P-Stim™ auricular electroacupuncture stimulation device for pain relief

Sabine M Sator-Katzenschlager† and Andrea Michalek-Sauberer

Acupuncture is now accepted as a complementary analgesic treatment. Auricular acupuncture is a distinct form of acupuncture. Electrical stimulation of acupoints (electroacupuncture) increases the effects of acupuncture. Recently, an auricular electroacupuncture device, the P-Stim™, has become available. Clinical studies in outpatients have investigated the P-Stim in chronic musculoskeletal pain and its use for minor surgery. In chronic cervical or low back pain, auricular electroacupuncture was more effective than conventional auricular acupuncture. The results in acute pain were controversial. Auricular electroacupuncture reduced pain and remifentanil consumption during oocyte aspiration when compared with conventional auricular acupuncture or a sham treatment. However, after third molar tooth extraction, auricular electroacupuncture and auricular acupuncture failed to reduce either postoperative pain or analgesic consumption. Further large-scale studies are required to evaluate the analgesic efficacy of auricular electroacupuncture.

Expert Rev. Med. Devices 4(1), xxx–xxx (2007)

Contents

†Author for correspondence
Department of Anesthesiology and Intensive Care Medicine (B), Medical University of Vienna, Waehringer Guertel 18–20, A-1090 Vienna, Austria
Tel.: +43 140 400 4144
Fax: +43 140 400 4165
sabine.sator-katzenschlager@meduniwien.ac.at

KEYWORDS:
acupuncture, auricular acupuncture, electroacupuncture, neurobiology, pain

Theoretical background of auricular & electroacupuncture

It has long been accepted that acupuncture, that is, puncturing or scraping certain points on the body surface with needles, can be therapeutically useful in various diseases and produces analgesic or anesthetic effects. The use of acupuncture, electroacupuncture (EA) and auricular acupuncture has become the subject of scientific research during the last few decades. Recently, an auricular electrical stimulation device, the so-called P-Stim™, has become commercially available. This article gives an overview of the theoretical background of auricular EA and discusses its use in the treatment of chronic and acute pain. Related techniques such as transcutaneous electrical nerve stimulation are excluded from the discussion.

Auricular acupuncture – traditional Chinese & nogier systems

Auricular acupuncture is a distinct form of acupuncture. The auricles' importance was first mentioned in the Huang Di Nei Jing (~100 BC): 'All the vessels congregate in the ear'. During the 1950s the French physician Paul Nogier developed a western concept of auricular acupuncture that is based on the assumption that each part of the body is represented in a specific zone on the external ear. He described a map of the arrangement of auricular acupuncture points. With the head represented towards the lower lobule, the hands and feet at the uppermost portion of the auricle and the body in between, the projection of different body regions can be compared with an inverted fetus. This somatotopic relation has been confirmed in double-blind studies investigating auricular diagnosis [1–3].

Auricular acupuncture points are discrete anatomic loci of the external ear, measuring approximately 1–5 mm in diameter [4]. The number of auricular acupuncture points is not well defined with reported numbers ranging from 43 to 900 [5]. Auricular acupuncture points are characterized by a lower electrical skin resistance and a heightened tenderness to touch compared with the surrounding tissue. The increased electrical conductivity is probably

10.1586/17434440.4.1.xxx

ISSN 1743-4440

related to the autonomic control of blood vessels rather than an increased sweat gland activity, whereas the tenderness of reactive auricular acupuncture points is possible due to the accumulation of noxious substances in the subcutis [2,3].

Mechanisms of auricular acupuncture

Several possible mechanisms have been proposed for acupuncture analgesia:

- Stimulation of A-δ fibers in the skin can inhibit painful stimuli from the periphery, thus, reducing pain perception [6,7];
- Activation of encephalin-containing interneurones in the substantia gelatinosa of the spinal grey matter results in inhibition of the conduction of pain signals to the brain;
- Acupuncture leads to a release of β-endorphin and met-encephalin in the brain [8–10];
- Activates descending pain control systems in the mid-brain [8–16];
- Modulating effects on the central pain network in the hypothalamus and the limbic system have been proposed [8–16].

Functional magnetic resonance studies demonstrate that stimulation of acupuncture points elicits effects in specific brain regions [8,9,13–19]. These effects of acupuncture are believed to be point specific as opposed to nonspecific inhibitory control mechanisms [20]. Further studies have shown that acupuncture activates multiple analgesia systems, stimulates pain modulation systems and leads to the release of neurotransmitters such as endogenous opioids [21]. Acupuncture has also been shown to normalizes the protein expression profile of the hypothalamus caused by neuropathic pain [22,23] and to exert neuroprotective effects on dopaminergic neurons [24]. These theories, however, are not undisputed. Some investigators have not been able to replicate the findings that endorphins play a role in acupuncture analgesia [25,26]. Critics have also noted that the vast majority of the research supporting acupuncture originates from China [27], and the percentage of 'negative' results published by these Chinese investigators is close to zero [28]. Doubts also arise from preclinical studies of acupuncture on experimental pain in human volunteers. Approximately half of these investigations show an analgesic effect whilst the other half fails to do so [29].

Mechanisms of electroacupuncture

In addition to the use of needles, acupuncture points can also be 'stimulated' with heat, electrical currents [30], pressure, laser light [31] or shock waves [32]. Electrical stimulation of acupuncture points is considered to increase the analgesic effects of acupuncture.

EA analgesia is mediated by humoral mechanisms, which was confirmed by a cerebrospinal fluid cross-infusion study. When cerebroventricular fluid obtained from rabbits that have been subjected to EA was infused to the third ventricle of an acupuncture-naïve rabbit, a transfer of the analgesic effect from the donor to the recipient rabbit was observed [33]. Han and colleagues proposed the involvement of various neurotransmitters including monoamines, favoring serotonin [34].

