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#### **Review Article**

# Modern acupuncture-like stimulation methods: a literature review



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#### ABSTRACT

Acupuncture therapy has been proved to be effective for diverse diseases, symptoms, and conditions in numerous clinical trials. The growing popularity of acupuncture therapy has triggered the development of modern acupuncture-like stimulation devices (ASDs), which are equivalent or superior to manual acupuncture with respect to safety, decreased risk of infection, and facilitation of clinical trials. Here, we aim to summarize the research on modern ASDs, with a focus on featured devices undergoing active research and their effectiveness and target symptoms, along with annual publication rates. We searched the popular electronic databases Medline, PubMed, the Cochrane Library, and Web of Science, and analyzed English-language studies on humans. Thereby, a total of 728 studies were identified, of which 195 studies met our inclusion criteria. Electrical stimulators were found to be the earliest and most widely studied devices (133 articles), followed by laser (44 articles), magnetic (16 articles), and ultrasound (2 articles) stimulators. A total of 114 studies used randomized controlled trials, and 109 studies reported therapeutic benefits. The majority of the studies (32%) focused on analgesia and pain-relief effects, followed by effects on brain activity (16%). All types of the reviewed ASDs were associated with increasing annual publication trends; specifically, the annual growth in publications regarding noninvasive stimulation methods was more rapid than that regarding invasive methods. Based on this observation, we anticipate that the noninvasive or minimally invasive ASDs will become more popular in acupuncture therapy.

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#### 1. Introduction

Stimulation of acupoints and meridians has been an important therapeutic modality in traditional Eastern medicine, and it has also become popular in the West, as its clinical effectiveness has been demonstrated through extensive research.

Acupuncture and related modern technologies are increasing in popularity worldwide. According to a 2002 World Health Organization report, acupuncture treatment was shown to be effective in controlled trials of 29 diseases, symptoms, or conditions. However, the safety of acupuncture has engendered controversy with respect to infection, inflammation, and pain management.

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Clinical effectiveness of acupuncture has widely been studied during the past four decades.<sup>2–6</sup> In addition to the demonstrated effectiveness of traditional acupuncture practices, increased demand has arisen for the development of modern acupuncture-like stimulation devices (ASDs), which are simpler to quantify and standardize and are less dependent on the manipulation techniques of individual clinicians.

The first modern ASD dates back to the early 1950s, which was based on electrical stimulation (ES). <sup>7,8</sup> In addition to its long history, ES is the most extensively studied ASD. <sup>9</sup> Recently, however, several types of ASDs have extensively been studied for their clinical effectiveness and noninferiority to manual acupuncture, including laser stimulation (LS) <sup>10</sup> and magnetic stimulation (MS). <sup>11</sup> In this review, we summarize recent studies of popular ASDs. We first describe the most popular types of ASDs, discuss their clinical effectiveness and target symptoms, and finally, discuss the annual research trends regarding popular ASDs.

#### 2. Methods

To analyze the popularity and features of methods for stimulation of acupoints, we searched for studies in the Medline, PubMed, Cochrane Library, and Web of Science electronic databases from their inception to June 2014. First, we searched for studies related to acupuncture or acupoint stimulation, which yielded > 22,000 studies, of which approximately 20,000 were redundant. Among the latter studies, approximately 3000 were related to moxibustion, 1600 to massage (or acupressure), 200 to the cupping method, 5400 to ES, 900 to LS, 700 to MS, and 300 to ultrasound stimulation (US). To narrow the search scope to ASDs, we refined the search to [(acupoint\* or "acupuncture point" or meridian") and (stimul\* or irritat\* or excit\* or response or respon\* or react\* or reflex or measur\* or diagnos\*) and (electric\* electro\* or magnet\* or infrared or IR or laser or ultraviolet or UV or ultraso\*) not (rat or monkey or dog or pig or cat or mouse or mice or rabbit or rodent\*)]. We excluded laboratory experiments on animals, studies that were not written in English, and reviews. We searched 728 articles obtained from the electronic databases, excluding 489 articles that included studies on animals, manual acupuncture-only clinical trials, non-English-language articles, and review articles by screening the titles and abstracts. A total of 44 studies were excluded from the selected 239 articles because of duplication. Finally, 195 studies met the inclusion criteria and were evaluated in detail. The topics of these 195 articles were ES (133), LS (44), MS (16), and US (2), as shown in Fig. 1. Prior to describing the results of the detailed analysis, we introduce the features and research history of ES, LS, MS, and US in the following sections.

#### 2.1. Electrical stimulation

Low electrical impedance and high conductance are recognized as typical electrical properties of acupoints and meridians. 12-14 In the Western hemisphere, the electrical properties of acupoints and meridians have been investigated since the 1950s. In 1958, Niboyet and Mery<sup>15</sup> reported the points with low skin impedance using the Wheatstone bridge, whereas in 1962, Kramar<sup>16</sup> showed that acupoints have high capacitance compared with neighboring points. Voll7 devised an ES device to apply to acupoints and meridians, thereby establishing a method that was called "electroacupuncture according to Voll." This method of Voll7 greatly stimulated clinical and research activities associated with ES at acupoints and meridians. In the East in 1956, Nakatani<sup>8</sup> reported that electrical pathways connected the points with low skin resistance and named them "Ryodoraku." Today, ES can be classified into five types: electroacupuncture (EA), transcutaneous electrical acupoint stimulation (TEAS), auricular electroacupuncture (AEA), transcutaneous electrical nerve stimulation (TENS), and electrical heat acupuncture (EHA). EA is an electrical, minimally invasive stimulation technique applied to acupoints. TEAS is an electrical, noninvasive stimulation technique applied to acupoints. AEA is a subtype of EA applied to acupoints of the ear. TENS is an electrical, noninvasive stimulation technique applied to the nervous system (nonacupoints). EHA is similar to EA with the exception that a needle heated by an electric current is used at acupoints. Of the 133 articles on ES, 54 pertained to EA, 69 to TEAS, six to AEA, three to TENS, and one to EHA. To simplify the discussion, we categorized ES into EAs and TEASs, where EAs represented

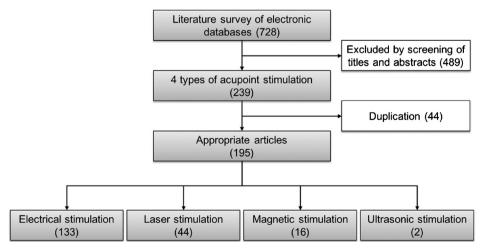


Fig. 1 - Flow diagram of literature survey.

all invasive techniques, such as EA, AEA, and EHA, and TEASs included all noninvasive techniques, such as TEAS, auricular TEAS, and TENS.

#### 2.2. Laser stimulation

Studied since the 1970s, LS is used to expose acupoints of the human body to low-energy laser beams. A review article 17 noted that studies using LS were conducted between 1970 and 1972 in the USSR. Nevertheless, Friedrich Plog's 18 study published in 1976 is well known as the first report of implementation of LS at acupoints. Since the 1980s, LS has been recognized as an effective method for stimulating acupoints without needles. Applications of LS at acupoints were mostly described as noninvasive in the studies reviewed, with only a few being described as invasive. Here, we do not distinguish invasive techniques from noninvasive stimulation.

#### 2.3. Magnetic and ultrasonic stimulation

MS is used to access the body's magnetic fields by stimulating acupoints, and MS of acupoints has been studied since the 1970s. Transcranial magnetic stimulation is one of the most frequently used MSs and was introduced by Barker<sup>19</sup> in 1985. In 1980, Inoue<sup>20</sup> applied for a patent for a device used for MS of body acupoints, and in 1982, Katayama<sup>21</sup> reported

the meridian magnetic analgesia of acupuncture stimulation (published in Japanese). The MS used in all 16 papers consisted of noninvasive stimulations at acupoints.

US is used to irritate acupoints using a narrow, cylindrical, high-frequency beam of sound. Characteristics of phonation and sound transmission in meridians were reported in the 1980s, and a study on US of acupoints was published by Jin<sup>22</sup> in 1984. Only two studies that we identified in the electronic databases were relevant.

