

## Manual and Electrical Needle Stimulation in Acupuncture Research: Pitfalls and Challenges of Heterogeneity

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on behalf of the Executive Board of the Society for Acupuncture Research

### Abstract

In the field of acupuncture research there is an implicit yet unexplored assumption that the evidence on manual and electrical stimulation techniques, derived from basic science studies, clinical trials, systematic reviews, and meta-analyses, is generally interchangeable. Such interchangeability would justify a bidirectional approach to acupuncture research, where basic science studies and clinical trials each inform the other. This article examines the validity of this fundamental assumption by critically reviewing the literature and comparing manual to electrical acupuncture in basic science studies, clinical trials, and meta-analyses. The evidence from this study does not support the assumption that these techniques are interchangeable. This article also identifies endemic methodologic limitations that have impaired progress in the field. For example, basic science studies have not matched the frequency and duration of manual needle stimulation to the frequency and duration of electrical stimulation. Further, most clinical trials purporting to compare the two types of stimulation have instead tested electroacupuncture as an adjunct to manual acupuncture. The current findings reveal fundamental gaps in the understanding of the mechanisms and relative effectiveness of manual versus electrical acupuncture. Finally, future research directions are suggested to better differentiate electrical from manual simulation, and implications for clinical practice are discussed.

### Introduction

**D**ESPITE SUBSTANTIAL GROWTH in the field of acupuncture research in the last decade, significant challenges still impede drawing overall conclusions from the available data. The indiscriminate use of the term *acupuncture*, which does not differentiate between diverse intervention styles and techniques, contributes to this challenge.<sup>1</sup> In particular, manual and electrical stimulation of the acupuncture needle are commonly assumed to be equivalent means of achieving therapeutic benefit, with electrical stimulation mainly considered as

a means to provide stronger treatment. Further, electrical stimulation is frequently favored in basic science research because of its readily quantifiable stimulation parameters of frequency, intensity, and duration. As a result of these assumptions and research preferences, the potential differences between the two most common modes of needle stimulation, manual and electrical, are poorly understood and largely unaddressed.

This article is the second in a series of white papers put forth by the Board of the Society for Acupuncture Research addressing methodologic issues in the field. The first white paper highlighted paradoxes in acupuncture research,

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specifically the challenges presented by incongruent findings between basic science experiments and clinical trials of acupuncture efficacy, as well as by the limited evidence on the benefit of verum acupuncture relative to sham needling.<sup>1</sup> The present paper systematically reviews clinical trials and basic science studies that report comparisons between manual (MA) and electrical (EA) acupuncture to determine whether evidence-based conclusions can be drawn concerning the similarities and differences between these needling techniques. In addition, this article examines systematic reviews and meta-analyses that have separately assessed trials that used each of the two types of needle stimulation. The literature was searched for basic science studies, clinical trials of acupuncture, systematic reviews, and meta-analyses. Tables 1–3 describe the search strategy and inclusion and exclusion criteria for each category.

The aim of this white paper is to evaluate a generally held but largely unexplored assumption in the field: that evidence derived from basic and clinical studies of EA and MA is generally interchangeable and can be used in a bidirectional approach to acupuncture research, translating between basic science and clinical studies. This article also discusses why it is imperative for future research to explore the relative clinical benefits and modes of action of MA versus EA to better inform clinical practice, and research guidelines to more directly compare these treatment modalities are proposed.

### Comparisons of MA and EA: Distinct Challenges for Basic and Clinical Research

Clinical research comparing the effectiveness of MA and EA asks a pragmatic question: Which treatment works better? This is a broad but clinically relevant question. Basic research comparing MA and EA, on the other hand, asks: Does stimulating a needle manually cause the same, or different, physiological effects than stimulating it electrically? This is specific question whose direct relevance is primarily scientific.

In basic research, experimental variables need to be “isolated,” such that any difference in outcome between two treatments can be ascribed to the variable that is being examined, as opposed to some other factor. In clinical trials of acupuncture, manual needle stimulation techniques are nearly always applied for a much shorter duration than is electrical stimulation (i.e., seconds rather than minutes). Even when manual stimulation is repeated a few times at intervals during the treatment, the total duration of active stimulation is much shorter in MA than EA. Furthermore, MA and EA are not always clearly separated. For example, in a study of EA, manual stimulation is frequently performed briefly first to “obtain *de qi*”, followed by electrical stimulation, such that MA is actually compared to a combination of MA plus EA. In any case, unless specifically addressed, the duration of active stimulation constitutes a confounding factor when comparing MA versus EA (or MA versus MA + EA).

From a scientific perspective, confounders can arise when the effect of a treatment is compared across two conditions in the presence of another variable that also systematically differs across the two conditions. For example, if one compares the physiologic effects of walking

for 5 minutes with that of running for an hour, one could not conclude that walking and running had different effects because, in this experiment, the type of exercise would be confounded with its duration. An analogous situation occurs in acupuncture research that compares continuous electrical stimulation for the duration of the treatment (about 20 minutes) versus intermittent manual stimulation (every few minutes, for just a few seconds) or just initial manual stimulation. If a difference were observed in some physiologic measurement (e.g., blood flow indicating brain region activation) between the two conditions, one could not conclude that this difference was due to the type of stimulation (manual versus electrical) because this was confounded by the duration (20 minutes versus a few seconds) or by the periodicity (intermittent versus continuous) of the stimulus. To answer this question, manual versus electrical stimulation would need to be performed for the same amount of time and periodicity (e.g., 10 seconds of stimulation every 5 minutes for 20 minutes).

A commonly heard rationale for comparing acupuncture stimuli of different durations is that while electrical stimulation is typically applied for at least 15–20 minutes, continuous MA for this amount of time is not done clinically because continuous manual stimulation would be too painful (while continuous electrical stimulation can be better tolerated because its intensity is adjustable). However, experiments in humans or animals comparing manual versus electrical stimulation for a short duration (e.g., 10 seconds total) would be feasible as well as scientifically important. Experiments in anesthetized animals comparing manual versus electrical stimulation for longer durations (e.g., 20 minutes) also would fulfill these criteria. Unfortunately, as shown below, few such experiments have been published to date.

