3g per day.

The treatment protocol was approved by the institutional review boards at Beth Israel Deaconess Medical Center, Joslin Medical Center, and Harvard Medical School.

Three experienced acupuncturists were enlisted in this trial. Two of the acupuncturists had more than 20 years of experience and were each considered 'Masters' in their respective style of acupuncture (Traditional Chinese and Japanese). The third acupuncturist was an experienced Japanese-style practitioner (~10 years of experience) who substituted the Japanese Master when she was not able to attend.

The primary outcome for the study was the 11-point Likert Scale daily pain severity score. It was recorded four times a day and measured the level of pain attributed to diabetic neuropathy on a scale of 0 to 10 (10 being worst). Due to the dynamic nature of diabetic neuropathy symptoms, this measure is capable of capturing the variations in pain levels and is therefore considered most reflective of patients' pain symptoms by most major studies.¹²⁻¹⁶ Other outcome measures obtained from the diaries included a sleep interference score (defined as the amount of sleep interference due to nocturnal pain), glucose control, and use of pain medication.

Other secondary measures were obtained at week 0, week 5, and week 10 after randomisation. These

measures included the Profile of Mood States scores, the pain rating index portion of SF-MPQ, SF36 Quality of Life Questionnaire, and blood tests (including complete blood cell count, creatinine, and haemoglobin A1C). Quantitative sensory tests based on cooling and warming sensations were obtained on both legs at week 0 and week 8 after randomisation. To assess for physiologic effects, pulse wave analysis and heart rate variability were obtained at weeks 0, 5, and 10 to measure arterial compliance and autonomic nervous system function, respectively. In addition to these outcome measures, a licensed acupuncturist was present at each acupuncture treatment to record the interventions performed. Recorded variables included diagnostic techniques, number of needles used, acupuncture points selected for needling, manipulation technique if any, needling depth, and assessment of treatment efficacy.

Because this study was not powered to detect differences in outcome between the two styles, comparative statistical analyses were not performed. Data are presented in a descriptive format. The primary outcome measure, the daily pain severity score, was averaged over a seven day period. For each treatment arm, the weekly scores were graphed against time (in weeks) to describe any time trends. For missing data, the last recorded value was carried over to the next time point following an intention-to-treat analysis.

Results

The study enrolled seven patients with chronic painful diabetic neuropathy – three were treated with TCM acupuncture and four were treated with Japanese acupuncture. The patient characteristics are shown in Table 1. All patients reported limited relief with pain modulating treatments (such as gabapentin) and had exhausted drug treatment options. Two subjects reported past enrolment in investigational drug trials. These participants, in general, had a long history of diabetes and diabetic neuropathy. The TCM acupuncture group compared to the Japanese acupuncture group had poorer glucose control as documented by the haemoglobin A1C levels. The Japanese acupuncture group had comparatively longer duration of diabetes and diabetic neuropathy.

Out of seven study subjects, six fully completed the 10 weekly treatments. One subject from the Japanese acupuncture treatment arm left the trial midway (about six weeks into treatment), citing worsening of symptoms.

Style differences in interventions

The treatments delivered by the two acupuncture styles differed substantially as shown in Table 2. Differences were noted in diagnostic techniques, choice of acupuncture points, and the manner in which the needles were handled and manipulated. In general, the TCM style relied on the radial pulse, tongue, and elicitation of tenderness along certain

Table 1 Baseline characteristics (mean values unless stated)

Characteristics	TCM acupuncture (n=3)	Japanese acupuncture (n=4)
	Mean [range]	Mean [range]
Age	63 years [42,79]	58 years [43,67]
DM type (number, I/II)	0/3	2/2
DM duration (yrs)	13 [8,19]	19 [6,32]
Neuropathy duration (yrs)	2.8 [1.3,5]	6.9 [1,10]
Hgb A1C (%)	8.8 [7.2,11.5]	6.6 [5.7,7.7]
MNSI* (maximum score = 8)	3.5 [2.5,5]	4.1 [3,4.5]
Pain Rating Index of the SF-MPQ† (maximum score = 45)	19 [10,41]	17.8 [15,40.5]
Expectancy for Acupuncture‡	1 [0,2]	2.3 [2,3]

* *Michigan Neuropathy Screening Instrument (MNSI)* assesses the appearance of feet (calluses, fissures), presence of ulceration, ankle reflex, and vibratory perception of great toe (or other if amputated). A score greater than 2 has both high specificity (95%) and sensitivity (80%) for the presence of diabetic neuropathy.