#### Results

The aforementioned four types of ASDs were classified into the following 13 categories according to the stimulation purposes: (a) analgesic effect; (b) pain relief; (c) physiological change; (d) improvement of the alimentary system; (e) prevention of nausea and vomiting; (f) recovery of muscle fatigue or improvement of muscle strength; (g) reduction of body weight; (h) treatment of depression; (i) treatment of addiction, such as addiction to tobacco, narcotics, and alcohol; (j) treatment of stroke; (k) treatment of various diseases; (l) characteristics of stimulation; and (m) brain activity. Fig. 2 shows how the four types of ASDs were distributed between the 13 categories for research purposes. It also shows the ratio of randomized controlled trials (RCTs) to efficacies for the 13 categories. The

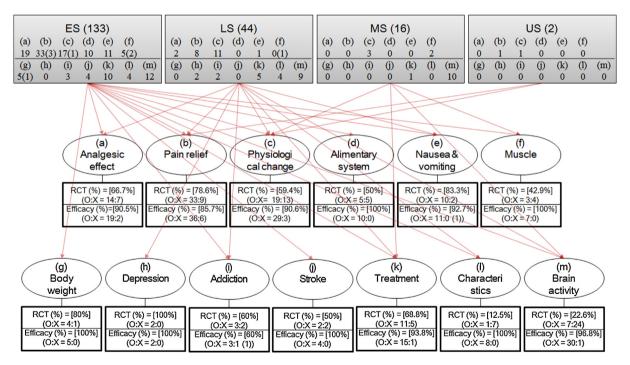


Fig. 2 – Distribution of the four ASDs with respect to the 13 research categories from (a) to (m) whereby the numbers of RCTs and the therapeutic effectiveness are shown for each category. Numbers reflect the article counts, with the numbers in parentheses for the four types indicating the number of cases of overlap between the stimulations, and the numbers in parentheses below the efficacy (%) are presented when the efficacy was unclear. In RCT (%) = A/(A + B) % and (O:X = A:B), A is the number of RCTs and B is the number of non-RCTs. The same formula was applied to the efficacy percentages. When the efficacy was unclear, indicated by the numbers in parentheses, we considered those studies as not effective in computing the percent values. For example, % value = A/(A + B + b) for efficacy [O:X = A:B(b)].

ASD, acupuncture-like stimulation device; ES, electrical stimulation; LS, laser stimulation; MS, magnetic stimulation; RCT, randomized controlled trial; US, ultrasound stimulation. O = yes, X = no. Example: RCT (O:X) = (RCT:non-RCT), Efficacy (O:X) = (efficacious:not efficacious).

Reference	Stimulation type	Stimulation site	Symptom	Control	Effect
iang et al <sup>23</sup>	TEAS	LI4, PC8	Healthy	46 individuals, TEAS/mock TEAS	Analgesic effect
Vang et al <sup>24</sup>	TEAS	LI4, PC6, ST36	Sinusotomy	60 patients, random TEAS/control:	Analgesic effect
Zhang et al <sup>25</sup>	TEAS	T3 acupoints	Ambulatory surgery	72 women, random TEAS/sham	Recovery & decrease o anesthesia
Wu et al <sup>35</sup>	EA	GV1, BL57	Hemorrhoids	120 cases, random EA (40)/sham EA (40)/blank (40)	Effects of preemptive analgesia
an et al <sup>26</sup>	TEAS	Bi PC6, LI14,	Total hip	68 elderly patients, random	Reduction of
		ipsilateral to surgery sire ST36, GB31	arthroplasty surgery	TEAS/sham TEAS	postoperative analgesi requirement
Zheng et al <sup>36</sup>	EA	GV24, EX-HN3	Orotracheally intubated patients	45 patients, random, no treatment/sham EA/EA	Sedation & analgesia
Cheing and & Chan <sup>27</sup>	TEAS/TENS	Right elbow LI11,	Healthy	Randomized controlled trial, 45 individuals, random TEAS (15)/TENS	Hypoalgesic effects (acupuncture points &
		Nonacupoint (right superficial radial nerve)		(15)/control-no stim (15)	nerve points)
DeSantana et al <sup>31</sup>	TENS	Around the incision	Unilateral inguinal herniorrhaphy with epidural anesthetic	Prospective, randomized, double-blinded, placebo-controlled study, 40 patients, TENS (20)/placebo-TENS (20)	Hypoalgesic effect for postoperative pain
darlas et al <sup>37</sup>	EA	Bi LI10, HT5/ipsilateral GB34, ST38	technique Healthy (acupuncture naïve)	Randomized, double-blinded, placebo-controlled study, 48 volunteers, control/placebo-EA no stim/high-intensity	Hypoalgesic response
eung et	EA	Left SP1, LR1	Healthy	EA/low-intensity EA  13 individuals, EA/before-EA/ after-EA (time sequence)	Analgesic benefit
itscher <sup>42</sup>	Acupressure/ MA/LS	EX-HN3	Healthy	Randomized, controlled, blinded crossover trial, 20 volunteers, acupress/MA/LA; APs/non-APs	ECG similarities of acupressure-induced sedation & general anesthesia (all)
Zhang et al <sup>38</sup>	EA	Acupoints	Healthy	Eight8 individuals, EA/mock-EA	Analgesic effect
Attele et	TEAS	LI4, PC6	Healthy	22 individuals, TEAS/control	Analgesic effect
Chesterton et al <sup>29</sup>	TENS/TEAS	GB34, radial	Healthy	Randomized, double-blind,	Hypoalgesic effect
et ai		nerve or extrasegmental		sham-controlled study, 240 participants, six6 TENS (180; 90 m, 90 f)/control (30; 15 m, 15 f)/sham TENS (30; 15 m, 15 f); 4/110 Hz, intensity, site	
⁄uan et al³0	TEAS	LI4, PC6	Healthy	20 individuals TEAS/morphine/TEAS + morphine/control	Analgesia effect
Morioka et al <sup>39</sup>	EA	ST36, GB34, BL60	Healthy	14 volunteers, EA/control	No difference in minimum alveolar anesthetic concentration
in et al <sup>41</sup>	EA	Bi ST36	Lower abdominal surgery	Randomly, 100 women, control (25)/sham-EA no stim (25)/LF-EA 2 Hz (25)/HF-EA 100 Hz (25)	Reduction of postoperative analges requirements & side effects (LF-EA, HF-EA)
Greif et al <sup>32</sup>	ATEAS	Auricular acupoints	Healthy	Randomized, double-blind, crossover trial, 20 volunteers (10 m, 10 f), ATEAS/no treatment	Reduction of anesthet requirement
hen et al <sup>33</sup>	TEAS/TENS	ST36/dermatomal level	Total abdominal hysterectomy or myomectomy procedures	Randomized controlled trial, 100 women, sham-TEAS no stim (25)/non-APs TEAS (25)/dermatomal-TENS (25)/TEAS	TENS was as effective TEAS, both were more effective than stim at non-APs

Table 1 (Con	Table 1 (Continued)									
Reference	Stimulation type	Stimulation site	Symptom	Control	Effect					
Wang et al <sup>34</sup>	TEAS	LI4	Healthy women undergoing lower abdominal procedures	Random, 101 participants, PCA (26)/PCA + LP-TEAS (25)/PCA + HP-TEAS (25)/PCA + sham-TEAS no stim (25)	Decrease in PCA opioid requirement & opioid-related side effects (HP-TEAS)					
Brokhaus and& Elger <sup>43</sup>	LS/MA	Bi LI4, EX-UE	Healthy	Double-blind, 40 probationers, MA-LI4/LA-LI4, EX	Analgesic effect of MA on painful heat stim, no effect on pain (LA)					

AP, acupuncture point; ASD, acupuncture-like stimulation device; ATEAS, auricular TEAS; EA, electroacupuncture; ECG, electrocardiogram; HF, high frequency; HP-TEAS, high power TEAS; LA, laser acupuncture; LF, low frequency; LP-TEAS, low power TEAS; LS, laser stimulation; MA, Manual acupuncture; PCA, patient-controlled analgesia; stim, stimulation; TEAS, transcutaneous electrical acupoint stimulation; TENS, transcutaneous electrical nerve stimulation.

numbers shown in the uppermost boxes in Fig. 2 signify the numbers of articles. The numbers of overlapping articles are shown in parentheses under the 13 categories of the four ASDs, and the numbers in parentheses below the efficacy (%) are presented when the efficacy was unclear.

To investigate the effectiveness of ASDs, we analyzed the efficacy of each stimulation type through the articles reporting effectiveness. The effectiveness of ES was stated in the fields of analgesic effect (94.7%), pain relief (90.9%), and reduction of nausea and vomiting (90.9%) based on the sample size of > 1000 trials. Based on the sample size of > 100 trials, ES was shown to be effective in improving the alimentary system (100%), improving muscle strength (100%), reducing body weight (100%), treating various addictions (60%), and treating stroke (100%), whereas LS was effective for pain relief (62.5%) and treating various addictions (100%). Based on a sample size of <100 trials, ES was shown to be a therapeutic possibility in various diseases such as orthostatic intolerance, autism spectrum disorders, supratentorial craniotomy, tinnitus, asthma, dyspnea, distress, and anxiety. LS presented potential in the treatment of nausea and vomiting, depression, menopausal symptoms, cholecystitis, renal failure, head injury, and interstitial cystitis. MS was a possible treatment for muscle and diving fatigue, whereas US demonstrated potential for relieving pain.

#### 3.1. Analgesic effect

All the studies that reported an analgesic effect are shown in Table 1. Twelve articles reported an analgesic effect using TEASs, 23-34 seven articles reported an analgesic effect using EAs, 35-41 and two articles discussed LS. 42,43 A total of 834 individuals received TEASs to enable estimation of the analgesic effect of their clinical application using RCTs, and all articles reported that the TEASs had an analgesic or hypoalgesic effect or decreased opioid requirements. A total of 348 individuals received EAs, and an effect of the EAs on analgesia, sedation, hypoalgesia, pre-emptive analgesia, and reduction of analgesic requirements was found in 334 patients. In 20 individuals who received acupressure, manual acupuncture (MA), and LS, a sedative effect was observed, and an anesthetic effect was observed in 60 individuals who received LS. Two of the 21 papers<sup>39,43</sup> reported no significant analgesic effect of the EAs and LS.