It is important to stress that the duration of manual versus electrical stimulation is not simply a nuisance to be dealt with methodologically. Ample evidence from basic studies of cell signaling, gene expression, and tissue plasticity suggests that the duration of a stimulus (from milliseconds to minutes to days) profoundly affects its biological function. Furthermore, habituation and refractoriness to further stimulation are well-described phenomena indicating that “more is better” does not always apply in physiology. Controlling the duration of MA or EA needle stimulation, as well as comparing the effects of different stimulus durations, should improve understanding of their physiologic effects. Furthermore, careful consideration of what is meant by “stimulation” is important as well. Electrical needle stimulation is typically continuous, while manual stimulation is brief or intermittent, with the needles left in place in between periods of stimulation. One could hypothesize that the tissue is still “stimulated” by the presence of the indwelling needle, even in between periods of manual needle manipulation. This type of stimulation could include static stretching of tissue that has wrapped around the needle and remained stretched after the manipulation stops. It is therefore imperative that these potential effects be tested while controlling one variable at a time.

In contrast to basic research, comparative effectiveness clinical research can readily ask whether prolonged electrical stimulation (treatment A) is more clinically effective than brief manual stimulation (treatment B) because in this

TABLE 1. CHARACTERISTICS OF BASIC SCIENCE ARTICLES EXAMINING ELECTRICAL AND MANUAL ACUPUNCTURE (TWO RESEARCH QUESTIONS)

Research question 1: Is there any evidence that electrical stimulation of needles has physiologic effects distinct from manual stimulation when performed under otherwise identical conditions?

Databases and dates: MEDLINE, AcuTrials, and PubMed through March 31, 2013

Search strings: “manual” AND “electrical” AND “acupuncture”

Author, year	MA methods	EA methods	Type of participants/ subjects	Participants/ subjects (n)	Outcomes	Results/study quality
Ernst and Lee, 1985 <sup>39</sup>	LI4; “twirling needle to elicit painful sensation”	LI4; needle manipulation as in MA, plus 1 Hz for 15 min; muscle contractions were generated	Human (healthy)	17 F/2M	Skin temperature	Both MA and EA increased skin temperature; EA showed transient decrease in temperature
Ernst and Lee, 1986 <sup>40</sup>	SI36; “twirling needle to elicit painful sensation”	SI36; needle manipulation as in MA, plus 1 Hz for 15 min; muscle contractions were generated but below pain threshold	Human (healthy)	17 F/2M	Skin temperature	Both MA and EA increased skin temperature; EA showed transient decrease in temperature
Ceccherelli et al., 2002 <sup>41</sup>	SI36, GB30; “left and right rotating movements for 30 seconds at the beginning of the session and every 5 minutes for 20 minutes”	SI36, GB30; insertion same as MA; stimulation with 5 Hz and 5 mAmp pulsed current lasting 500 s with whole event lasted 2.8 ms	Animal (rat)	105 M (15 per group)	Inflammation	Both MA and EA equally reduced paw swelling following inflammation, and both treatments were blocked by local and systemic naloxone
Kong et al., 2002 <sup>42</sup>	LI4; “the needle was rotated clockwise and counterclockwise at a rate of about 180 times per minute” (3Hz) during two 1-min blocks within a 5-min run; <i>de qi</i> was obtained	LI4; same as MA plus 3 Hz electrical stimulation with a 30-ms continuous rectangular wave form pulse; attempt was made to match <i>de qi</i> sensation during MA	Human (healthy)	5 F/6M	Brain response to needling (fMRI)	EA activated insula (and other regions) whereas MA deactivated insula (and other regions); direct comparison of EA versus MA showed greater activations in precentral gyrus during EA as compared to MA
Zhou et al., 2005 <sup>36</sup>	PC5-6; 2 Hz for 2 min of needle stimulation	PC5-6; same as MA with 2-Hz stimulation, 0.3–0.5 mAmp, 0.5-ms duration, and for 2 min; also compared 40- and 100-Hz stimulation	Animal (rat)	15 M	Blood pressure	Equivalent decrease in blood pressure responses for MA and EA; also similar afferent neural impulses/s recorded from MA and EA somatosensory afferents; no effects of EA with higher frequency, 40 or 100 Hz
Kong et al., 2005 <sup>43</sup>	LI4, SI36, Sp6; rotation frequency 3 Hz, three 7-min stimulation periods, manually stimulated 1 point for 30 s, followed by a 15-s break; <i>de qi</i> was elicited	LI4, SI36, Sp6; EA was performed with alternating 2-Hz and 15-Hz stimulation every 30 s simultaneously at the 3 points in three 7-min blocks; <i>de qi</i> was elicited	Humans (healthy)	F 8/M 23	Evoked pain (thermal)	EA and MA evoked analgesia but were not significantly different; different subjects responded to EA and MA; EA and MA had similar sensory sensations

(continued)

TABLE 1. (CONTINUED)