Later studies have demonstrated that opioid peptides in the periaqueductal gray are involved in EA analgesia. The type of neuropeptides to be released by EA is dependent on stimulation frequency. A low frequency of 2 Hz accelerates the release of enkephalin, β-endorphin and endomorphin, while a high frequency of 100 Hz selectively increases the release of dynorphin. A combination of both frequencies with a simultaneous release of all four opioid peptides, results in a maximal therapeutic effect [35,36]. Cumulative analgesic effects may be achieved by longer electrical stimulation periods [37].

Recent evidence demonstrates that nitric oxide is also involved in mediating the cardiovascular responses to EA stimulation through the gracile nucleus–thalamic pathway. The role of other substances (e.g., serotonin, catecholamines, inorganic chemicals and amino acids such as glutamate and α-aminobutyric acid), that have also been proposed to mediate analgesic, as well as cardiovascular effects of acupuncture, is poorly understood.

Mechanisms of auricular electroacupuncture

The mechanism of auricular EA is still not fully understood. In one study, a change in the blood flow of cerebral arteries was demonstrated after electrical stimulation of an auricular acupoint [38]. Further studies are needed to define the underlying mechanisms of auricular EA.

Indications of auricular acupuncture

Auricular acupuncture is most commonly used in acute and chronic pain states, and as complementary therapy for addiction and obesity.

The analgesic effects of auricular acupuncture have been proven in numerous studies in acute [39–41] and chronic pain states [42–46]. A case report has also suggested that auricular acupuncture is effective for acute migraine pain [47]. However, there have been contradictory results. Ceccherelli failed to demonstrate a therapeutic effect when auricular acupuncture was combined with body acupuncture for the treatment of cervical myofascial pain [48]. There is a need for further well-designed clinical trials [49].

Wen and Cheung broadened the indication of auricular acupuncture by using it for the treatment of opioid addiction [50–52], thus, providing the basis for the National Acupuncture Detoxification Association protocol [53]. Although auricular acupuncture has since been widely used in the treatment of both cocaine and alcohol addiction, a recent review could not confirm a therapeutic effect [54–56]. The addition of auricular acupuncture to conventional treatments for alcoholism also had no benefit [57,58]. In addition, no relevant benefit could be found with auricular laser acupuncture for the treatment of alcohol withdrawal [43]. The studies on the use of auricular acupuncture for cocaine addiction were controversial, which emphasizes the need for further large-scale, controlled studies [43,58–60].

The results for auricular acupuncture therapy for nicotine abuse are also controversial. While a recent review concluded that auricular acupuncture, laser therapy and electroacupuncture were ineffective adjunctive treatments for the cessation of smoking [61], Kang and colleagues found a significant tendency towards a reduction of cigarette consumption with auricular acupuncture [62].

Therapeutic effects of auricular acupuncture and some effects on blood lipids in juvenile simple obesity have been described [63]. Acupuncture supposedly affects appetite, intestinal motility and metabolism, as well as emotional factors such as stress [64]. Transcutaneous electrical nerve stimulation of specific auricular acupuncture points concave an effect on appetite suppression, which can lead to weight loss [65]. However, most trials thus far are descriptive in nature and use nonstandard treatment protocols. Therefore, further high-quality, controlled studies are needed to confirm the role of auricular acupuncture for weight loss [66].

Auricular electroacupuncture using a P-Stim™ device

P-Stim™ development

The P-Stim is a device that has been developed for the continuous, ambulatory application of auricular EA. First-generation P-Stim devices resembled a hearing aid (FIGURE 1). The rechargeable device was fixed by an anchor behind the ear. The apparatus was rather stiff, which limited patient comfort. In 2000 an improved version of the P-Stim device became commercially available in Europe (FIGURE 2). The new device is a single-use product, smaller (13 × 8 mm) and mounted on adhesive foam.

Description

The P-Stim device consists of a microcontroller that delivers electrical pulses with alternating polarity via three specially designed, permanent auricular acupuncture needles. The counter-electrode is an adhesive electrode (hydrogel), which also serves to fix the whole P-Stim device behind the ear. Three serial nickel metallic heart cells with 1.20-V batteries provide the required stimulation energy for a maximum of 96 h. This constant current source guarantees equivalent stimulation energy regardless of the individual impedance of the skin.

Usually the stimulation pattern consists of 1 Hz single pulses (pulse duration 1 ms) with a rectangular wave form. The current direction is inverted every second pulse, which is intended to avoid polarization effects. To minimize the risk of adaption or tolerance to the electrical stimulation, stimulation is applied for 3 h, followed by a pause of 3 h.

Technical details

Technical details of the P-Stim device are summarized in TABLE 1 and FIGURE 3. The stimulator consists of a microcontroller and a bit-coded ST62T60BM6 interface. The P-Stim has a read-only-memory capacity of 4 kB static and 512 bytes dynamic space, using five interrupt vectors with 8 MHz clock frequency. In the output stage, the current is amplified to drive three parallel stimulation channels.