#### 3.2. Pain relief

As shown in Table 2, presenting the studies reporting the effect on pain relief, 15 articles reported using TEASs, 44-58 EAs were used in 18 studies, <sup>59–76</sup> other acupoint stimulations such as US were used in one study,77 and LS was used in eight studies.78-85 TEASs and EAs were compared in a total of 872 individuals to evaluate their effect on pain relief. Both had an effect on pain relief in two studies; however, the effect of EAs was reported to be superior to that of TEASs in one study. Of 1046 individuals who received TEASs, 926 experienced relief or a reduction in various types of pain. Of the 877 individuals who received EAs, 628 also experienced pain relief. Of the 435 individuals who received LS, 230 experienced relief of dysmenorrhea pain or carpal tunnel syndrome pain, whereas 50 individuals who received US experienced an effect on short-term segmental antinociception. Six of the 42 papers44,47,64,79,82,84 reported no statistically significant effect on pain relief when TEASs, LS, EAs, LS combined with paracetamol and chlormezanone, and LS were applied to the acupoints of study participants.

#### 3.3. Treatments of the alimentary system

As summarized in Table 3, ES (TEASs and EAs) was the primary ASD method for treating digestive disorders. Of these studies, seven that investigated TEAS<sup>86–92</sup> and three that evaluated EA<sup>93–95</sup> comprise this category. In total, 149 individuals who received TEAS experienced a beneficial effect on the alimentary system, as did 68 individuals who received EA. No study reported statistically insignificant results regarding stimulation of the alimentary system.

#### 3.4. Prevention of nausea and vomiting

All the studies shown in Table 4 employed ASDs for the prevention of nausea and vomiting. ES was primarily applied for the prevention or treatment of nausea and vomiting, except for one study that used LS for this purpose. TEAS was the main method used for preventing nausea and vomiting: we retrieved nine articles on TEAS, <sup>96–104</sup> two on EA, <sup>105,106</sup> and one on LS. <sup>107</sup> A total of 830 individuals who received TEAS experienced an effect on prevention, reduction, or treatment of postoperative nausea and vomiting and nausea or vomiting. A total of 224 individuals who received EA also

Reference	Stimulation type	Stimulation site	Symptom	Control	Effect
Mucuk & Baser <sup>44</sup>	TEAS	LI4, SP6	Pregnant women	Bi LI4-TEAS (40)/SP6-TEAS (40)/control (40) no stim	Labor pain relief, not statistically significant
Sun et al <sup>45</sup>	TEAS	PC6	Driver fatigue		Able to withstand drive fatigue
Vassal et al <sup>46</sup>	TENS	Left common peroneal nerve	Healthy	20 individuals, TENS/sham TENS (left thigh)	Pain relief
Kim et al <sup>59</sup>	EA	Bi LI4, TE3, GV39, GV41, SP6, LR3, Ba Feng, Ba Xie	CIPN	Randomized, patient-assessor-blinded, controlled trial, 40 patients, EA (20)/sham EA (20)	Treatment for CIPN, trials
Lee et al <sup>60</sup>	EA	Bi ST36, GB39, SP9, PC6, LR3, GB41	PDN	3-armed, randomized, controlled pilot trial, EA (15)/sham EA (15)/usual care (15)	Treatment for PDN, trials
Mucuk et al <sup>47</sup>	TEAS	Bilateral LI4	Labor pain	Random TEAS/control no TEAS; all standard treatments	Pain relief, not statistically significant
Ni et al <sup>48</sup>	TEAS	Bilateral PC6	Children with congenital heart defects	70 eligible children, random, TEAS (34)/control-no stim (36)	Attenuation of myocardial injury in children undergoing cardiac surgery
Wu et al <sup>49</sup>	TEAS	LI4, SP6	Gynecology patients (primary dysmenorrhea)	Randomized controlled trial, 66 patients (f), TEAS (34)/control non-APs (32)	Mitigation of pain in dysmenorrhea
Yoshimizu et al <sup>72</sup>	EA/TEAS	For acupoints in trapezius muscle	Shoulder & neck pain	Randomized crossover trial, 90 patients, EA/TENS	Reduction in pain (EA : TEAS)
Musial et al <sup>73</sup>	EA	LI4, LI10	Healthy	Double-blind design, 125 individuals, EA (25)/tramadol (25)/ibuprofen (25)/placebo pill (25)/no treatment (25)	Reduction of experimentally induce ischemic pain
Choi et al <sup>61</sup>	EA/meditation	LI4, LI10	Vipassana meditators	Semirandomized trial, medita- tors(8)/nonmeditators (20)-EA/nonmeditators (20)- no EA	Reduction in the pain induced by SETT
Yeh et al <sup>50</sup>	TEAS	BL40, GB34, HT7, PC6	Spinal surgery receiving patients	Placebo- & sham-controlled study, random TEAS (30)/TEAS-sham point (30)/no TEAS (30)	Reduction in postoperative pain, analgesic usage
Montenegro et al <sup>51</sup>	TEAS	TE5, CV6	Healthy	32 volunteers, random TEAS/sham TEAS	Increase in the latency of pain threshold
Yeh et al <sup>53</sup>	TEAS	Acupoints	Lumbar spinal surgery	Randomized controlled repeated measures design, 99 patients, ES/sham-AP ES/no ES	Improvement of acute postoperative pain management without adversely affecting vita signs
Гакатјапі et al <sup>81</sup>	LS	Acupoints	Wrist pain	Randomized controlled trial, 70 women, LS (33)/control (37) no LS	Increase in mean valu of pain threshold
ee & Lee <sup>62</sup>	EA	Bi BL32, BL33, GB30	Chronic prostatitis/chronic pelvic pain syndrome	39 men, random 3 group exercise + EA/exercise + sham EA/exercise	Pain relief effect
Kempf et al <sup>78</sup>	LS	Bi SP6, LR3, LI4; right CV3, ST36	Minimum menstrual pain	Randomized controlled double blind pilot trial, 48 women, LA (18)/placebo-LA (30)	Dysmenorrhea treatment
Glazov et al <sup>82</sup>	LS	Acupoints	Chronic nonspecific low-back pain	Double blind, 2-group parallel randomized controlled trial, 100 participants, LA/sham-LA	Not showing a specific effect for chronic low-back pain

Pafaranca	Stimulation	Stimulation	Simnton	Control	Effect
Reference	type	site	Symptom	Control	Effect
Chan et al <sup>74</sup>	EA	Acupoints on	Chronic neck pain	Single-blind, randomized,	Significant
		the wrist	•	sham-controlled trial, 49	improvements of
				patients, EA (22)/sham-EA (27)	chronic neck pain
ubb et al <sup>63</sup>	EA	Acupoints	Osteoarthritic knee	Blinded randomized trial,	Symptomatic
		-	pain & disability	MA (34)/EA (34)/sham MA (34)	improvement
rbely et	US	Right	Identifiable	Randomized controlled	Short-term segmental
al <sup>77</sup>		supraspinatus	myofascial trigger	study, 50 individuals,	antinociceptive effects
		trigger point	points	random US/sham US (off)	on TPs
e et al <sup>54</sup>	TEAS + PCA	LI4, PC8;	Craniotomy &	Randomized control, 40	Enhancement of the
		Jiaogan,	required pain relief	patients, PCA + TEAS	effect of pain relief &
		Shenmen,	following surgery	(20)/PGA (20)	reduction of adverse
		Shen, Waifei,			reactions
		Naogan,			
		Pizhixia (ear			
ficholol-	AFA	acupoints) Auricular	Molor to ath	Prognostive was descired	No rodustion in sit
lichalek- Sauberer	AEA		Molar tooth extraction	Prospective, randomized,	No reduction in either
et al <sup>64</sup>		shenmen, mouth, tooth	extraction	double-blind, placebo-controlled study,	pain intensity or analgesic consumption
etai		moun, tooth		placebo-controlled study, 149 patients, AEA (76)/AMA	in a molar tooth
				(37)/sham AEA no stim no	extraction model
				needle (36)	extraction model
Zhang et	EA	GB34, GB39	Healthy (right	12 volunteers,	Pain relief
al <sup>65</sup>	LA	GD34, GD39	handiness)	EA/sham-points EA/shallow	raili lellei
aı			Handinessy	EA subcutaneous needling	
rip et al <sup>55</sup>	TEAS +	_	Subacute neck or	Randomly, 47 individuals,	Reduction in pain
p ccu.	EMMW		low-back pain	TEAS + EMMW (23)/control	intensity, stress, &
				(24)	stiffness level
Fang et al <sup>52</sup>	TEAS/EA	Acupoints	Periarthritis of	360 cases, TEAS (186)/EA	Therapy for periarthri
Ü		•	shoulder at different	(174)	of shoulder, no
			stages		significant differences
					(TEAS/EA)
Aigner et	LS +	22 acupuncture	Whiplash injuries	Prospective, randomized	Ineffective in
al <sup>79</sup>	paracetamol,	points		placebo-controlled trial, LA	management of
	chlormezanone			(23)/placebo-LA (22)	whiplash injuries
Sator-	AEA	Auricular 29,	In vitro fertilization	94 women, random, AEA	Reduction of pain
Katzenschlage et al <sup>66</sup>	•	55, 57		(32)/AMA (32)/pharm. (30)	intensity
Wong et al <sup>75</sup>	EA	LI4, GB34,	Operable non-small	Random, 25 patients, EA	Management of
		GB36, TE8	cell lung carcinoma	(13)/sham-EA (12)	post-thoracotomy
			patients who		wound pain
			received		
			thoracotomy		
Weng et al <sup>56</sup>	TEAS	LI10, LI11	Tennis elbow pain	Randomly, 20 patients,	Effective in the
			for at least 3 mo	5 kHz modulated LF-TEAS	treatment of patients
				2 Hz (20)/5 kHz modulated	with tennis elbow pai
				HF-TEAS 100 Hz	(LF-TEAS, HF-TEAS)
				(20)/sham-TEAS, different time slots	
Гsui &	EA/EHA	6 acupuncture	Chronic low-back	ume siots 42 individuals, random	Treatment of chronic
Cheing <sup>67</sup>	LI V LI IA	points	pain	EA/EHA/control; all exercise	low-back pain
Sator-	AEA	Auricular	Chronic low-back	Prospective, randomized,	Treatment of chronic
Katzenschlage		acupuncture	pain	double-blind, controlled	low-back pain
et al <sup>68</sup>		points 29, 40, 55	1	study, 61 patients, random	, Puil.
		15, 10, 55		AEA (31)/sham-AEA no stim	
				(30)	
Sator-	AEA	Cervical spine,	Chronic cervical	Prospective, randomized,	Treatment of chronic
Katzenschlage		shenmen,	pain patients	double-blinded, controlled	cervical pain
et al <sup>69</sup>		cushion	without radicular	study, 21 patients, EA	
			symptoms with	(10)/control (11)	
			insufficient pain		