Author, year	MA methods	EA methods	Type of participants/ subjects	Participants/ subjects (n)	Outcomes	Results/study quality
Napadow et al., 2005 <sup>44</sup>	St36; “manual stimulation consisted of even motion twisting technique at 1 Hz”; two 1-min stimulations	St36; 2-Hz or 100-Hz stimulation at 0.7–3.6 mAmp “set midway between the sensory and pain thresholds for each subject”	Humans (healthy)	F 7/M 6	Brain response to needling	MA evoked greater deactivation of limbic system as compared to EA; EA evoked greater activation of somatosensory system; There were some shared regions
Inoue et al., 2008 <sup>45</sup>	“The needle was manually rotated...in the neighboring muscle of lumbar vertebra L6...rotation stimulation was conducted in the same direction after insertion until the needle stopped and then the needle was left in place for 3 min before being removed...For a total of 58 stimulations.”	10-Hz “stimulation of the pudendal (or sciatic) nerve was performed...the nerve was exposed and after amputation the distal stump was placed on a platinum bipolar electrode and efferent electrical stimulation.”	Animal (Rat)	M 13	Blood Flow	EA and MA increased sciatic nerve blood flow, with more robust effects seen with EA (MA increased 57% versus EA increased 100%)
Johansson et al., 2013 <sup>46</sup>	Needles rotated back and forth 5 times every 5 min for 15 min	Continuous stimulation at 2 Hz for 15 min	Animal (rat)	n = 10 per group	Glucose tolerance, insulin sensitivity, gene expression	EA and MA both influenced glucose homeostasis but had different effects on insulin sensitivity
Lang et al., 2010 <sup>47</sup>	Sp6, Sp9, St36, GB39; treatments lasted 30 minutes; second stimulation was given midway through the session by rotation of the needle; elicited <i>de qi</i> both following needle insertion and midway through treatment	Sp6, Sp9, St36, GB39; EA involved 2 Hz and 100 Hz; “stimulus intensity was increased, so that the patient felt the stimulation strongly, but not painfully (2–8 mAmp)”; Each treatment lasted 30 min; elicited <i>de qi</i> with needle before EA	Humans (healthy)	12 F/12 M	Evoked pain (thermal, mechanical, and pressure)	EA (both 2 Hz and 100 Hz) was superior to MA for mechanical pin prick pain; both EA and MA equivalently increased thermal heat pain and pressure pain thresholds
Zheng et al., 2010 <sup>48</sup>	St36, St40; “needles were rotated 180–360 degrees between the fingers at 3–5 Hz in a bidirectional manner, first clockwise then anticlockwise”; stimulation was repeated 9 times and took approximately 10 s; this manipulation was repeated every 5 min 6 times over a period of 25 min; <i>de qi</i> was elicited	St36, St40; “Needles were inserted...and manipulated to achieve <i>De qi</i> sensations. The needles were then connected to the EA stimulator...and electrical stimuli...were delivered at an alternating frequency of 2 and 100 Hz every 6 sec”; intensity of stimulation was strong but comfortable with visible muscle contraction; the total duration of EA treatment was 25 min	Humans (healthy)	15 F/11 M	Evoked pain (electrical)	EA greater than MA for both single and temporal summation of electrical pain thresholds immediately and 24 h after intervention

(continued)

TABLE 1. (CONTINUED)

<i>Author, year</i>	<i>MA methods</i>	<i>EA methods</i>	<i>Type of participants/ subjects</i>	<i>Participants/ subjects (n)</i>	<i>Outcomes</i>	<i>Results/study quality</i>
Schliessbach et al. <sup>49</sup> 2011	LI4, LI11; "rotated the needle in an angle of approximately 180°, both clockwise and anticlockwise, and at the same time lifting and thrusting it 2-3 mm along its vertical axis"; this maneuver was performed every 30 s during the 5 min of needling	LI4, LI11; 100 Hz for 3 seconds, followed by 2 Hz for 3 s; current was applied during the whole 5 min; "current intensity was gradually increased... patients were repeatedly asked whether they felt muscle twitches, tingling, or burning sensations. Current intensity was finally set at a level that created perceptible but well-tolerable sensations."	Humans (healthy)	23 F/22 M	Evoked pain (pressure)	EA engenders greater analgesia during stimulation than with MA; after stimulation EA and MA were equivalent at increasing pain thresholds
Yamamoto et al. <sup>30</sup> 2011	"An acupuncture needle... was inserted into a point below the knee joint just lateral to the tibia in the left or right leg. The needle was twisted clockwise and counter-clockwise, and moved up and down at a frequency of 1-2 Hz for a duration of 120 s."	"An acupuncture needle was inserted into a point approximately 1 cm from the MA needle toward the ankle joint and used as the ground"; the stimulation frequency was set at 10 Hz in 6 and at 20 Hz in 3 of the 9 rats	Animal (rat)	9 M	Blood pressure and heart rate	Both EA and MA attenuated heart rate and arterial blood pressure, and these effects were both blocked by a stretch-channel blocker involved in mechanosensation

*Research Question 2: "Does electrical stimulation delivered via an inserted acupuncture needle have effects different from electrical stimulation percutaneously when performed under otherwise identical conditions?,"*

<i>Author, year</i>	<i>TENS methods</i>	<i>EA or MA methods</i>	<i>Type of participants/ subjects</i>	<i>Participants/ subjects (n)</i>	<i>Outcomes</i>	<i>Results/study quality</i>
Wang et al., 1992 <sup>51</sup>	St36, Sp6; "surface silver plate electrodes (5 × 6 mm) were bilaterally placed in contact with the skin. The same stimulation procedures as EA were employed and such TENS usually produced similar behavioral changes as EA stimulation"; 2-, 15-, and 100-Hz stimulation	EA: St36, Sp6; "stimulation delivered via the needles for a total of 30 min duration. In each EA session, intensity of stimulation was always increased stepwise...lasting for 10 min each"; 3 different frequencies used: 2, 15, and 100 Hz	Animal (rat)	32 (sex not reported)	Evoked pain (thermal)	2- and 15-Hz EA and TENS blocked by naloxone; 100-Hz EA and TENS not naloxone sensitive; tolerance to EA reduced TENS effects, and tolerance to TENS reduced EA effects

MA, manual acupuncture; EA, electrical acupuncture; F, female; M, male; TENS, transcutaneous electrical nerve stimulation.

TABLE 2. CHARACTERISTICS OF CLINICAL TRIALS EXAMINING ELECTRICAL AND MANUAL ACUPUNCTURE

Research question: "Is there any evidence that electrical stimulation of acupuncture points results in significantly distinct clinical outcomes when compared to manual stimulation?"

Search strategy:

Databases and dates: MEDLINE and AcuTrials, from inception through December 31, 2012

Search strings: PubMed: "Electroacupuncture" [Title/Abstract] AND "Acupuncture" [Title/Abstract]; limits - Limits: Humans AND Randomized Controlled Trial AND English; AcuTrials: "Acupuncture vs. acupuncture AND electroacupuncture"

Inclusion criteria: Trials that reported testing MA and EA in separate groups and that needed the same acupoints in each group. Case studies, case series, non-controlled trials, and interventions that did not use acupuncture needling were excluded (e.g., TENS, laser, other nonfiliform needle procedures).