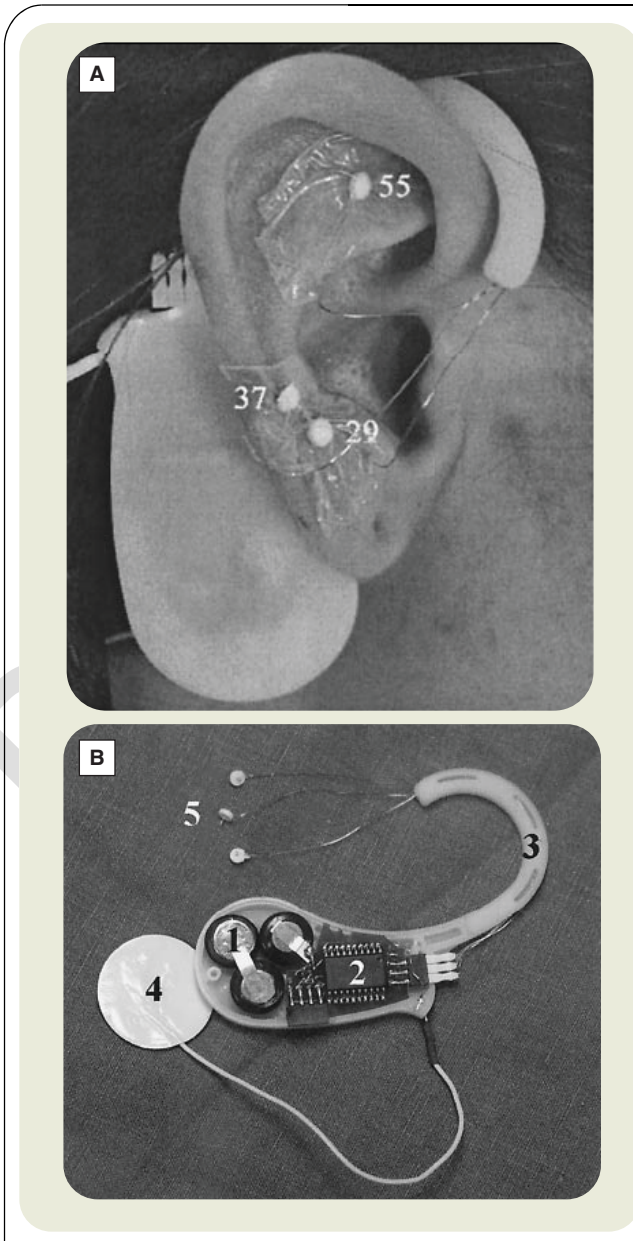

Figure 1. The electrical point stimulation device P-Stim™ – first generation. (A) P-Stim device – first generation *in situ*: acupuncture points are indicated by bullets and numbered according to the nomenclature of Nogier [1]: 37 (cervical spine), 55 (shen men) and 29 (cushion). **(B)** The P-Stim device consists of an automated accucharger for the nickel metal hydride cells (1) and a microcontroller with a bit-coded RS232 interface (2). This first-generation P-Stim model is fixated via an anchor (3) behind the patient's ear. The neutral electrode (4) is positioned behind the ear. Three wires connect the P-Stim with the acupuncture needles (5).

Safety

For safety reasons, the maximum current is limited to 4 mA for all channels. Reliability of the function mode is controlled by an integrated watchdog and automatically switched off by low voltage.

The risk of processor failure resulting in continuous voltage at the stimulation electrodes at the level of the battery voltage (~3.8 V) is prevented by the series connection of a capacitor in

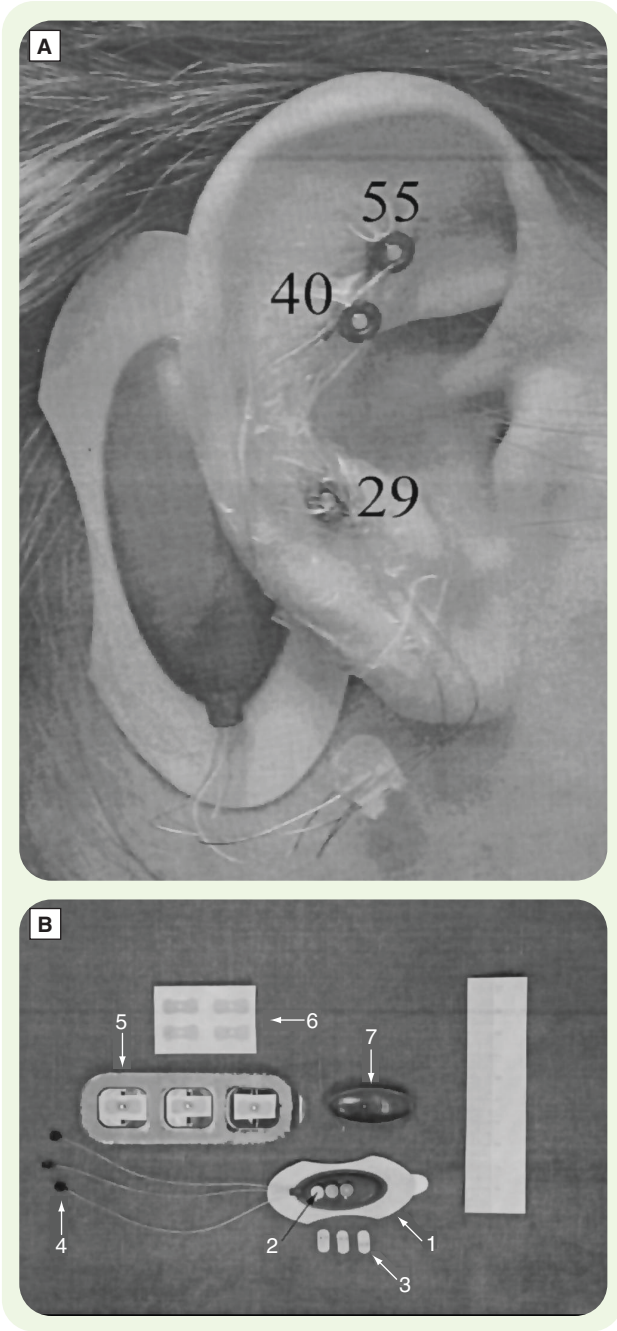

Figure 2. Electrical auricular point stimulation device P-Stim™.
(A) P-Stim device *in situ*: acupuncture points are indicated by closed circles and numbered according to the nomenclature of Nogier [1]: lumbar spine (40), shen 6 men (55) and cushion (29). **(B)** The P-Stim device consists of the microcontroller and interface (7) and is mounted on adhesive foam (1) that keeps it behind the patient's ear. The batteries (2) are protected by a cover (3) to prevent accidental activation and energy loss before the intended activation. The device is connected by three wires (4) with the disposable titanium auricular acupuncture needles (5). Adhesive tape for needle fixation (6). Scale: 10 cm.

the stimulation lead. This means that there is no risk to the patient of excessive exposure to direct voltage if the microcontroller should come to an uncontrolled stop.