Reference	Stimulation type	Stimulation site	Symptom	Control	Effect
Ng et al <sup>70</sup>	EA/TEAS	ST35/EX-LE4	OA-induced knee pain	Single-blinded randomized controlled trial, 24 individuals (1 m, 23 f), EA (8)/TEAS (8)/control standard therapy (8)	Reduction of OA-induced knee pain
Naeser et al <sup>80</sup>	LS/TENS	Shallow acupuncture points/wrist	CTS	Randomized, double-blind, placebo-controlled, crossover trial, 11 cases, red LS/IR LS/TEAS/sham (off)	Treating CTS pain
Tsui & Leung <sup>71</sup>	EA	GB34, ST38	Chronic tennis elbow	Single-blinded randomized controlled trial, 20 patients, MA/EA	Treating patients with tennis elbow
Zoghi & Jaberzadeh <sup>57</sup>	ATEAS/ATENS	4 auricular acupoints	Healthy	Double-blind within-subject design, randomly, 90 individuals, HV-ES (30)/HV-sham-ES non-APs (30)/no ES (30)	Increase in experimental pain threshold (HV-ES, sham)
Lorenazana <sup>58</sup>	TEAS	HT7, LI4	Episiotomy pain	Randomized, double-blind, controlled trial, 68 patients, TEAS (38)/control (30)	Relief of episiotomy pain (TEAS > lidocaine)
King et al <sup>83</sup>	ALS	Auricular acupoints	Healthy	80 individuals, ALS (41)/control (39) sham-ALS	Increase in mean pain threshold after treatment
Waylonis et al <sup>84</sup>	LS	Acupoints	Myofascial pain syndromes (fibrositis, fibromyalgia)	Crossover double-blind trials, 62 patients, LS/placebo	No statistical difference between the treatment and placebo groups
Kreczi & Klingler <sup>85</sup>	LS	Acupoints	Radicular and pseudoradicular pain syndromes	Prospective randomized single-blind crossover study, 21 patients, LS/mock LS	Mean pain levels (lower)
Ernst & Lee <sup>76</sup>	EA	LI4	Normal individuals	Crossover repeated-measure design, 5 individuals, control/EA/EA + naloxone/EA + placebo	Pain threshold increase

AEA, auricular electroacupuncture; ALS, auricular laser stimulation; AMA, auricular manual acupuncture; AP, acupuncture point; ASD, acupuncture-like stimulation device; ATEAS, auricular TEAS; ATENS, auricular TENS; CIPN, chemotherapy-induced peripheral neuropathy; CTS, carpal tunnel syndrome; EA, electroacupuncture; EHA, electrical heat acupuncture; EMMW, electromagnetic millimeter wave; ES, electrical stimulation; f, female; m, male; HF, high frequency; HV, high voltage; IR, infrared; LA, laser acupuncture; LF, low frequency; LS, laser stimulation; MA, manual acupuncture; OA, osteoarthritis; PCA, patient-controlled analgesia; PDN, painful diabetic neuropathy; pharm, pharmacological treatment; SETT, submaximum effort tourniquet technique; stim, stimulation; TEAS, transcutaneous electrical acupoint stimulation; TENS, transcutaneous electrical nerve stimulation; TP, trigger point; US, ultrasound stimulation.

experienced either the same effect or controlled emesis, whereas 40 individuals who received LS experienced a decrease in the incidence of vomiting. We observed that TEAS has been steadily applied in the prevention of nausea and vomiting, and exceeded EA in the number of clinical studies since 2003. This finding implies that the effectiveness of TEAS in preventing nausea and vomiting has been confirmed, and that TEAS was preferred to EA because of the infection risk and pain due to the use of needles with EA.

#### 3.5. Improvement of the muscle system

Studies regarding ASDs that were related to the recovery of muscle fatigue or improvement of muscle strength are shown in Table 5. MS and ES were used to reduce muscle fatigue or improve muscle strength. This category included two studies on MS<sup>108,109</sup> and five studies<sup>110–114</sup> on ES. The two MS studies, which were conducted by the same research group, reported

the effective recovery of muscle fatigue. One study<sup>109</sup> reported better performance of MS than TEAS with respect to the therapeutic effect on muscle fatigue, and we expect more studies to validate this report.

#### 3.6. Reduction in body weight

All the papers investigating the reduction in body weight were associated with ES, as shown in Table 6. EAs \$^{115,118,119}\$ and TEASs \$^{116,117}\$ were applied to facilitate the reduction in body weight. One study \$^{117}\$ stated that TEAS was as effective as EA in weight reduction. A total of 193 individuals who received ES experienced a reduction in body weight or fat, and an improvement in body mass index or body composition. All the studies reporting on the reduction in body weight claimed significant effects. More studies are required to substantiate the effectiveness of ES for body weight reduction.

Reference	Stimulation type	Stimulation site	Symptom	Control	Effect
McNearney et al <sup>86</sup>	TEAS	PC6, ST36	SSc	17 patients, all TEAS	Enhancement of gastric myoelectrical functioning in SSc
Leung et al <sup>87</sup>	TEAS	LI4, PC6, ST36	Healthy	40 individuals, random TEAS/placebo TEAS	Reduction of rectal discomfort
Chen et al <sup>93</sup>	EA	ST36, ST37, ST25, ST28, CV4, CV6	Female constipation	Single-blind, randomized trial, 30 females, EA (14)/sham EA (16)	Improvement of constipation
Liu et al <sup>88</sup>	TEAS	PC6, ST36	Functional dyspepsia	Double-blind, crossover study, 27 patients, random acute-TEAS/chronic (2w) TEAS	Improvement of dyspepsia symptoms
Wang et al <sup>94</sup>	EA	ST36, LI4	Type 2 diabetes (symptoms of gastroparesis)	Single-blind, randomized pilot study, 19 patients, EA (9)/sham EA (10)	Reduction of the dyspeptic symptoms of diabetic gastroparesis
Sallam et al <sup>89</sup>	TEAS	Gastrointestinal (GI) acupoints	SSc	17 patients, TEAS/baseline	Treatment of upper GI symptoms
Xu et al <sup>95</sup>	EA	ST36, PC6	Functional dyspepsia	19 patients, acute-EA (10)/short-term (2w) EA (9)	Relief of dyspeptic symptoms
Zou et al <sup>92</sup>	TEAS	PC6	Healthy	Random, 26 volunteers, TEAS/sham APs-TEAS/naloxone	Inhibition of frequency of transient lower esophageal sphincter relaxations
Xing et al <sup>90</sup>	TEAS	ST36, PC6	Diarrhea- predominant IBS	7 patients, TEAS/sham-TEAS/control	Reduction of rectal sensitivity in IBS patients
Chang et al <sup>91</sup>	TEAS	ST36	Healthy (males)	15 volunteers (males) EA/TEAS	Enhancement of gastric myoelectrical regularity, bradygastria not significant

AP, acupuncture point; EA, electroacupuncture; GI, gastrointestinal; IBS, irritable bowel syndrome; SSc, scleroderma; TEAS, transcutaneous electrical acupoint stimulation.