Study, year	Condition	Design	Participants (n)	No. of TXs	MA methods	EA methods	Outcome measures	Result(s)	Findings (EA vs. MA)	Comments
Ghaly, 1987 <sup>53</sup>	Emesis: postoperative	(1) MA; (2) EA; (3) cyclizine; (4) no Tx	50	1	No description re: <i>de qi</i>	No description re: <i>de qi</i> ; EA stimulation: 10 Hz to participant tolerance	(1) Vomiting without nausea and (2) nausea alone	No between-group differences in 1-3; groups 1-3 > 4	MA + EA = MA	High dropout rate; findings based on observational data
Zang, 1999 <sup>54</sup>	Facial paralysis	(1) MA; (2) EA	150	30	No <i>de qi</i> elicited; intermittent needle vibration technique	<i>De qi</i> elicited; EA stimulation: 15-20 Hz to induce muscle twitch	Practitioner assessed response to care: cured, improved, failed	Both groups improved; no between-group differences	MA + EA = MA	Designed to assess effect of MA vibrating needle technique
Bao et al., 2006 <sup>55</sup>	Vascular dementia	(1) MA; (2) EA; (3) Medication	60	40	<i>De qi</i> elicited	<i>De qi</i> elicited; EA stimulation: 240 Hz to participant tolerance	(1) Dementia Scale; (2) MMSE; (3) functional activity; and (4) Serum levels (T3, T4, and FT3)	All groups improved; no between-group differences	MA + EA = MA	MA Tx lasted 10 h vs. EA 30 min
Frisk et al., 2009 <sup>56</sup>	Hot flushing: prostate cancer	(1) MA; (2) EA	31	14	<i>De qi</i> elicited	<i>De qi</i> elicited; EA stimulation: 2 Hz; no other details given	(1) Number/distress from hot flushes and (2) change in hot flush score	Both groups improved	MA + EA = MA	
Freire et al., 2010 <sup>57</sup>	Sleep apnea	(1) MA; (2) EA 2 Hz; (3) EA 10 Hz; (4) no Tx	40	1	<i>De qi</i> elicited	<i>De qi</i> elicited; EA stimulation: 2 or 10 Hz to induce muscle twitch	(1) Apnea indices and (2) respiratory events	MA and EA (10 Hz): significant improvements in 3 measures; EA (2 Hz) and no Tx: no significant changes in any measures	MA + EA = MA	

(continued)

TABLE 2. (CONTINUED)

Study, year	Condition	Design	Participants (n)	No. of TXs	MA methods	EA methods	Outcome measures	Result(s)	Findings (EA vs. MA)	Comments
Moon et al., 2003 <sup>58</sup>	Stroke: elbow spasticity	(1) MA; (2) EA; (3) MA + Moxa	35	8	No description re: <i>de qi</i>	No <i>de qi</i> elicited; EA stimulation: 50 Hz to induce muscle twitch	Modified Ashworth scale	EA reduced elbow spasticity; group 2 > 1 and 3	MA + EA > MA	All groups received ROM exercises
Zheng et al., 2012 <sup>59</sup>	Analgesia/sedation: intubation	(1) MA; (2) EA; (3) no Tx	45	1	<i>De qi</i> elicited	<i>De qi</i> elicited; EA stimulation: 2/100 Hz at 10–15 mA (not detectable by participants); 30 min on, 30 min off (6 h total)	(1) Ramsey sedation scale and (2) bispectral index	EA reduced use of midazolam monitored by bispectral index; no between-group difference	MA + EA > MA	All groups received usual care (midazolam)
Mackenzie et al., 2011 <sup>60</sup>	Analgesia: labor induction	(1) MA; (2) EA; (3) sham MA; (4) sham EA; (5) no Tx	105	1	<i>De qi</i> elicited	No <i>de qi</i> elicited; EA stimulation: 2 Hz to induce muscle twitch	Rate of epidural analgesia	No between-group differences	EA = MA	Trend of more epidurals in EA vs. MA
Michalek-Sauberer et al., 2007 <sup>61</sup>	Dentistry: tooth extraction	(1) MA (ear); (2) EA; (3) sham EA	149	1	No description re: <i>de qi</i> (auricular acupuncture)	No description re: <i>de qi</i> ; EA stimulation: 100/2 Hz (no other information reported)	(1) Pain intensity (VAS) and (2) medication consumption	No between-group differences	MA + EA = MA	“... neither MA nor EA reduce acute pain”
Tam et al., 2007 <sup>62</sup>	Rheumatoid arthritis	(1) MA; (2) EA; (3) sham acupuncture	36	20	<i>De qi</i> elicited; connected to EA device without current; intermittent twirling to select needles	<i>De qi</i> elicited; EA stimulation: 4/20 Hz; no other details given	Pain (VAS)	No change in pain for any group; groups 1 > 2 > 3 in number of tender joints	MA + EA = MA	No effect on pain for any group
Tao, 2000 <sup>63</sup>	Back pain: superior cluneal nerve entrapment	(1) MA; (2) EA	157	10	<i>De qi</i> elicited	<i>De qi</i> elicited; EA stimulation: 80 Hz to participant tolerance	Practitioner assessed response to care: cured, improved, failed	Both groups improved on all measures; group 2 > 1	MA + EA > MA	
Tsui and Leung, 2002 <sup>64</sup>	Tennis elbow	(1) MA; (2) EA; (3) no treatment	40	6	<i>De qi</i> elicited	No description re: <i>de qi</i> ; EA stimulation: 4 Hz to participant tolerance	(1) Pain (VAS) and (2) grip strength	EA improved pain and grip strength; groups 2 > 1 > 3	MA + EA > MA	
Guo, 2003 <sup>65</sup>	Analgesia (ligamentous sprains)	(1) MA; (2) EA	72	10	<i>De qi</i> elicited	<i>De qi</i> elicited; EA stimulation: 40–80 Hz to participant tolerance	Practitioner assessed response to care: cured, improved, failed	Both groups improved on all measures; group 2 > 1	MA + EA > MA	

(continued)

TABLE 2. (CONTINUED)