Table 1. Technical details of the P-Stim™ device.

Microcontroller	
Type	S3C9444 MTP/Flash
Manufacturer	Samsung
Memory	2K
Voltage Digital Driving	2–5.5 V
Timing	Int. RC oscillator 0.5 MHz
Operating temp	-40 to +85°C
Package	8-SOP-225
Development tools	
System	OPENice i500 Version 2.15 SAM8
Manufacturer	AIJI System Co., Ltd
Program language	Assembler

Indications & contraindications

In Europe the P-Stim device is a medical product registered for the use in all indications of auricular acupuncture. Studies support its use for the treatment of various acute and chronic pain states.

Contraindications against the use of the P-Stim device include the usual contradindications for auricular acupuncture with permanent needles (e.g., immunocompromised patients), the presence of a pacemaker and the concomitant use of transcutaneous electrical nerve stimulation.

Studies on the use of the P-Stim™ device for acute & chronic pain states

Use of the P-Stim™ in acute pain

So far, studies on the use of the P-Stim in acute pain are contradictory. One randomized, double-blind study evaluated the use of auricular EA during oozyte aspiration for *in vitro* fertilization [67]. A total of 94 women received either auricular acupuncture with (EA: n = 32) or without (A: n = 32) 1 Hz electrical stimulation using a P-Stim device at the auricular acupuncture points 29 (cushion), 55 (shen men) and 57 (uterus). Thirty patients in the control group (CO) had the P-Stim device without electrical stimulation connected to small metal plates instead of needles at the respective auricular acupoints. All patients received patient-controlled analgesia with remifentanil (20 µg bolus over 30 s, lockout period 1 min). Pain intensity and psychological well-being were assessed by means of visual analogue scales (VAS); tiredness, nausea and vomiting, and analgesic drug consumption were documented. Pain relief and subjective well-being were significantly greater in group EA during and after the procedure as compared with group A and CO. Patients in group CO were significantly more tired than in group A and EA. Remifentanil requirement and nausea were significantly lower in the EA group (FIGURE 4).

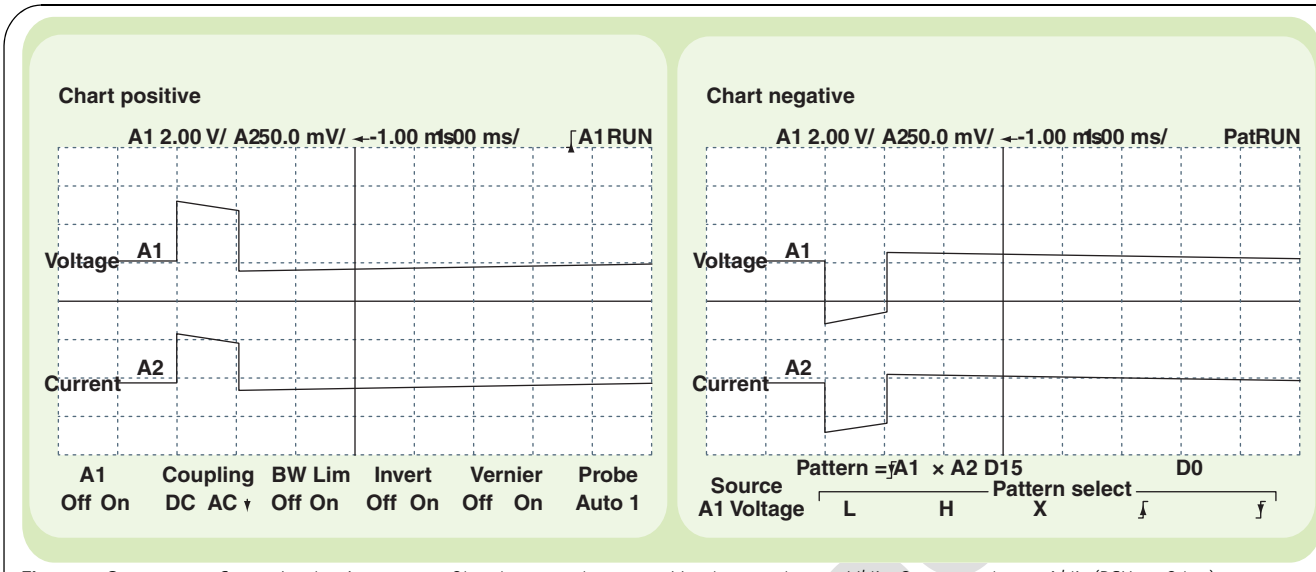

Figure 3. Output waveforms. Load resistance: 500 Ohm; battery voltage: 3,84 V; voltage scale: 2,00 V/div; Current scale: 5 mA/div (RSH=100 hm).

Another prospective, randomized, double-blind, placebo-controlled study investigated the effects of auricular EA on pain and analgesic drug consumption in the first 48 h after unilateral mandibular third molar tooth extraction, a model of acute pain [68].

Patients received either auricular acupuncture with (EA: n =76) or without (A: n = 37) electrical stimulation at an alternating frequency of 2/100 Hz, or a sham auricular EA with metal plates instead of needles and no electrical stimulation (CO: n = 36) at the auricular acupuncture points one (tooth), 55 (Shen men) and 84 (mouth) during the entire study period. Regularly rated pain intensity (five-point-verbal rating scale), consumption of acetaminophen 500-mg tablets and additional rescue medication with mefenamic acid 500 mg were assessed. Median fraction of time when pain was rated as moderate or worse (upper and lower quartile): EA: 33% (12%, 64%); A: 22% (6%, 56%); CO: 30% (7%, 53%); did not differ significantly between the treatment groups. There were no significant differences in mean number of acetaminophen 500-mg tablets (range): EA: 5.2 (0–12); A: 4.6 (0–11); CO: 5.4 (0–10); or percentage of patients requiring additional mefenamic acid: EA: 19%; A: 18%; and CO: 19%. It was concluded that neither auricular EA nor auricular acupuncture alone reduced either pain intensity or analgesic consumption in the molar tooth extraction model of acute pain.