† *Short-Form McGill Pain Questionnaire (SF-MPQ)* Pain Rating Index assesses both the sensory and affective components of pain using 15 descriptors, each scored from 0 to 3. A higher score indicates more pain.

‡ *Expectancy 4-Likert Scale* measures the patient's perceived efficacy of acupuncture in treating his or her pain.

Table 2 Differences in treatment approach between styles

Aspects of style	TCM acupuncture	Japanese acupuncture
Diagnosis	tongue & pulse	'reflex points'
Number of needles used	6-14	18-25
Acupuncture points used	mostly leg points (ST36, ST40, SP4, SP9, LR3, KI3, BL22-25)	points all over body ('Sphincter of Oddi', scalp points, 'immune' and 'sugar' points)
Needle depth	>25mm	<5mm
Manipulation	frequent	minimal or none
Therapeutic end point	<i>de qi</i> , pulse	release of reflex tenderness

meridians for diagnoses. Compared to the Japanese style, fewer needles were used, more needles were localised to the symptom area, needles were inserted deeper, and they were manipulated more frequently. The Japanese style relied on the radial pulse as well, but placed more emphasis on strategic reflex points – where tenderness could be elicited with pressure and released by shallow needling at related acupuncture points.

Diabetic neuropathy-related outcomes

The weekly pain severity scores are charted in Figure 1. Individuals in the Japanese Acupuncture group, on the average, noted a greater decrease in pain scores, although this difference appeared to diminish with time.

For the quantitative sensory testing, the TCM acupuncture group noted greater improvement in sensation by both cooling and warming compared to the Japanese group, as charted in Figure 2. Interestingly, both groups noted a decrease in pain according to the Pain Rating Index of the SF-MPQ. This index measures the pain level using sensory and affective descriptors and is scaled from 0 to 45 (45 being worst). The TCM acupuncture group had a decrease from 19 at week 0 to 14.3 at week 10, while the Japanese Acupuncture group had a decrease from 17.8 at week 0 to 13.5 at week 10.

There were no notable differences in changes of profile of mood states (POMS) or blood test results, such as white blood cell count, creatinine, and haemoglobin, with the exception of haemoglobin A1C. The Hgb A1C levels in the TCM acupuncture group were consistently elevated at 8.8 (week 0) and 9.2 (week 10), whereas the Japanese acupuncture group had levels of 6.6 (week 0) and 6.5 (week 10). The weekly blood glucose levels and insulin usage

did not reliably change with acupuncture (Figure 3). The sleep interference score and SF36 Quality of Life Questionnaire proved to be either too confusing or time consuming for the study participants to complete. As a result, the data could not be meaningfully analysed.

Physiological markers

The Holter monitor readings showed evidence of multiple atrial ectopic beats in two of the six subjects – one from each acupuncture group. Atrial ectopic beats are found commonly in elderly individuals and can interfere with heart rate variability analysis – as it did with these two subjects. For the remaining four subjects, there were no notable differences in heart rate variability seen with acupuncture by time-domain, frequency-domain, and non-linear measures. The quality of the pulse wave readings proved to be too poor for adequate interpretation.

Qualitative outcomes

Within the confines of the study protocol, the acupuncturists reportedly did not feel at complete liberty to utilise their full repertoire of treatments. Were it not for these restrictions, the TCM acupuncturist would have used herbal treatments and moxa (burning of herb over acupuncture points) while the Japanese acupuncturist would have used moxa and electrical or magnetic stimulation. In addition, the TCM acupuncturist would have ideally recommended visits twice a week rather than once a week.