#### 3.7. Treatment of depression, addiction, and stroke

Two studies investigating the treatment of depression using LS, 120,121 five studies evaluating the treatment of various addictions (i.e., alcoholism and addictions to tobacco and narcotics) using ES122-124 and LS, 125,126 and four studies examining the treatment of stroke using ES127-130 are shown in Tables 7-9, respectively. LS was used by a research group to treat depression 120,121, whereas two studies used ES devices 123,124, one used LS125 to treat tobacco dependence, one used an ES device in the treatment of drug abuse, 122 and one used LS to treat alcoholism. 126 Five studies showed that the use of ES and that of LS for treating various addictions were appropriate treatment adjuncts. ES was applied for treating stroke in four studies. All the studies in which stroke was treated, including treatment with a combination therapy consisting of TEAS and task-related training, reported treatment efficacy of TEAS or EA based on clinical trials involving 421 individuals. These results showed that ES is feasible for treating stroke. All the studies in these three categories claimed beneficial effects on the treatment of depression, various addictions, or stroke.

## 3.8. Physiological changes, diverse diseases, miscellaneous characteristics, and brain activities

All the papers regarding ASDs that induced physiological changes, treated various diseases, affected miscellaneous

characteristics, and induced brain activities are shown in Tables 10–13, 131–174 respectively. Most studies in these categories were focused on phenomenological observations or consisted of a small number of clinical trials. Many more case studies are required to demonstrate the effects of ASDs on diverse diseases. These various investigations may expand the application of modern ASDs. Due to the limited scope of this review, we did not further investigate the diverse aspects of these studies.

#### 4. Discussion

EAs, which are invasive types of ES, were the first and most intensively studied modern applications of ASDs. Recently, the number of publications regarding the clinical effectiveness of noninvasive stimulations, such as TEAS, LS, MS, and US, has been increasing (Fig. 3). The increase is more substantial for noninvasive acupuncture-like techniques, most likely due to the growing demands for painless acupuncture or acupoint stimulations. Among the 195 articles analyzed, the studies involving ES (EAs and TEASs) predominated (133 articles, 68%), followed by LS studies (44 articles, 23%). Studies involving MS (16 articles, 8%) or US (2 articles, 1%) were less common. The publication of ES studies has steadily increased since the early 2000s, whereas LS and MS showed similar increment patterns with delayed start-up points (i.e., the increases began in 2009 and 2011, respectively). Despite its long history, ES had a steady

Reference	Stimulation type	Stimulation site	Symptom	Control	Effect
Xu et al <sup>96</sup>	TEAS	PC6	PONV	Prospective, blind, & randomized study, 119 patients, TEAS/sham TEAS	Prevention of PONV after infratentorial craniotomy
Wang et al <sup>97</sup>	TEAS	Right PC6	Supratentorial craniotomy	Random TEAS (40)/control-nonacupoint (40),all standard general anesthesia	Prevalence of nausea, vomiting
Larson et al <sup>98</sup>	TEAS	Acupuncture points	Patients undergoing cosmetic surgery	Prospective, randomized, blinded, clinical trial, 122 patients, random standard pharm./pharm. + EA	Postoperative nausea & vomiting
Liu et al <sup>99</sup>	TEAS	Left-side PC6	Patients undergoing laparoscopic cholecystectomy	96 patients, random EA/placebo-EA no stim	Reduction of nausea & vomiting, pain relief
Habib et al <sup>102</sup>	TEAS	PC6/dorsum of wrist	Cesarean delivery with spinal anesthesia	Random, 91 patients, TEAS (47)/sham-APs TEAS (44)	No difference between the 2 groups (less PONV in 2 groups)
Kabalak et al <sup>100</sup>	TEAS	PC6, CV13	Tonsillectomy under general anesthesia	Randomized, controlled, prospective study, 90 children, TEAS (30)/pharm. dose (30)/no treatment (30)	Prophylaxis of postoperative retching & vomiting in pediatric tonsillectomy
Kramer et al <sup>101</sup>	TEAS	PC6	Patients receiving electroconvulsive therapy	11 patients, TEAS (9 good, 1 mixed, 1 no response)	Treating nausea & vomiting
Rusy et al <sup>105</sup>	EA	PC6	Tonsillectomy	120 patients, random EA (40)/sham-EA sham needle(40)/control no needle (40)	PONV prevention
Zárate et al <sup>103</sup>	TEAS	PC6	Laparoscopic cholecystectomy with standardized general anesthetic technique	Sham-controlled, double-blinded study, random, 221 outpatients, TEAS/placebo no stim	TEAS reduced postoperative nausea, but not vomiting
Shen et al <sup>106</sup>	EA	Antiemetic acupoints	High-risk breast cancer patients undergoing highly emetogenic chemotherapy regimen	3-arm, parallel-group, randomized controlled trial, LF-EA (37)/mock-EA (33)/no-EA (34)	Effective in controlling emesis (EA > pharm.)
Schlager et al <sup>107</sup>	LS	Bi PC6	Postoperative vomiting in children undergoing strabismus surgery	Double-blind, randomized, controlled study, 40 children, LS (20)/placebo (20)	Incidence of vomiting significantly lower
McMillan & Dundee <sup>104</sup>	TEAS	PC6	Cancer chemotherapy	- (-5)	Antiemetic action, useful adjunct to both the older antiemetics & the new antagonist ondansetron

ASD, acupuncture-like stimulation device; EA, electroacupuncture; LF, low frequency; PONV, postoperative nausea and vomiting; pharm, Pharmacological; stim, stimulation; TEAS, transcutaneous electrical acupoint stimulation.

but limited publication rate prior to 2000, whereas during the 1980s and 1990s, the number of publications on ES remained between zero article and two articles per year.

Fig. 4 shows the yearly publications of invasive (EAs) and noninvasive (TEASs) ES techniques. The total number of studies was similar between EAs (63 articles) and TEASs (70 articles). However, differences were observed in the number of publications per year; the publications associated with TEASs

showed a steady increase over time, which is in contrast to the stable annual publication pattern of EAs. Notably, the number of TEAS publications surpassed that of EAs in 2010. Specifically, TEASs were studied more than EAs over the past 5 years in the context of diseases with high therapeutic benefits, such as analgesic effect, pain relief, improvement of the alimentary system, and prevention of nausea and vomiting. The rising popularity of TEASs is presumably due to the increasing needs

Table 5 – Sun	nmary of studies on the re	ecovery of muscle	fatigue or im	provement of muscle s	trength with the four ASDs
Reference	Stimulation type	Stimulation site	Symptom	Control	Effect
Kim et al <sup>108</sup>	MS	LR9	Healthy (males)	20 participants (males), MS (10)/no MS (10)	Recovery of muscle fatigue
Kim et al <sup>109</sup>	TEAS/MS	An acupoint	Muscle fatigue	TEAS/MS/no stim	Therapeutic effect on muscle fatigue (MS better)
Zhou et al <sup>110</sup>	EA	ST36, ST39	Healthy (males)	randomized controlled trial, 43 young men, control/MA/ EA-APs/EA-non-APs	Improvement of muscle strength in both limbs
Ngai et al <sup>111</sup>	TEAS	Bi LU7, EX-B1	Healthy (males)	11 individuals (males), TEAS/placebo-TEAS no stim	Higher postexercise FEV1, prolongation of submaximal exercise
Huang et al <sup>112</sup>	EA	ST36, ST39	Healthy (males)	30 men, random EA/control	Improvement of muscle strength of both limbs
Chiu et al <sup>113</sup>	TEAS + LS/exercise + LS/LS	Acupoints	Chronic neck pain	Randomized clinical trial, 218 patients, TEAS + IR/Exercise + IR (LS)/IR (LS)	Improvement in disability, isometric neck muscle strength, pain (TEAS, exercise)
Milne et al <sup>114</sup>	TEAS/EA	LI4, LI11	Healthy	TEAS/EA	Relief of muscle spasm & musculoskeletal pain, & restoration of mobility (TEAS)

AP, acupuncture point; ASD, acupuncture-like stimulation device; EA, electroacupuncture; FEV1, forced expiratory volume in 1 second; IR, infrared; stim, stimulation; LS, laser stimulation; MA, manual acupuncture; MS, magnetic stimulation; TEAS, transcutaneous electrical acupoint stimulation.

Table 6 – Summary	y of studies on t	he reduction in	body weight with the	e four ASDs	
Reference	Stimulation type	Stimulation site	Symptom	Control	Effect
Schukro et al <sup>115</sup>	AEA	18, 87, 91 at ear	Obese females	Prospective, randomized, double-blinded study, 56 patients (females), AEA (28)/placebo dummy (28)	Reduction of body weight & BMI
Chien et al <sup>116</sup>	TEAS	ST36	Postmenopausal obese women	Prospective study, 49 women, random TEAS (24)/control no-TEAS (25)	Reduction in percentage body fat
Rerksuppaphol & Rerksuppaphol <sup>117</sup>	TEAS/EA	10 acupoints	Obese women	Prospective randomized open-label study, 45 women, TEAS/EA	Effective method for weight reduction as seen with EA
Lin et al <sup>118</sup>	EA	ST36, SP6	Postmenopausal women with obesity	Randomized controlled trial, 41 women, EA (20)/control (21)	Improvement of body composition
Jeong & Lee <sup>119</sup>	EA	Acupoints	Factitial panniculitis	2 cases (females), EA	Weight reduction

AEA, auricular electroacupuncture; ASD, acupuncture-like stimulation device; EA, electroacupuncture; TEAS, transcutaneous electrical acupoint stimulation.