Use of the P-Stim™ chronic pain

Two studies in patients with chronic musculoskeletal pain found that pain relief with auricular EA was more effective than conventional manual auricular acupuncture [69].

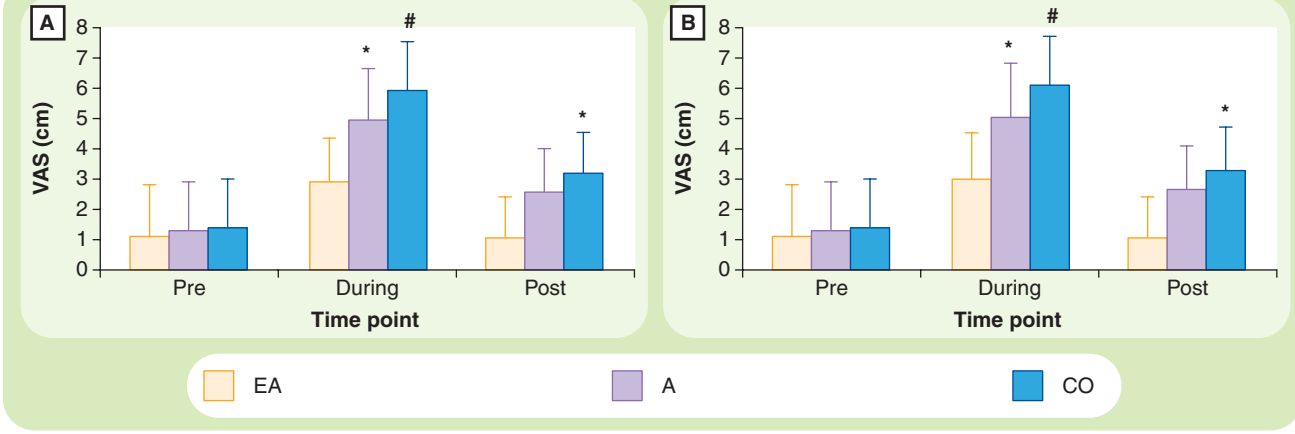

Figure 4. Effect of auricular electroacupuncture (group EA), acupuncture (group A) or placebo (group CO) on pain intensity (A), subjective well-being (B) in patients during oocyte aspiration in *in vitro* fertilisation treatment [67]. Data are presented as means ± SD.
*p < 0.005 versus group EA. #p < 0.005 versus group A. Pain intensity and subjective well-being were assessed by visual analogue scales (VAS) ranging from 0 mm (no impairment) to 100 mm (worst deterioration imaginable). The degree of tiredness and nausea were assessed by using a verbal rating scale (0 = no, 1 = mild, 2 = moderate, 3 = severe).