Study, year	Condition	Design	Participants (n)	No. of TXs	MA methods	EA methods	Outcome measures	Result(s)	Findings (EA vs. MA)	Comments
Sator-Katzenschlager et al., 2003 <sup>66</sup>	Neck pain	(1) MA (ear); (2) EA	21	6	No <i>de qi</i> elicited (auricular acupuncture); connected to P-Stim™ device without current	No <i>de qi</i> elicited; needle connected to P-Stim™ device; EA stimulation: 1 Hz at 2 mA (not detectable by participants)	(1) Pain (VAS), (2) psychological well-being, (3) activity, (4) sleep, and (5) medication use	Group 2 > 1 in all outcomes	MA + EA > MA	
Sator-Katzenschlager et al., 2004 <sup>67</sup>	Low back pain	(1) MA (ear); (2) EA	61	6	No <i>de qi</i> elicited (auricular acupuncture); connected to P-Stim™ device without current	No <i>de qi</i> elicited; needle connected to P-Stim™ device; EA stimulation: 1 Hz at 2 mA (not detectable by participants)	(1) Pain (VAS), (2) psychological well-being, (3) activity, (4) sleep, and (5) medication use	Both groups improved on all measures; EA significantly better vs. MA	MA + EA > MA	
Sator-Katzenschlager et al., 2006 <sup>68</sup>	Analgesia: IVF-Tx	(1) MA (ear); (2) EA; (3) sham MA	94	1	No <i>de qi</i> elicited (auricular acupuncture); connected to P-Stim™ device without current	No <i>de qi</i> elicited; needle connected to P-Stim™ device; EA stimulation: 1 Hz at 2 mA (not detectable by participants)	Pain (VAS)	Pain relief (and well-being) were significantly greater in EA (perioperative and postoperative); group 2 > 1 > 3	MA + EA > MA	All groups received usual care analgesia
Xue et al., 2007 <sup>69</sup>	Neck pain (cervical spondylopathy)	(1) MA; (2) EA	58	20	<i>De qi</i> elicited	<i>De qi</i> elicited; EA stimulation: 10–12 Hz to participant tolerance	Practitioner assessed response to care: cured, improved, failed	Both groups improved; EA significantly better vs. MA	MA + EA > MA	

TX, treatment; MMSE, Mini-Mental Status Examination; T3, triiodothyronine; T4, thyroxine; FT3, free triiodothyronine; ROM, range of motion; VAS, visual analogue scale; IVF, in vitro fertilization.

TABLE 3. CHARACTERISTICS OF SYSTEMATIC REVIEWS THAT INCLUDED META-ANALYSES COMPARING MANUAL AND ELECTRICAL ACUPUNCTURE TRIAL OUTCOMES

Study, year	Condition	Design, relevant trials	Trials with MA	Trials with EA	Comparison analyzed	Results	Comments
Direct comparisons Manheimer et al., 2010 <sup>70</sup>	Osteoarthritis	Meta-analysis, 9 trials	4 trials, 1215 patients	5 trials, 614 patients	Comparing effect sizes as SMDs in single analysis with test of interaction	Effect size of MA trials: SMD, -0.11 (95% CI, -0.29 to -0.11); EA trials: SMD, 0.50 (95% CI, -0.81 to -0.20); <i>p</i> for interaction=0.042	EA superior to MA
Indirect comparisons White et al., 2011 <sup>71</sup>	Smoking cessation	Meta-analysis, 14 trials	All 14 trials, <sup>a</sup> 2206 patients	4 trials, 462 patients	Separately comparing vs. sham control using RRs	MA vs sham MA: RR, 1.18 (95% CI, 1.03–1.34); EA vs sham EA: RR, 1.17 (95% CI, 0.89–1.54)	Difference not directly evaluated, but EA vs. sham statistically significant
Lu et al., 2007 <sup>72</sup>	Chemotherapy-induced leukopenia	Meta-analysis, 10 trials	All 7 trials, 270 patients	3 trials, 169 patients	Comparing WMD for leukocyte increase vs. control	Leukocyte increase in those trials with EA: WMD, 1.863 (95% CI, 1.096–2.629); <i>p</i> =0.041; no increase for MA	Significant leukocyte increase in the 3 EA trials
Smith et al., 2010 <sup>73</sup>	Depression	Meta-analysis, 5 trials	3 trials, 175 patients	2 trials, 117 patients	Separately comparing vs. SSRIs using SMDs	MA vs SSRI: SMD, -0.02 (95% CI, -0.33 to 0.28); EA vs SSRI: SMD, 0.07 (95% CI, -0.38 to 0.53)	Difference not directly evaluated; neither comparison statistically significant

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Research question: “Is there any evidence that electrical stimulation of acupuncture points results in significantly distinct clinical outcomes when compared to manual stimulation?”

Databases and dates: MEDLINE and AcuTrials, January 1, 2000–December 31, 2012

Search strings: PubMed: “electroacupuncture” AND “acupuncture”; AcuTrials: “Acupuncture vs. acupuncture AND electroacupuncture”

Inclusion criteria: Reviews that reported pooling of data in a meta-analysis in which comparisons were made between outcomes associated with MA and EA. Reviews listed only as abstracts or protocols, previous reviews by the same researchers, reviews of interventions that did not use acupuncture needling, and reviews in the form of editorials or commentaries were excluded.

TABLE 3. (CONTINUED)

<i>Study, year</i>	<i>Condition</i>	<i>Design, relevant trials</i>	<i>Trials with MA</i>	<i>Trials with EA</i>	<i>Comparison analyzed</i>	<i>Results</i>	<i>Comments</i>
Cho et al., 2009 <sup>74</sup>	Obesity	Meta-analysis	2 trials, 43 patients	2 trials, 53 patients	Separately comparing vs. lifestyle control, using RRs	MA vs. lifestyle control: mean difference, 2.16 (95% CI, 0.47–3.84); EA vs. lifestyle control: mean difference, 1.20 (95% CI, –0.65 to 3.05)	Difference not directly evaluated, MA vs. lifestyle control statistically significant
Lee et al., 2009 <sup>75</sup>	Schizophrenia	Meta-analysis, 7 trials	All 7 trials, <sup>a</sup> 457 patients	5 trials, 365 patients	Separately comparing with adjunctive drug vs. drug alone, using RRs	MA + drug vs. drug: RR, 1.15 (95% CI, 1.04–1.28); EA + drug vs. drug: RR, 1.19 (95% CI, 1.00–1.43)	Difference not directly evaluated, both comparisons statistically significant
Langhorst et al., 2010 <sup>76</sup>	Fibromyalgia	Meta-analysis, 7 trials	5 trials, 175 patients	2 trials, 104 patients	Separately comparing effect sizes vs. control using SMDs	MA vs. control SMD, –0.19 (95% CI, –0.52 to –0.14); EA vs. controls: SMD, 0.43 (95% CI, –0.81 to –0.04)	Difference not directly evaluated, but EA vs. sham statistically significant ( $p < 0.03$ )