The acupuncture treatments were uniformly described as relaxing and comforting. Adjectives commonly used to describe the sessions included 'relaxing', 'skilful', 'comfortable', 'serene', 'calm', and 'warm'. One subject in the Japanese

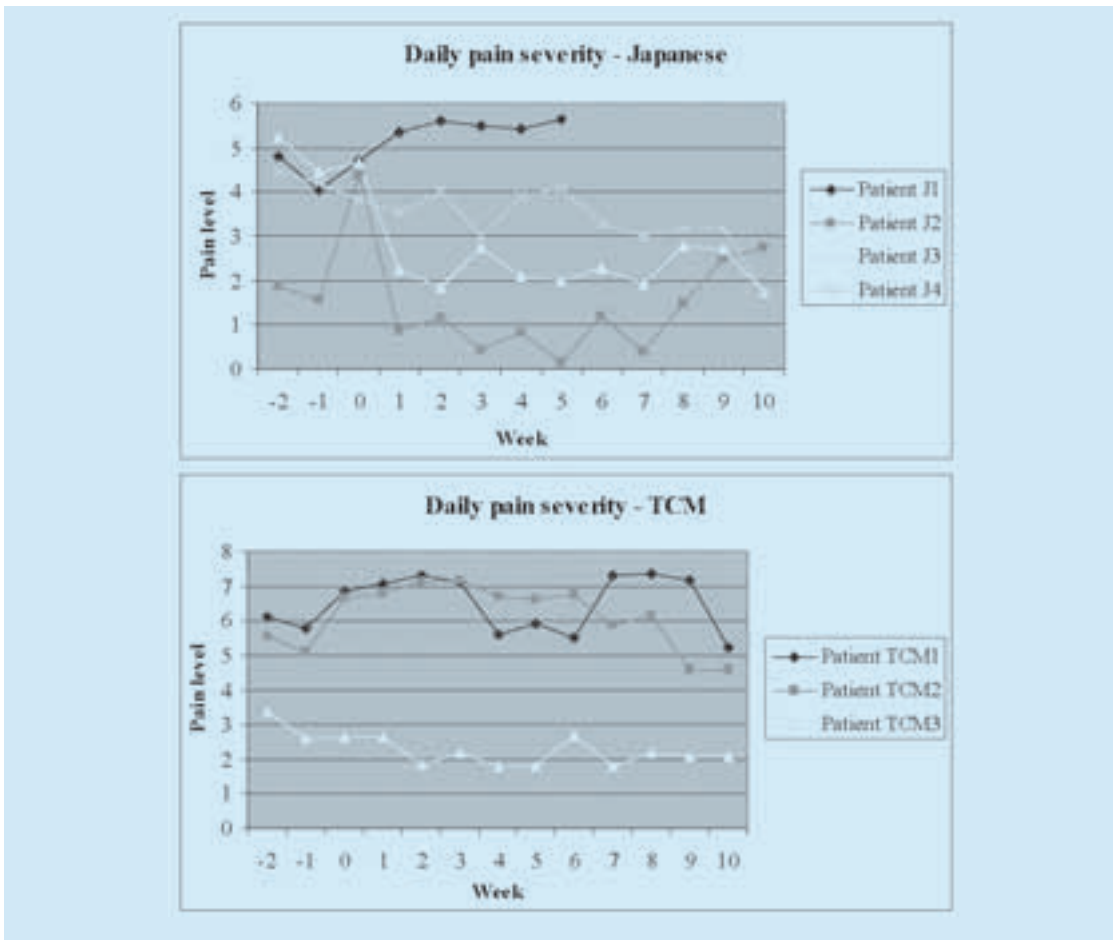


Figure 1 Weekly average of daily pain severity scores by acupuncture style.