Reference	Stimulation type	Stimulation site	Symptom	Control	Effect
Quah-Smith et al <sup>120</sup>	LS	LR14, LR8, CV14, HT7	Depressed participants	Random block on–off design, 10 nondepressed participants, 10 depressed participants	Antidepressant effect
Quah-Smith et al <sup>121</sup>	LS	LR14, CV14, LR8, HT7, KI3	major depressive disorder	Randomized, double blinded, placebo controlled trial, 47 participants, LA/placebo LA	Reduction of symptoms of depression

Reference	Stimulation type	Stimulation site	Symptom	Control	Effect
Penetar et al <sup>122</sup>	TEAS	PC6, TH5; LI4, PC8	Cocaine dependent or cannabis dependent	Single-blind, sham-controlled, crossover design, 20 volunteers (11 m, 9 f) TEAS/sham- TEAS/baseline ST	Modulation of mood & anxiety, no significant reduction in drug use or drug cravings
Lambert et al <sup>123</sup>	TEAS	LI4, PC8, PC6, TE5	Smoking	2 double-blind studies, 98 smokers, random TEAS-10 mA (20)/TEAS-5 mA (20)/placebo TEAS-0 mA (16)/TEAS-5 mA (19); intermittent 5 mA	Antagonizing the urge to smoke in dependent smokers
Kerr et al <sup>125</sup>	LS	4 acupoints	Smoking	Double-blind, randomized controlled trial, 387 volunteers, 3-LS 1-sham LS/4-LS/4-sham LS no stim	Assisting in smoking cessation by reducing the physical symptoms of withdrawal
Zalewska-Kaszubska & Obzejta <sup>126</sup>	ALS	Neck; 10 auricular acupoints	Alcoholics	53 patients, He–Ne LS (neck) + argon ALS	Adjunct treatment for alcoholism
Georgiou et al <sup>124</sup>	TEAS	SJ18, SJ17	Smoking cessation	Randomized controlled trial, 216 smokers, TEAS/control TEAS no stim	Insufficient power to detective real but small differences between treatment conditions

ALS, auricular laser stimulation; ASD, acupuncture-like stimulation device; f, female; LS, laser stimulation; m, male; stim, stimulation; ST, standard treatment; TEAS, transcutaneous electrical acupoint stimulation.

Reference	Stimulation type	Stimulation site	Symptom	Control	Effect
Ng & Hui-Chan <sup>127</sup>	TEAS + TRT	ST36, LV3, GB34, UB60	Poststroke	Case study, 1 man (age 61 y), TEAS + TRT	Decreased impairment & improved function in an individual with long-term chronic stroke
Gong et al <sup>128</sup>	EA	ST36	First-time cerebral infarction or hemorrhage, or a stroke history	Randomized, controlled, clinical study, 240 patients, EA (124)/control (116)	Effects on lower extremity motor function in stroke patients
Kim et al <sup>129</sup>	TEAS	Acupoints	Ischemic stroke with motor dysfunction	62 patients, 2 Hz-TEAS/120 Hz-TEAS	Helpful for motor recovery after ischemic stroke (LF-TEAS)
Wong et al <sup>130</sup>	TEAS	Acupoints	Patients with hemiplegia in stroke	Randomized, 118 patients, comprehensive rehabilitation + TEAS (59)/comprehensive rehabilitation (59)	Convenient & effective therapy for stroke

for safety without needling, low infection risk, and relatively expedient utilization of clinical trials. The recent increase in studies of LS and MS, which are noninvasive, may be understood based on the same rationale.

TRT, task-related training.

According to a recent analysis, approximately 41% of clinical studies in acupuncture research from 1991 to 2009 addressed pain and analgesia. Among the studies evaluating the four types of ASDs published through 2014, the percentage

of clinical studies addressing pain and analgesia was 33%. This reduction in the percentage of studies focused on pain and analgesia is directly related to the recently heightened interest in acupuncture research on brain activities. The percentage of publications focused on brain activities that have been published since 2010 constitutes 61% (19 articles) of all such publications since 2001 (31 articles). Excluding the emerging category of brain activity, approximately 38%

Reference Stimulatio type		Stimulation site	Symptom	Control	Effect	
Cafaro et al <sup>131</sup>	LS	Bi LI2, ST5,	Sjögren's	26 female, patients, LA/sham	Salivary flow rate	
		ST6, ST7, SI19, BL 13	syndrome		improvement	
Kim et al <sup>175</sup>	MS	LI4	Healthy	-	Improvement of peripheral vascular system circulation	
Li et al <sup>176</sup>	EA	LI4, TE5,	Supratentorial	29 patients, control (10)/EA	Prevention of decrease of	
		BL63, LR3, ST36, BL40, BL10, BL20, BL2, EX-HN4	craniotomy	(9)/sham EA (10)	immunoglobulin after surgery, no significant difference between EA & sham EA	
Litscher et al <sup>132</sup>	LS	GV20, PC6	Healthy	Randomized crossover study, 11 volunteers (3 m, 8 f), MA (GV20;PC6)/red LA (GV20;PC6)/violet LA (GV20;PC6)	HR & HRV control	
Tsuruoka et al <sup>177</sup>	US	LR3	Healthy	50 volunteers (40 m, 10 f), random US/MA	Increase of blood flow volume	
Wang et al <sup>133</sup>	LS	Right LI4	Healthy	28 volunteers, random LA-LI4/LA-non LI4	Increase of left LI4 MBF, 40 min later after stimulation ceased, the MBF still increasing significantly	
Raith et al <sup>134</sup>	LS	LI4	Premature neonates	10 neonates (7 m, 3 f), initial temp/5 min stim temp/10 min stim temp	Increase in the skin temperature	
Lee et al <sup>178</sup>	MS	PC9	Healthy	1 individual	Parasympathetic activity of the autonomic nervous system	
Jia et al <sup>179</sup>	EA	Bi ST36, ST37	Healthy	20 volunteers, EA/sham EA	Effect on autonomic function	
Jones et al <sup>180</sup>	TEAS	Bilateral PC6	Healthy	16 volunteers, random TEAS/sham-TEAS non-APs/no TEAS no-stim	Change in artery	
Lee et al <sup>181</sup>	EA	LI4, LI11	Healthy	Randomized crossover design, 14 participants, HF-EA 120 Hz/LF-EA 2 Hz	Increase in autonomic nervous activity (HF-EA), enhancing sympathovagal balance (both)	
Chang et al <sup>182</sup>	EA	ST36, LI10	Healthy	15 volunteers, LF EA (low freq. 2 Hz)/HF EA (high freq. 100 Hz)	Not affecting cardiovagal activity in normal volunteers	
Cunha et al <sup>140</sup>	LS/MA	10 acupoints	Circulatory deficiency	40 individuals, LS (20)/MA (20)	Significant increase in systolic pressure of lower limbs, consequent improvement of the revascularization index	
Litscher et al <sup>135</sup>	LS	PC6	Healthy	Randomized, controlled study, 13 volunteers, LS/control-laser off	Decrease of HR	
Kim et al <sup>183</sup> Lu et al <sup>184</sup>	EA MA, EA, TENS	PC5, PC6 Bi ST36, ST37, palm, dorsum	Healthy Healthy	EA (10)/sham-EA no stim (10) 20 volunteers, random sham-MA/MA/EA/TENS; before-A, during-A, after-A (time sequence)	EEG, ECG, HR change Cutaneous blood flow & temperature change	
Zhang et al <sup>185</sup>	TEAS	LI4, LI11	Normal & elevated blood pressure	Randomly, 27 individuals, TEAS (13, 8 m, 5 f)/control (14, 9 m, 5 f)	Reduction of systolic blood pressure, but not diastolic blood pressure	
Zhang et al <sup>136</sup>	LS	LI4, LI11	Healthy	Randomized controlled pilot study, 45 students + faculty, LA/sham-LA laser off	Reduction of blood pressure	
Cakmak et al <sup>186</sup>	EA	ST29, ST25	Healthy (m)	Prospective, randomized study, 80 volunteers, MA/2 Hz-EA/10 Hz-EA	Increase in testicular blood flow, helpful in clinical treatment of infertile men (ST29, 10 Hz)	