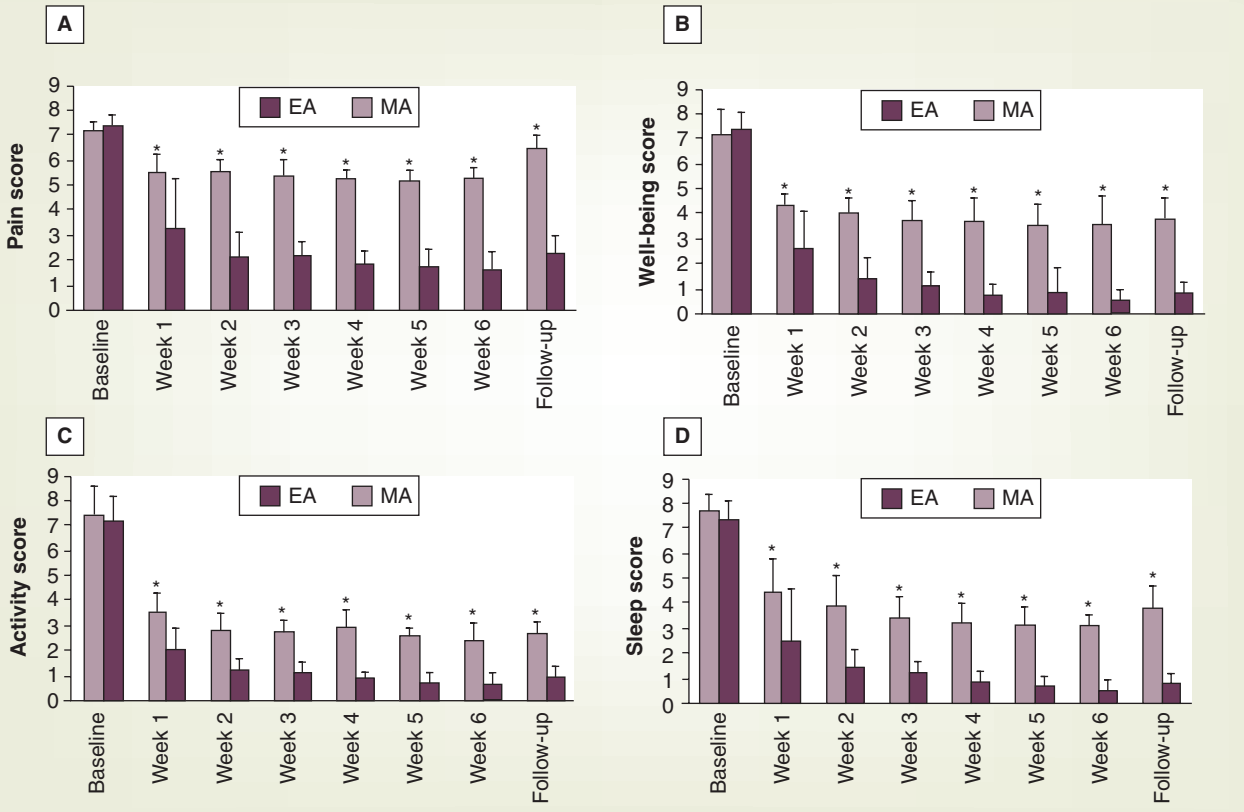

Figure 5. Effect of MA and EA on pain intensity, physical activity, psychological well-being and sleep in chronic cervical pain patients [69,70]. Subjective scores ranging from 0 (no impairment) to 10 (worst deterioration imaginable). Data are reported as mean ± SD of, *p < 0.05 between the groups. The reduction in pain scores is significantly higher in the EA group than in the conventional MA group **(A)**. Similarly, psychological well-being **(B)**, activity **(C)**, and sleep **(D)** are significantly improved in patients receiving electrical point stimulation during the 6-week treatment period and a follow-up 4 after weeks.
EA: Electroacupuncture; MA: Manual auricular acupuncture.

In the first study, 21 patients suffering from chronic cervical pain (>6 months) without radicular symptoms and insufficient pain relief (>5 on a 11-point VAS) under standard analgesic medication were included. All patients received auricular acupuncture at the acupuncture points 37 (cervical spine), 55 (shen men) and 29 (cushion). In ten patients, the needles were stimulated with 1 Hz, monophasic 2 mA constant current using a first-generation P-Stim device (FIGURE 1). To avoid tolerance to EA, the duration of electrical stimulation was limited to cycles of 3 h, followed by a 3 h pause. Eleven control patients also wore a P-Stim, but no electrical stimulation was administered. All needles were withdrawn 48 h after insertion. Acupuncture was performed once a week for 6 weeks. Patients had to complete a questionnaire assessing pain intensity (VAS), psychological well-being, activity, sleep and demand for rescue medication (lornoxicam and tramadol). The reduction in pain scores was significant in the auricular EA group (FIGURE 5). Similarly, psychological well-being, activity and sleep were significantly improved in patients receiving electrical acupuncture, and consumption of rescue medication was significantly less compared with the control group. No adverse effects were observed in either group.

The second randomized, double-blind study included 61 patients with chronic (>6 months) low back pain without radicular symptoms and insufficient pain relief (VAS >5) under standard analgesic medication [70]. In this study, second-generation P-Stim devices were used (FIGURE 2). All patients received auricular acupuncture at the auricular acupoints 29 (cushion), 40 (lumbar spine) and 55 (shen men). Patients in the EA group (n = 31) had low-frequency auricular EA as previously described. Patients in the control group (n = 30) wore the P-Stim device without receiving electrical stimulation. Treatment was performed once weekly for 6 weeks and in each group needles were withdrawn 48 h after insertion. During the study period and at 3 months follow-up, patients were asked to complete the McGill questionnaire. Psychological well-being, activity level, quality of sleep and pain intensity were assessed by means of a VAS; moreover, analgesic drug consumption was documented. Pain relief was significantly better in the EA group during the study and the follow-up period as compared with manual auricular acupuncture. Similarly, psychological well-being, activity and sleep were significantly improved in the EA group versus the CO group. Consumption of analgesic rescue medication was also less in the EA group, and more patients returned to full-time employment (FIGURE 6).