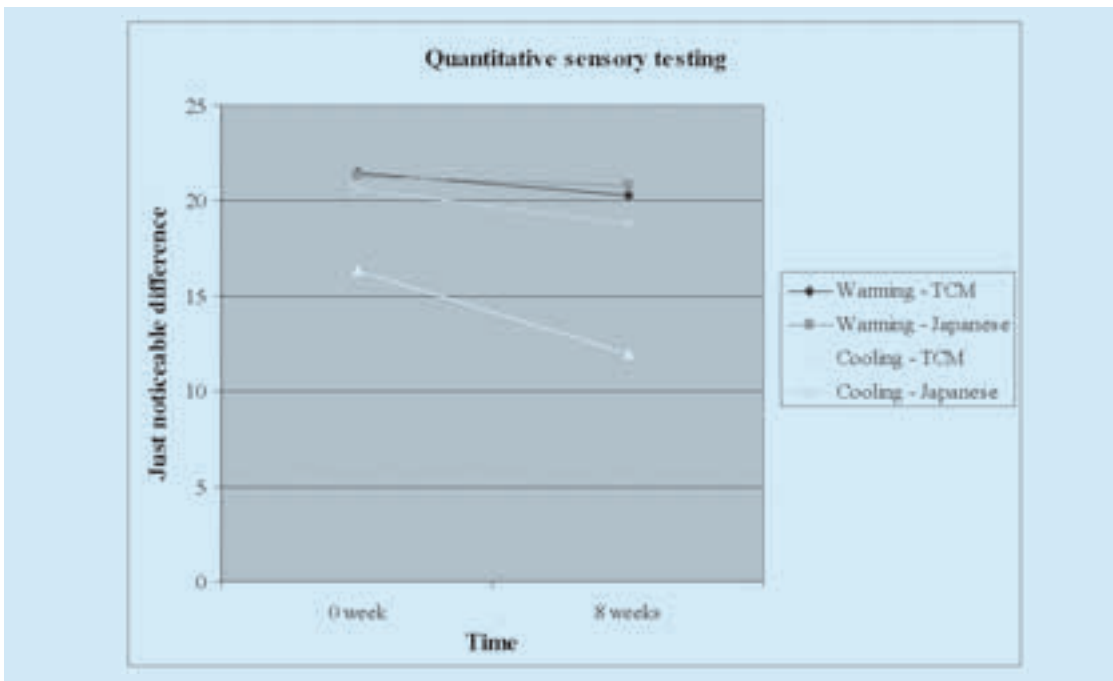


Figure 2 Quantitative sensory testing: 'just noticeable difference' marks a patient's ability to distinguish a certain sensation at a range of stimulation levels; the lower 'just noticeable difference' score indicates improved sensation.

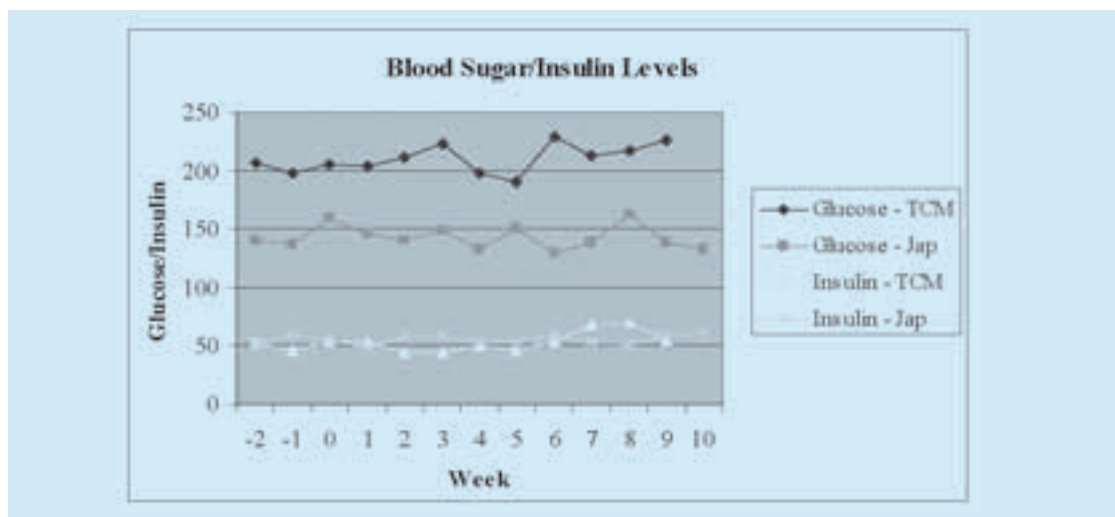


Figure 3 Weekly average of blood glucose and insulin use levels.