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Reference	Stimulation type	Stimulation site	Symptom	Control	Effect
Arai et al <sup>187</sup>	TEAS	Bi PC5, PC6/shoulder	Parturients undergoing cesarean section under spinal anesthesia	Random, 36 singleton parturients, TEAS (12)/sham-APs TEAS (12)/no treatment (12)	Reduction of the severity & incidence of hypotension after spinal anesthesia in parturients
Cheung & Jones <sup>188</sup>	TEAS	Bilateral PC6	Healthy (m)	Single-blinded, randomized controlled trial, 28 individuals, treadmill, TEAS/pre-TEAS/placebo-TEAS	HR recovery after exercise
Banzer et al <sup>137</sup>	LS	Right forearm PC6	Healthy (nonsmoking males)	Randomized, double-blinded, placebo-controlled trial, 33 healthy (m), LA (18)/control no laser (15)	Improvement of blood flow
Szeles & Litscher <sup>189</sup>	AEA	Ear acupuncture	Healthy (f)	2 healthy (f), AEA	Modulation of blood flow
Litscher <sup>138</sup>	LS	Acupuncture points	Healthy	Randomized crossover study, 22 volunteers, LS	Changes in peripheral microcirculation & surface temperature of skin
Li et al <sup>190</sup>	MS (magni- topuncture)	GV14, PC6	Healthy (m)	Randomly, 40 individuals, MS/control MS non-APs	Modulating effect on sympathetic & parasympathetic nerve activities
Hsieh et al <sup>191</sup>	EA	ST36	Healthy	8 volunteers, before/during /after EA	Physiological mechanisms responsible
Litscher & Schikora <sup>139</sup>	LS	Vision- related acupoints	Healthy	Randomized crossover trial, 27 volunteers (13 m, 14 f), LA/MA	Increases of blood flow in ophthalmic artery
Cramp et al <sup>192</sup>	TENS/TEAS	Median nerve/LI4	Healthy	Randomly, 30 individuals (15 m, 15 f), control (10)/TENS (10)/TEAS (10)	Increase in cutaneous blood flow in the TENS median nerve
Litscher et al <sup>141</sup>	LS	Vision- related acupoints	Healthy	15 volunteers (10 m, 5 f), LS/MA	Increases in blood flow velocity in posterior cerebral artery
Balogun et al <sup>193</sup>	TEAS (HVG)	ST36, ST37	Healthy	11 individuals (5 m, 6 f), 2 Hz-TEAS/120 Hz-TEAS	No increase in peripheral hemodynamic functions in asymptomatic individuals
Williams et al <sup>194</sup>	TEAS	LR3, ST36, LI11	Diastolic hypertension	Random, 10 individuals, TEAS/sham-TEAS non-APs.	Reduction of diastolic blood pressure for TEAS
Dunn et al., <sup>195</sup>	TEAS	SP6, LR3	Pregnant women	Randomly, TEAS/control no stim	Increase in frequency & strength of uterine contractions

AEA, auricular electroacupuncture; AP, acupuncture point; ASD, acupuncture-like stimulation device; EA, electroacupuncture; ECG, electrocardiogram; EEG, electroencephalogram; f, female; HF, high frequency; HR, heart rate; HRV, heart rate variability; HVG, high voltage galvanic; LA, laser acupuncture; LF, low frequency; LS, laser stimulation; m, male; MA, manual acupuncture; MBF, meridian blood flow; MS, magnetic stimulation; stim, stimulation; TEAS, transcutaneous electrical acupoint stimulation; TENS, transcutaneous electrical nerve stimulation; US, ultrasound stimulation.

of the studies were focused on pain and analgesia, which is similar to the percentage of MA studies focused on pain and analgesia.

The effectiveness analysis showed that the effectiveness of ES with respect to the analgesic effect, pain relief, and reduction of nausea and vomiting was confirmed by clinical trials involving > 1000 individuals and many RCTs. Based on clinical trials involving > 100 individuals, ES was effective in improving the alimentary system, improving muscle strength, reducing body weight, and treating stroke. Likewise, LS was shown to be useful for providing pain relief and in treating various addictions. Interestingly, the addiction treatment effect was confirmed by LS studies but not by ES studies.

#### 4.1. Limitations

Our review is based on the four most influential databases, specifically Medline, PubMed, Cochrane Library, and Web of Science; moreover, we primarily analyzed Science Citation Index (SCI) or Science Citation Index Expanded (SCI-E) journal articles. The advantage of this approach is the inclusion of quality-guaranteed articles only. Laboratory experiments on animals, MA-only clinical trials, non-English-language articles, and review articles were excluded from the analysis. The details regarding device specifications or interventional designs, including stimulation strength, duration and interval, and patient and environmental conditions, were not analyzed due to space limitations.

Reference	Stimulation type	Stimulation site	Symptom	Control	Effect
Sun et al <sup>142</sup>	**		OI	Randomized, controlled, crossover design, EA (20)/no EA (10)	Treatment in attenuating OI
Zhang et al <sup>196</sup>	TEAS	LI4, PC6, ST36, SP6	Autistic children receiving rehabilitation training	76 children, TEAS (37)/no treatment (39)	Effective for treatment of autistic children with passive & aloof social interaction style
Yang et al <sup>197</sup>	TEAS	LI4, SJ5, ST36, BL63, LR3, GB40	Supratentorial craniotomy	Randomized controlled trial, EA/sham-EA	Significantly shortened speed of postoperative recovery
Sahmeddini et al <sup>198</sup>	EA	PC6, PC5	End-stage liver disease patients undergoing orthotropic deceased donor liver	Randomized, 40 patients, norepinephrine- vasoconstrictor/EA	Reduction of severity & incidence of hypotension during anesthesia for liver transplantation
Ng et al <sup>199</sup>	TEAS	Bi PC6	transplantation Open heart surgery	40 patients, random TEAS (20)/placebo-TEAS no stim (20)	Earlier return to preoperative BP, HR, & RPP values
Wang et al <sup>200</sup>	MA/EA	Bi GB8, TE17, GB2, GB20, GV20, TE3, ST36 (MA)/bi GB8, TE17 (EA)	Tinnitus	Randomized, single-blinded, placebo-controlled design, 50 patients (46 m, 4 f), MA/EA/placebo	Short-term general effects on tinnitus (EA)
O'Brien et al <sup>201</sup>	LS	10 acupoints	Active symptoms of menopause	Double-blind, randomized, placebo-controlled study, 40 women, LS/placebo LS (off)	Treatment of menopausal symptoms (no more efficacious than MA)
Ngai et al <sup>202</sup>	TEAS	Bi EX-B1, LU7	Patients with asthma	Randomized controlled trial, 30 individuals, random TEAS/TEAS + ST/sham-TEAS + ST	Reduction in the decline of forced expiratory volume in 1s FEV (1) following exercise training
Burduli & Ranyuk <sup>203</sup>	LS + ST	Acupuncture points	Chronic noncalculous cholecystitis	73 patients, ST (35)/LA + ST (38)	Cholecystitis treatment
Su et al <sup>204</sup>	LS	Acupoints	Renal failure patients receiving regular hemodialysis	Randomized controlled trial, before/after LS	Decrease in both stress & fatigue levels
Lau & Jones <sup>205</sup>	TEAS	Bi Ex-B1	Chronic obstructive pulmonary disease	Randomized, placebo-controlled trial, 46 patients, TEAS/placebo-TEAS no stim	Management of dyspnea
Hsu et al <sup>206</sup>	EA	BL15	Healthy	10 volunteers, sham-EA/2 Hz-EA	Relaxation, calmness, & reduced feeling of tension or distress
Bray et al <sup>207</sup>	EA	Uni PC6, HT3, LR3/bi GB34, LI11, SI3	Healthy	80 individuals, EA-PC6, HT3, LR3/ EA-GB34, LI11, SI3/no stim; 5/60/100 Hz; uni/bilateral	Adjunct therapy for disorders of hypervigilance (to decrease arousal levels)
Litscher et al <sup>208</sup>	LS	ST7, TE22	Intensive care patient after severe head injury	34 volunteers (10 m, 24 f), 1 patient (head injury), acupressure/MA/LA	Reproducible functional changes in the brain
O'Reilly et al <sup>209</sup>	LS	SP6	Interstitial cystitis	Double-blind trial, random LS (29)/placebo (27)	Treatment & control cohorts experiencing similar improvements, no difference between active & sham
Li et al <sup>210</sup>	MS	GV14, PC6	Healthy	Randomly, 40 individuals, MS/control MS non-APs	Effects of driving fatigue

AP, acupuncture point; ASD, acupuncture-like stimulation device; BP, blood pressure; EA, electroacupuncture; f, female; FEV1, forced expiratory volume in 1 second; HR, heart rate; LA, laser acupuncture; LS, laser stimulation; m, male; MA, manual acupuncture; MS, magnetic stimulation; OI, orthostatic intolerance; RPP, rate pressure product; ST, standard treatment; stim, stimulation; TEAS, transcutaneous electrical acupoint stimulation.

Reference	Stimulation type	Stimulation site	Symptom	Control	Effect
Chen et al <sup>143</sup>	LS	LU9, PC7, HT7, SI4, SJ4, LI5, SP3, LR3, KI4, BL65, GB40, ST42	Healthy	76 candidates	Complementary & interaction for current flow of meridians
Gopalan et al <sup>211</sup>	EA	Acupuncture points	Implanted with cardiac device	-	Safety in patients with a total artificial heart
Irnich et al <sup>212</sup>	LS/Seirin (sham-LS)	LI4, LU7, LR3	Healthy	Randomized, double-blinded, crossover design, 34 volunteers, LS (18)/sham-LS (16)	Valid placebo control in laser acupuncture studies (Seirin)
Litscher & Wang <sup>213</sup>	MA/LS	LU6	Healthy	1 person, MA/LA	Changes of electrical skin impedance
Thompson & Cummings <sup>214</sup>	EA	Acupuncture points in a limb	Healthy	-	No detectable currents in the chest (safety)
Leung et al <sup>215</sup>	TEAS/MA/EA	LI4	Healthy	15 individuals, TEAS/MA/EA	Difference in electrical conductance between APs & non-APs
Litscher et al <sup>216</sup>	LS	Acupuncture points	Healthy	29 volunteers (9 m, 20 f), LA/placebo-LA; before/after	Change in the median value of cold pain, no significant changes in parameters of thermal sensory & pain thresholds
Chang et al., <sup>217</sup>	EA/TEAS	Left LI4	Healthy	13 volunteers, 2 Hz-EA/2 Hz-TEAS/100 Hz-TEAS	Changes of cutaneous reflex

AP, acupuncture point; EA, electroacupuncture; f, female; LA, laser acupuncture; LS, laser stimulation; m, male; MA, manual acupuncture; TEAS, transcutaneous electrical acupoint stimulation.