<sup>a</sup>Trials include those with MA and EA, with data on number of trials and number of patients not separated out. SMD, standardized mean difference; CI, confidence interval; RR, risk ratios; WMD, weighted mean difference; SSRI, selective serotonin reuptake inhibitor.

case one is simply asking, Which treatment works better? However, an important caveat to this question is that if differences were found between the treatments, one would not know whether this had anything to do with the electrical stimulation.

### Brief History of MA and EA

Descriptions of manual acupuncture techniques date at least as far back as the *Neijing* (ca. 300 BCE) and include a wide variety of needle manipulation techniques, such as rotation, lifting, and thrusting techniques. In contrast, the use of electrical methods to stimulate acupuncture needles is considerably more recent, with origins in both Europe and Asia.<sup>2,3</sup> In France, the late 18th-century interest in the medical uses of electricity was contemporaneous with the introduction of acupuncture by Jesuit missionaries returning from China.<sup>4,5</sup> Use of electrical stimulation of needles, however, did not necessarily imply that the technique was informed by knowledge of Chinese or other East Asian theory. Early 20th-century British studies of electrical stimulation of acupuncture needles to treat sciatica describe needle placement as guided by sites of pain, with no mention of traditional Chinese practice.<sup>6</sup> Acupuncture and electricity were coupled in a different manner in the 1950s and 1960s with the independent explorations in Germany (Voll), France (Niboyet), and Japan (Nakatani) of electrodermal activity at acupoints as a means of objectifying diagnosis.<sup>7</sup> The mid 20th century also saw practitioners in Japan beginning to apply EA methods, apparently as a result of contact with their Western counterparts,<sup>7</sup> while Chinese acupuncturists were studying electrical stimulation at acupoints as a result of the emphasis on integration of Western medical concepts into Traditional Chinese Medicine.<sup>3,8</sup>

The early 1970s interest in acupuncture in the United States and Europe led to Western studies of both MA and EA for experimental pain.<sup>9,10</sup> Identification of the endogenous opioids in the mid-1970s led to pioneering animal research by Pomeranz in Toronto<sup>11</sup> and Han in Beijing.<sup>12</sup> This research, implicating endogenous opioids in EA-induced analgesia, set the stage for the use of EA to explore a wide range of biochemical and physiologic correlates of acupuncture treatment.<sup>13–16</sup> Clinical trials of EA soon followed, with publications first appearing in the early to mid-1980s.<sup>17–20</sup>

### Current Patterns of Use

Patterns of use of MA versus EA vary greatly by condition treated, practitioner preference and training, and stimulation parameters. Needling techniques, whether MA or EA, are widely heterogeneous. Manual stimulation techniques may include rotation of the needle in one or both directions and lifting and thrusting of the needle in myriad combinations. These techniques may range from subtle and barely perceptible to vigorous, rapid, and forceful.<sup>7,21–27</sup> EA techniques vary by stimulation amplitude, frequency, waveform, and duration. Clinically, EA is often performed after the needle has been manually stimulated sufficiently to obtain *de qi*, the characteristic needling sensation commonly associated with acupuncture. From this perspective, EA may be seen as additive to MA rather than as a distinct technique.

A recently published survey of practitioners compared acupuncture patterns of use in the European Union ( $n=559$ ) and China ( $n=461$ ).<sup>28</sup> Use of EA was reported by 39.7% of European acupuncturists (with pain as the most frequently treated condition) and 28.2% of Chinese practitioners (with neurologic conditions, mainly stroke, as most frequently treated). Because some European practitioners refer to the Voll electrodiagnosis system as EA, it is possible that this survey overestimates the number of European acupuncturists who practice traditional EA as defined in this paper.

Analyses of surveys and insurance claims in the United States indicate that EA is used in 12–15% of all acupuncture treatments.<sup>29,30</sup> When treating chronic back pain, the reported use of EA in the United States increases to 24–32%.<sup>31</sup> The decision to use EA appears to be practitioner dependent: Thirty-five percent of United Kingdom acupuncturists reported never using EA, while 13% reported using it “most or all of the time.”<sup>32</sup> Finally, use of EA appears to be based on the perception that it will improve clinical effectiveness in patients with more severe conditions or those more resistant to treatment. In a survey of United States acupuncturists treating chronic low back pain, 51% of practitioners reported using EA because “something simpler hadn’t worked.”<sup>33</sup>

### Physiologic Effects of Manual Versus Electrical Needling Stimulation

In basic science animal studies, both MA and EA have been observed to activate all four types of afferent nerve fibers.<sup>34</sup> These fibers include the thick myelinated A $\alpha$  and A $\beta$  fibers, the thin myelinated A $\delta$  fibers, and the thin unmyelinated C-fibers, all of which innervate skin and muscle. The innervation of fascia is less well known but is thought to include abundant nociceptors.<sup>35</sup> Single afferent fiber recordings found predominantly C and A fiber activation in response to both EA and MA.<sup>36</sup> However, from a broader physiologic perspective there is reason to suspect different physiologic responses to manual versus electrical stimulation of acupuncture needles. As the acupuncture needle traverses the epidermis, dermis, fascia, and muscle it contacts multiple tissues and cell types, and it is reasonable to suspect that these differing tissues and cells respond differently to electrical current added to an indwelling metal needle versus manual needle stimulation alone. For example, EA may depolarize the resting membrane potential of neighboring excitable cells that in turn could lead to action potentials along peripheral nerves and subsequent signaling cascades. On the other hand, manual manipulation of the needle, typically including lifting and thrusting to elicit *de qi*, dynamically alters the extracellular milieu, resulting in rotational deformation of fascia tissue,<sup>37</sup> which may affect the physiology and gene expression of fibroblasts. Another potentially important difference in the physiologic effects of MA and EA is that during EA in animal models, the intensity of the pulsed electrical current is often adjusted to produce repetitive contractions of local muscles. This does not happen with MA. Indeed, low-frequency (2 Hz) EA modulates muscle sympathetic activity, similar to the effect of exercise.<sup>38</sup> In summary, it is not yet known whether and to what extent the effects of EA result from sensory afferent stimulation, fascial deformation, and/or muscle contractions

or whether the effects of MA are qualitatively and quantitatively similar to those of EA.