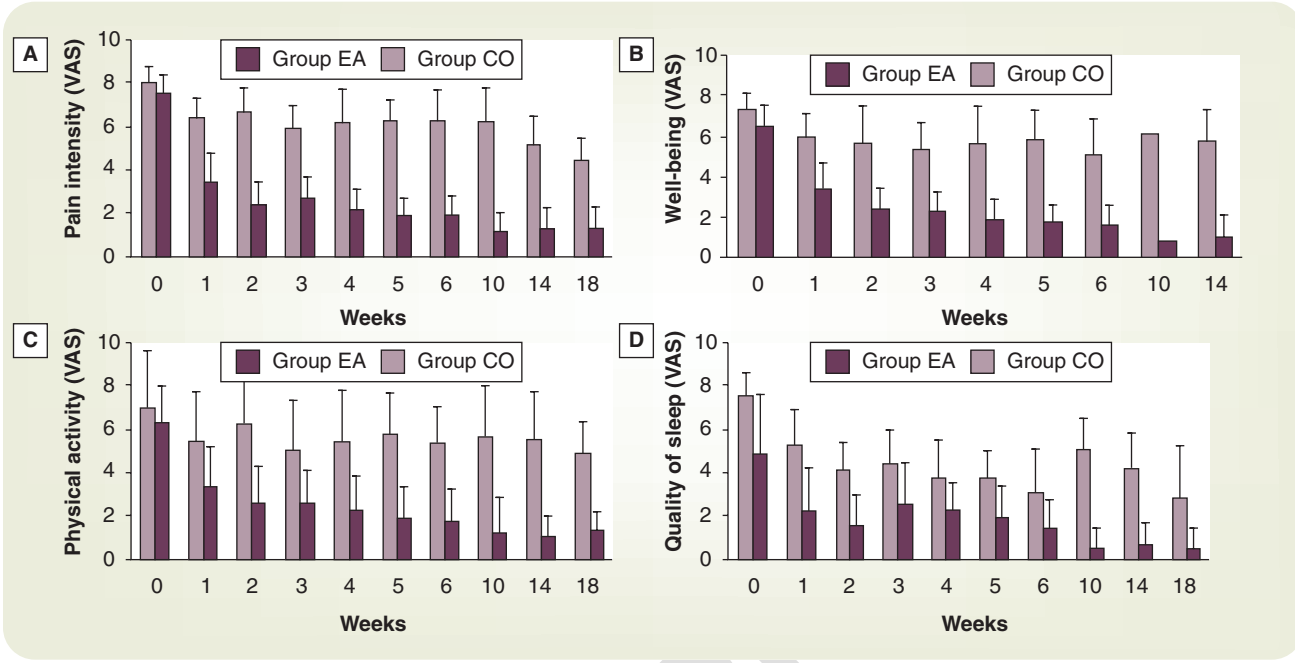

Figure 6. Effect of auricular electroacupuncture (group EA) versus sham-electroacupuncture (group CO) on pain intensity (A), physical activity (C), psychological well-being (B) and the quality of sleep (D) in chronic low back pain patients. Subjective VAS ranging from 0 (no impairment) to 10 (worst deterioration imaginable) [70]. Data are presented as means + SD, significance *P < 0.05 between the two groups. From the first week on, the reduction in pain scores was significantly larger in group EA than in group CO (A). Similarly, psychological well-being (B), physical activity (C), and to some degree quality of sleep (D) significantly improved in patients of group EA during the 6-week treatment period and a follow-up after 3 months.
CO: Control group; EA: Electroacupuncture; VAS: Visual analog scales.

There were no adverse effects. These results are the first to demonstrate that continuous EA stimulation of auricular acupuncture points improves the treatment of chronic low back pain in an outpatient population.

Conclusion

In summary, auricular EA is likely to become a more widely used adjuvant to other analgesic modalities for the management of a wide variety of acute and chronic pain syndromes. Further studies are desirable to broaden the spectrum of indications for auricular EA.

Expert commentary

Auricular EA is a new field of acupuncture. Studies support its use as an adjuvant to other analgesic modalities for the management of acute and chronic pain. Two studies in outpatients with chronic musculoskeletal pain showed a significant pain reduction with auricular EA [69–71]. In acute pain patients one positive

Key issues

- Auricular acupuncture and related techniques are increasingly used as an adjuvant to other analgesic modalities in acute and chronic pain.
- Postulated mechanisms of electroacupuncture (EA) analgesia include neuronal and humoral pathways.
- Depending on the frequency of electrical stimulation, different neurotransmitters are released including endorphins, endomorphins, dynorphins, nitric oxide and serotonin.
- The mechanisms of auricular EA are still poorly understood.
- So far, studies support the use of auricular EA as an alternative therapeutic option in the treatment of chronic cervical and low back pain.
- Auricular EA reduces the analgesic requirements in acute pain management during oocyte aspiration in *in vitro* fertilisation treatment but has no effect after third molar surgery.
- The recently introduced P-Stim™ auricular EA device offers the advantage of a small size and the possibility to administer the therapy on an ambulatory basis, obviating the need for frequent clinic visits to receive treatments.
- Further studies are desirable to broaden the spectrum of indications for auricular EA.

result during oocyte aspiration for *in vitro* fertilization [67] is contrasted by one negative result after third molar surgery [68].

The recently introduced P-Stim auricular EA device offers the advantage of a small size and the possibility to administer the therapy on an ambulatory basis, obviating the need for frequent clinic visits to receive treatments.

Five-year view

Future studies must clarify potential useful indications for the P-Stim auricular acupuncture device in the multimodal management of acute, subacute and chronic pain, as well as for treating other medical conditions. Comparative studies should evaluate efficacy of transcutaneous electrical stimulation at auricular acupuncture points and true auricular EA using needles, as with the P-Stim auricular acupuncture device. In addition, whether auricular EA underlies the same mechanism as body EA should be ascertained. Further research is clearly needed to establish the effects of different stimulation frequencies, intensity and the optimal duration and timing of electrical stimulation. It will also be important to determine how long the beneficial effects of auricular acupuncture persist after the therapy is discontinued.

Technical improvements could modify the P-Stim to make it more cost effective and enhance its ease of use.

References

Papers of special note have been highlighted as:
- • of interest
- •• of considerable interest

1 Nogier P. Face to face with auriculotherapy. *Acupunct. Electrother. Res.* 8, 99–100 (1983).

2 Oleson TD, Kroening RJ, Bresler DE. An experimental evaluation of auricular diagnosis: the somatotopic mapping or musculoskeletal pain at ear acupuncture points. *Pain* 8, 217–229 (1980).

•• **First study to prove the somatotopic relationship of external ear to different body regions.**

3 Oleson T. Auriculotherapy stimulation for neuro-rehabilitation. *Neurorehabilitation* 17, 49–62 (2002).

4 Falk CX, Birch S, Avants SK, Tsau Y, Margolin A. Preliminary results of a new method for locating auricular acupuncture points. *Acupunct. Electrother. Res.* 25, 165–177 (2000).

5 Chen G. Advances in researches on auriculo-acupoints. *J. Trad. Chin. Med.* 11, 216–223 (1991).

6 Pomeranz B, Warma N. Electroacupuncture suppression of a nociceptive reflex is potentiated by two repeated electroacupuncture treatments: the first opioid effect potentiates a second non-opioid effect. *Brain Res.* 452, 232–236 (1988).

7 Shen J. Research on the neurophysiological mechanisms of acupuncture: review of selected studies and methodological issues. *J. Altern. Complement Med.* 7(Suppl. 1), S121–S127 (2001).

8 Fang J, Krings T, Weidemann J, Meister IG, Thron A. Functional MRI in healthy subjects during acupuncture: different effects of needle rotation in real and false acupoints. *Neuroradiology* 46, 359–362 (2004).

9 Hsieh CL, Chang QY, Lin IH *et al.* The study of electroacupuncture on cerebral blood flow in rats with and without cerebral ischemia. *Am. J. Chin. Med.* 34, 351–361 (2006).

10 Hsieh CL. The physiological mechanisms of 2 Hz electroacupuncture: a study using blink and H reflex. *Am. J. Chin. Med.* 30, 369–378 (2002).

11 Napadow V, Makris N, Liu J, Kettner NW, Kwong KK, Hui KK. Effects of electroacupuncture versus manual acupuncture on the human brain as measured by fMRI. *Hum. Brain Mapp.* 24, 193–205 (2005).