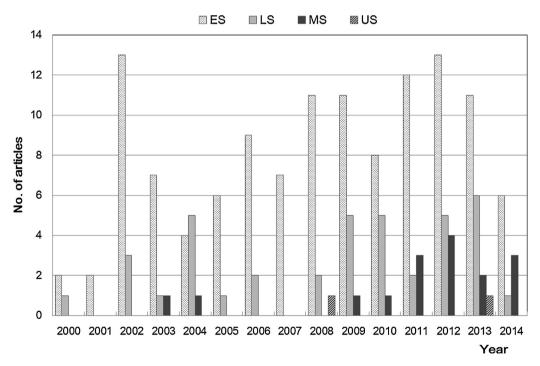


Fig. 3 – The number of published articles on the four ASDs per year.
ASD, acupuncture-like stimulation device; ES, electrical stimulation; LS, laser stimulation; MS, magnetic stimulation; US, ultrasound stimulation.

Reference	Stimulation type	Stimulation site	Symptom	Control	Effect
Guo et al., <sup>144</sup>	MS	PC6	Healthy	6 right-handed volunteers (3 m, 3 f)	Brain activity
Zhang et al <sup>145</sup>	MS	Left GB37	Healthy	GB37-MS/mock point-MS	Brain activity
Raith et al <sup>146</sup>	LS	Bi LI4	Term &	20 neonates (12 m, 8 f), LA	Brain activity
			preterm neonates	period/postintervention period	·
Quah-Smith et al <sup>147</sup>	LS	LR8	Healthy	16 participants, random on-off block design, LA/MA	Brain activity
Zhang et al <sup>148</sup>	TEAS	LI4, PC8	Healthy	18 individuals (9 m, 9 f), all individuals TEAS	Brain activity
⁄in et al <sup>149</sup>	MS	PC6	Healthy	_	Brain activity
ee et al <sup>150</sup>	MS	PC9	Healthy	_	HRV & brain activity
itscher <sup>151</sup>	LS	PC6	Healthy	40 volunteers, LA/MA	Brain activity
<i>W</i> u et al <sup>152</sup>	LS	Palm	Healthy	single-blind randomized trial, 40 individuals (m), random LS (20)/sham LS (20)	Brain activity
itscher et al <sup>153</sup>	LS	Bi PC6	Healthy (f)	1 volunteer (f), LA	Brain activity
<i>ľ</i> u et al <sup>154</sup>	MS	PC6	Healthy	MS-PC6/ MS-mock point	Brain activity
iang et al., <sup>155</sup>	TEAS	LI4, PC8	Healthy	40 individuals, TEAS (40)	Brain activity
Hsieh et al <sup>156</sup>	LS	KI1	Healthy right handed	36 right-handed volunteers, random MW LA (12; 8 m, 4 f)/CW LA (12; 9 m, 4 f)/placebo LA(12)	Brain activity
ru et al <sup>157</sup>	MS	PC6	Healthy	before MS/during MS/after MS	Brain activity
Kim et al <sup>158</sup>	MS	PC9	Healthy	_	Vascular & brain activity
o & Jo <sup>159</sup>	MS	HT4, HT6	Healthy	23 young adults (aged 19–22 y)	Brain activity (pole direction)
Zyloney et al160 <sup>160</sup>	EA	LI3, LI4 right hand	Healthy, right handed	48 individuals, random EA/sham EA	Brain activity
Quah-Smith et al <sup>161</sup>	LS	LR14, CV14, LR8, HT7	Healthy	10 individuals, random LA/LA-sham point	Brain activity
Ku et al <sup>162</sup>	MS	ST36, LI4	Healthy	MS/MS-mock point	Brain activity
Na et al <sup>163</sup>	EA	GB34	Healthy	12 individuals, EA/EA-sham points,	Brain activity
Ku et al <sup>164</sup>	MS	ST36	Healthy	Pre-MS/post-MS (0.5 Hz/1 Hz/3 Hz)	Brain activity
An et al <sup>165</sup>	EA	LI4, LI11	Healthy	Brain SPECT EA (20)/PET EA (13); before/during /after EA	Brain activity
Vang et al <sup>166</sup>	EA	Right LI4	Healthy	EA (9)/sham-point EA (5)	Brain activity
Zeng et al <sup>167</sup>	EA	LI4	Healthy (right handed)	EA	Brain activity
Litscher et al <sup>168</sup>	LS	Acupoints	Healthy	Randomized controlled crossover trial, 18 volunteers (7 m, 11 f), before/during-LA/after	Modulation of blood flow brain activity
Zhang et al <sup>169</sup>	EA	Left leg ST36, SP6	Healthy (right handed)	48 individuals, 2 Hz-EA/100 Hz-EA	Analgesia effect/brain activity
i et al <sup>170</sup>	EA	TE8, GV15	Healthy (Chinese males)	17 volunteers (m), EA-TE8 (11)/EA-GV15 (6)	Brain activity, typical language areas in the le inferior frontal cortex n activated
Kong et al <sup>171</sup>	EA	Left hand LI4	Healthy (right handed)	11 volunteers (6 m, 5 f), EA/MA	Brain activity
Siedentopf et al <sup>172</sup>	LS	Left foot BL67	Healthy (m)	10 volunteers (m), LA/dummy LA	Brain activity
<i>W</i> u et al <sup>173</sup>	EA	GB34	Healthy	45 volunteers, EA (15)/mock-EA no stim (7)/minimal-EA superficial & light stim	Modulation of hypothalamus limbic system
Chang et al <sup>174</sup>	MA/TEAS	LI4	Healthy	(8)/sham-EA non-Aps (15) Randomly, control TEAS no stim/MA/2 Hz-TEAS/100 Hz-TEAS	Increases in amplitude H-reflex (TEAS), 100 Hz TEAS has greater effect

AP, acupuncture point; ASD, acupuncture-like stimulation device; EA, electroacupuncture; f, female; HRV, heart rate variability; LA, laser acupuncture; LS, laser stimulation; m, male; MA, manual acupuncture; MS, magnetic stimulation; PET, positron emission tomography; SPECT, single-photon emission computed tomography; stim, stimulation; TEAS, transcutaneous electrical acupoint stimulation.

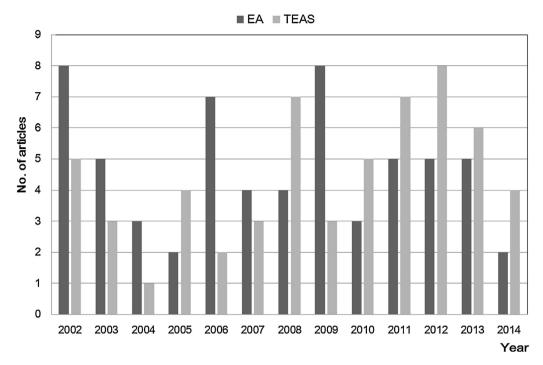


Fig. 4 – The number of articles on ES methods with years, where EAs include the invasive techniques of EA, AEA, and EHA, and TEASs include the noninvasive techniques of TEAS and TENS.

AEA, auricular electroacupuncture; EA, electroacupuncture; EHA, electrical heat acupuncture; ES, electrical stimulation; TEAS, transcutaneous electrical acupoint stimulation; TENS, transcutaneous electrical nerve stimulation.

#### 5. Conclusions

In the past decade, modern ASDs have been studied extensively for their clinical effectiveness and to test equivalence or noninferiority with traditional MA. Among the modern ASDs, ES was found to be most widely studied, and its popularity was sequentially followed by LS, MS, and US. Specifically, EAs, which are invasive types of ES, were the first and most intensively studied types of ASDs, whereas TEASs, which are noninvasive types of ES, have surpassed EAs in publication number since 2010. Very recently, noninvasive techniques, such as TEASs, LS, MS, and US have gained research attention, as evidenced by increasing annual publications.

The most extensively studied treatment effects were for analgesia and pain relief, whereas rapid growth has occurred in the research field of the effects of treatments on brain activities. The overall quality of the study designs was moderate, as 58% of the studies were based on RCTs and 96% of the RCT-based outcomes reported therapeutic benefits. ES was effective in providing an analgesic effect, pain relief, and a reduction of nausea and vomiting, based on clinical trials involving > 1000 individuals. Based on > 100 clinical trials, ES was shown to be effective in improving the alimentary system, improving muscle strength, reducing body weight, and treating stroke. LS was effective in pain relief and for treating various addictions. We anticipate more studies on the therapeutic effects of ASDs, particularly concerning noninvasive methods, to meet the growing needs of guaranteed safety, decreased risk of infection, decreased pain, and improved convenience.

#### **Conflicts of interest**

No conflicts of interest are declared.

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