For this component of the white paper, the basic science peer-reviewed literature was systematically searched for acupuncture research studies that specifically compared electrical and manual stimulation with respect to biological outcomes (see Table 1 for search strategy). Given the wide breadth of possible outcomes to investigate, the main domains of interest were limited to animal and human experimental studies that evaluated: (1) peripheral receptors and their ligands; (2) cardiovascular responses, including blood pressure; (3) central nervous system effects, including brain-based outcomes; and (4) subjective outcomes in experimental settings, such as pain reports.

Thirteen physiological studies (5 in animals, 8 in humans) met our selection criteria (Table 1).<sup>36,39–51</sup> Significant heterogeneity existed across studies, with variability in needle insertion location, electrical stimulation frequency, and stimulation duration. In searching for studies that compared the two stimulation modalities while controlling for confounding factors such as needle location, insertion depth of needle, and treatment duration, it was discovered that the duration of needle stimulation during EA was nearly always much longer than in MA (e.g., 15–30 minutes for EA and a few seconds for MA).

Moreover, most studies failed to specify whether they were directly comparing EA versus MA or whether EA was studied as an addition to MA. For instance, EA can be performed with needles simply inserted or both inserted and manipulated to achieve *de qi* sensation before electrical current stimulation. This ambiguity complicated the interpretation and integration of findings across studies. Of note, all studies identified were in healthy humans or rats, with no studies conducted in clinical populations or preclinical models of human disease. That said, some tentative conclusions were drawn.

In one study, EA and MA performed at the same frequency (2 Hz), location, and duration had nearly identical effects on centrally driven sympathetic nervous system activity (decreased blood pressure in a hypertensive rodent model).<sup>36</sup> However, some studies did report differences between EA and MA. In two human studies, EA evoked a transient decrease in temperature that was not seen in MA,<sup>39,40</sup> and the authors suggested that the cooling with EA could be a vasomotor spinal reflex response. More recent data from functional magnetic resonance imaging studies of healthy humans, in which stimulus duration (continuous manual stimulation and time of EA) was matched between conditions, showed greater activation in the somatosensory cortex with EA; in contrast, MA resulted largely in the deactivation of limbic system structures.<sup>42,44</sup> These findings were substantiated by a recent meta-analysis of acupuncture functional magnetic resonance imaging studies, which noted that while multiple areas were activated by both, EA produced greater activation in primary somatosensory cortex while MA produced greater deactivation in the putamen.<sup>52</sup>

With respect to behavioral responses in humans, three separate studies noted significant differences between EA and MA for analgesic responses to experimental pain stimuli. While EA had a greater effect than MA for pinprick pain, thermal and mechanical (i.e., pressure stimuli) behavioral tests did not show differences between EA and

MA,<sup>47</sup> suggesting that the analgesic effects of EA and MA may have overlapping but not identical mechanisms, similar to the neuroimaging findings above. Further, in healthy humans significantly greater analgesia for EA was observed compared with MA, with the analgesic effect of EA occurring immediately following treatment and peaking hours after needle removal.<sup>48</sup> This last finding is of significance because no other studies reported outcomes hours after needle removal, which raises the possibility that the window of observation needed for determining analgesic effects of EA may need to extend long after treatment. Finally, a recent study looking at mechanical pressure pain found EA superior to MA at increasing pain thresholds in healthy humans.<sup>49</sup> Of note, not all human experimental pain studies identified in our search showed differences between EA and MA. For example, no difference was reported between EA and MA for experimental thermal pain.<sup>43</sup>

Overall, while modest evidence suggests a potential difference between the physiologic effects of electrical and manual stimulation of acupuncture needles, the very small number of studies in which needle stimulation method was not confounded by other factors and the variability in methods used greatly reduce the ability to extend findings outside of individual research reports and to draw generalizable conclusions.

### Clinical Trials Comparing MA and EA

The literature on randomized controlled clinical trials of acupuncture was searched to identify comparative effectiveness research on MA versus EA. The aim was to assess whether the clinical trials data reflect survey data on patterns of use of these needle stimulation techniques.

The literature search from inception through December 31, 2012, initially identified 118 randomized controlled trials published in English, of which 17 met our selection criteria (see search strategy in legend to Table 2).<sup>53–69</sup> Next, trials that used EA adjunctively to MA (designated as MA versus MA + EA) were differentiated from trials that directly compared the two procedures (MA versus EA). If all procedures in the EA group before electrostimulation were the same as procedures in the MA group (e.g., *de qi* was initially elicited in each group), the trial was considered MA versus MA + EA; if the pre-electrostimulation procedure in the EA group was different (e.g., if *de qi* was elicited only in the MA group), the trial was considered MA versus EA. On the basis of these considerations, only one trial directly compared MA vs EA;<sup>60</sup> the remaining 16 trials were designated MA versus MA + EA. Consistent with acupuncture research in general and with reported patterns of use in clinical practice, most trials evaluated pain conditions ( $n=10$  [59%]). Of these, 7 trials (70%) reported MA + EA to have a superior “clinical effect” compared with MA alone; one study found a trend in favor of EA, while the other two studies found no difference (Table 2).