acupuncture group described ‘cramping when acupuncturist pressed hard’. A subject in the TCM acupuncture group described ‘heat going up some sections of legs’. Generally, the subjects randomised to the TCM acupuncture group reported more sensations (‘achiness’ and ‘warmth’) during needling than the subjects allocated to the Japanese acupuncture group.

Discussions after the completion of the trial indicated that four of the six patients would definitely consider continuing the acupuncture treatments, if given the option. Three were in the Japanese acupuncture group and one was in the TCM acupuncture group. One subject in the Japanese acupuncture group recorded: ‘My feet feel much better after the treatment. The circulation is perfect! The bottoms of the feet are not sensitive to the touch. The feet hurt less.’ Another subject in the Japanese acupuncture group summarised: ‘The acupuncture helps my arthritis as well as lowering my insulin level (Hgb A1C). Stress is a major factor in my diabetes and acupuncture helps me to deal with my stress more effectively. My pain level from my neuropathy has dropped. I do not wake up as frequently as I did before acupuncture started ... I will continue with the acupuncture because it has helped me so much. I was very sceptical at first but I am a believer now.’

Discussion

Based on our observational records, TCM and Japanese acupuncture differed significantly in the

manner in which diagnosis and treatments were administered. For clinical outcomes, Japanese acupuncture lowered neuropathy-associated pain according to our primary outcome measure (the daily pain severity score) while the TCM acupuncture had minimal effect. Both styles, however, lowered pain according to the Pain Rating Index of the SF-MPQ. In addition, the TCM style improved nerve sensation according to quantitative sensory testing while the Japanese style had a more equivocal effect. No notable differences were seen in glucose control or use of insulin.

Given the very small sample size, no conclusion can be drawn about the efficacy of either acupuncture style for the treatment of diabetic neuropathy. A larger study is needed to address this issue appropriately and a placebo control would also be critical. Nevertheless, it is encouraging to see that individuals with refractory pain noted some improvement. Decreased pain in the Japanese acupuncture group, despite including the individual with worsened symptoms, suggests that acupuncture may truly be effective for particular individuals with diabetic neuropathy. Furthermore, the improved sensations of the TCM acupuncture group as shown by quantitative sensory testing are promising. If replicated in a larger study, TCM acupuncture may be able to do what other medications have failed to consistently do thus far, namely improve sensation in persons with diabetic neuropathy.

The differences in treatment techniques and clinical outcomes support the hypothesis that the

Summary points

A small pilot study in patients with painful diabetic neuropathy compared traditional Chinese acupuncture with Japanese acupuncture

Japanese acupuncture was superior according to some measures, and Chinese according to others

two acupuncture styles differ in their clinical and mechanistic effects on diabetic neuropathy. The results from the study's physiologic markers were unable to disclose why these clinical differences were observed. In order to fully address this hypothesis, a future study should have a large enough sample size to confirm these clinical differences and should also incorporate more physiologic markers that are wisely chosen and properly administered. Even if this larger study were performed, however, it would be important not to make broad-based conclusions. While the techniques and principles were quite distinct, the two styles of acupuncture used in this study do not fully represent the myriad acupuncture styles available in the clinical setting. In addition, because the acupuncturists expressed some restrictions with the protocol, we cannot conclude fully that the study findings accurately reflect the results seen in real acupuncture treatments. Furthermore, our outcome measures did not mirror the very positive sentiments expressed by many of the study participants. Hopefully, future studies will be able to elaborate why this discrepancy between quantitative and qualitative results can occur.

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