In clinical trials for pain conditions, better analgesia appears to be obtained when prolonged electrical stimulation is added to manual stimulation compared with brief or intermittent manual acupuncture needle stimulation alone. However, too few randomized controlled trials specifically assessed this question to draw robust conclusions. Most of these trials included few participants (range, 21–157) and

their findings may not be generalizable. More specifically, clinical differences between MA and MA augmented by EA may depend on the location of acupuncture points (e.g., ear versus body), patient population (e.g., elderly versus young athletes), condition (e.g., back pain versus headache), and cause of pain (e.g., inflammation versus neuropathy).

### Systematic Reviews and Meta-Analyses on MA Versus EA

In addition to examining individual clinical trials, we explored the literature to assess whether systematic reviews and meta-analyses might shed light on the relative effectiveness of MA and EA (search strategy included in Table 3).<sup>70-76</sup> Of the 188 identified reviews, 89 met our initial inclusion criteria. Of these 89 reviews, 15 did not pool data in a meta-analysis, so that no quantitative comparison was conducted, and only 7 of the remaining reviews presented pooled data that included a quantitative comparison of outcome for MA and EA. These 7 were meta-analyses that used quantitative methods to pool trial data either comparing MA with EA in the same analysis (a direct comparison) or comparing MA versus controls with EA versus controls in 2 separate analyses (an indirect comparison).

Of the 7 reviews, only 1 included a direct comparison of MA versus EA.<sup>70</sup> In this analysis, through a statistical test for an interaction, acupuncture for osteoarthritis using EA (pooled effect from 4 trials,  $n=614$ ) was superior to the use of only MA (pooled effect of 5 trials,  $n=1215$ ) ( $p=0.042$ ) (Table 3). The other 6 reviews made comparisons of the two stimulation procedures in an indirect manner, using different data in separate analyses to compare the effects of MA versus controls against EA versus controls. These indirect comparisons, which make comparability more limited, included acupuncture for smoking cessation,<sup>71</sup> chemotherapy-induced leukopenia,<sup>72</sup> depression,<sup>77</sup> obesity,<sup>74</sup> schizophrenia,<sup>75</sup> and fibromyalgia<sup>76</sup> (Table 3). Across these 6 reviews, the findings are inconclusive as to whether EA or MA was associated with better outcomes.

In summary, the identified systematic reviews and meta-analyses provided limited pooled data relevant to the aims of this white paper. From 89 eligible systematic reviews, there were only 1 direct quantitative comparison of MA versus EA, which suggested that EA might be superior to MA for treating pain in knee osteoarthritis, and 6 indirect comparisons that were inconclusive. Thus, the evidence from systematic reviews on the comparative effectiveness of MA versus EA is difficult to interpret. Most clinical trials within the reviews are underpowered, and therefore any subgroup analysis conducted within trials is even more likely to be underpowered.

### Conclusions and Recommendations

Research on both manual and electrical acupuncture is typically lumped together to constitute scientific evidence on “acupuncture.” However, the following important question is rarely addressed: Is there a fundamental difference between stimulating manually and electrically?

This white paper was motivated by the recognition of two areas of weakness in the acupuncture evidence base. First, models of the mechanisms of action of acupuncture are often based on basic science studies using solely EA or MA

without rigorous testing of whether the physiologic effects are similar in both cases. Second, clinical recommendations and individual practitioner decisions for when to use EA or MA are based far more on clinical experience than on clinical research.

This review of 40 years of acupuncture research explored differences between manual and electrical modes of stimulation. Very few clinical trials have directly compared MA to EA stimulation, and meta-analyses have often been performed across a broad spectrum of clinical trials of acupuncture without discriminating between the two stimulation techniques. Furthermore, in basic science studies directly comparing the effects of MA versus EA stimulation, the mode of stimulation has almost always been confounded by the stimulus duration (i.e., a few seconds for MA versus 15–30 minutes for EA). Whenever manual and electrical acupuncture have been compared in basic research, the main concern of researchers has been to compare treatments that are clinically relevant rather than design experiments in which the mode of stimulation (MA versus EA) is not confounded by some other factor. In other words, in basic science, clinical relevance has systematically trumped scientific rigor. It is therefore important to recognize that while comparing physiologic effects of manual acupuncture to an electrical stimulus of identical duration may not be clinically relevant, it is of scientific importance. Controlling for stimulus duration may require testing shorter EA durations to match the duration of the MA stimulus, assuming prolonged MA is not feasible. Controlling the frequency of stimulation also may require lower frequencies of electrical stimulation, such as 2 Hz, a frequency that can be achieved with manual manipulation. Controlling other factors with high-tech solutions, such as robotics or mechanical devices to standardize needle placement, rotation, and duration, might also be beneficial and necessary.

In contrast to basic science experiments, comparing two different clinically relevant methods of delivering acupuncture (i.e., short-duration MA and prolonged EA) in clinical trials is valid as long as the aim is truly comparative effectiveness: that is, pragmatically asking what works best with no attempt at understanding why. If it is found, for example, that electrical stimulation for 20 minutes produces greater clinical improvement than 20 minutes of MA during which the needles are manipulated for only a few seconds at the outset, one cannot conclude that the electrical current itself was responsible for the difference in clinical improvement between the two methods. Moreover, mechanisms identified from basic research using EA (e.g., neurophysiologic basis of pain) cannot be assumed to be relevant to clinical trials that use MA. Unless this is specifically emphasized, the tendency to attribute clinical benefits to the electrical stimulation will remain, which will perpetuate the current level of confusion. However, as long as one remains conscious of these caveats, pragmatic recommendations for clinical practice can be based on the comparative effectiveness of EA and MA.

Finally, patterns of use, which differ widely among practitioners, should be more thoroughly explored. EA is commonly added as an adjunct to MA, and the decision to include EA in a treatment is based on numerous factors, including condition treated, severity of symptoms, individual patient differences, and practitioners' preference and

training. It is of fundamental interest to understand what should guide clinical decision-making (e.g., when to include EA and what specific stimulation parameters to use to learn from clinical observations what seems to work best for particular patients and specific conditions, as well as to assess patients' experiences with EA versus MA). Finally, criteria informed by the clinical experience of both practitioners and patients, obtained through well-designed surveys and focus groups, should be developed and applied to inform the design of clinical trials comparing EA versus MA.

#### Author Disclosure Statement

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