12 Pomeranz B, Bibic L. Electroacupuncture suppresses a nociceptive reflex: naltrexone prevents but does not reverse this effect. *Brain Res.* 452, 227–231 (1988).

13 Wu MT, Sheen JM, Chuang KH *et al.* Neuronal specificity of acupuncture response: a fMRI study with electroacupuncture. *Neuroimage* 16, 1028–1037 (2002).

14 Audette JF, Ryan AH. The role of acupuncture in pain management. *Phys. Med. Rehabil. Clin. N. Am.* 15, 749–72 (2004).

15 Zhang RX, Lao L, Wang L *et al.* Involvement of opioid receptors in electroacupuncture-produced anti-hyperalgesia in rats with peripheral inflammation. *Brain Res.* 1020, 12–17 (2004).

16 Zhang RX, Lao L, Wang X, Ren K, Berman BB. Electroacupuncture combined with indomethacin enhances antihyperalgesia in inflammatory rats. *Pharmacol. Biochem. Behav.* 78, 793–797 (2004).

17 Liu JH, Li J, Yan J *et al.* Expression of c-fos in the nucleus of the solitary tract following electroacupuncture at facial acupoints and gastric distension in rats. *Neurosci. Lett.* 366, 215–219 (2004).

18 Liu W-C, Feldman SC, Cook DB *et al.* fMRI study of acupuncture-induced periaqueductal gray activity in humans. *Neuroreport* 15, 1937–1940 (2004).

19 Yan B, Li K, Xu J *et al.* Acupoint-specific fMRI patterns in human brain. *Neurosci. Lett.* 383, 236–240 (2005).

20 Cho ZH, Chung SC, Jones JP *et al.* New findings of the correlation between acupoints and corresponding brain cortices using functional MRI. *Proc. Natl Acad. Sci. USA* 95, 2670–2673 (1998).

21 Han JS. Acupuncture and endorphins. *Neurosci. Lett.* 361, 258–261 (2004).

22 Sung HJ, Kim YS, Kim IS *et al.* Proteomic analysis of differential protein expression in neuropathic pain and electroacupuncture treatment models. *Proteomics* 4, 2805–2813 (2004).

23 Liu X-Y, Zhou H-F, Pan Y-L *et al.* Electro-acupuncture stimulation protects dopaminergic neurons from inflammation-mediated damage in medial forebrain bundle-transected rats. *Exp. Neurol.* 189, 189–196 (2004).

24 Park HJ, Lee HS, Lee HJ *et al.* Decrease of the electroacupuncture-induced analgesic effects in nuclear factor-kappa B1 knockout mice. *Neurosci. Lett.* 319, 141–144 (2002).

25 Chapman CR, Benedetti C, Colpitts YH, Gerlach R. Naloxone fails to reverse pain thresholds elevated by acupuncture: acupuncture analgesia reconsidered. *Pain* 16, 13–31 (1983).

26 Bossut DF, Mayer DJ. Electroacupuncture analgesia in rats: naltrexone antagonism is dependent on previous exposure. *Brain Res.* 549, 47–51 (1991).

27 Ramey DW. Dr. Ramey remains unconvinced about acupuncture. *J. Am. Vet. Med. Assoc.* 227, 1064; author reply 1064–1065 (2005).

28 Vickers A, Goyal N, Harland R, Rees R. Do certain countries produce only positive results – a systematic review of controlled trials. *Control Clin. Trials* 19, 159–166 (1998).

29 White A. Neurophysiology of acupuncture. In: *Acupuncture: a Scientific Appraisal.* Ernst E, White A (Eds). Butterworth Heinemann, Oxford, 60–92 (1999).

30 White PF. Electroanalgesia: does it have a place in the routine management of acute and chronic pain? *Anesth. Analg.* 98, 1197–1198 (2004).

•• **Excellent review of electroanalgesia as an adjuvant to other analgesic modalities for the management of acute and chronic pain.**

31 Whittaker P. Laser acupuncture: past, present, and future. *Lasers Med. Sci.* 19, 69–80 (2004).

32 Diehl DL, Kaplan G, Coulter I, Glik D, Hurwitz EL. Use of acupuncture by American physicians. *J. Altern. Complement Med.* 3, 119–126 (1997).

33 Research Group of Acupuncture Anesthesia PMC. The role of some neurotransmitters of brain in acupuncture analgesia. *Sci. Sin.* 17, 112–130 (1974).

34 Han JS, Chou PH, Lu CH, Yang TH, Lu LH, Ren MF. The role of central 5-HT in acupuncture analgesia. *Sci. Sin.* 22, 91–104 (1979).

35 Tang NM, Dong HW, Wang XM, Tsui ZC, Han JS. Cholecystokinin antisense RNA increases the analgesic effect induced by electroacupuncture or low dose morphine: conversion of low responder rats into high responders. *Pain* 71, 71–80 (1997).

36 White PF, Craig WF, Vakharia AS, Ghoname E, Ahmed HE, Hamza MA. Percutaneous neuromodulation therapy: does the location of electrical stimulation effect the acute analgesic response? *Anesth. Analg.* 91, 949–954 (2000).

37 Ghoname ES, Craig WF, White PF *et al.* The effect of stimulus frequency on the analgesic response to percutaneous electrical nerve stimulation in patients with chronic low back pain. *Anesth. Analg.* 88, 841–846 (1999).

38 Szeles JC, Litscher G. Objectivation of cerebral effects with a new continuous electrical auricular stimulation technique for pain management. *Neurol. Res.* 26, 797–800 (2004).

39 Usichenko TI, Dinse M, Hermsen M, Witstruck T, Pavlovic D, Lehmann C. Auricular acupuncture for pain relief after total hip arthroplasty – a randomized controlled study. *Pain* 114, 320–327 (2005).

•• **A randomized controlled study of auricular acupuncture for the treatment of acute postoperative pain.**

40 Usichenko TI, Pavlovic D, Groth M. The effect of auricular acupuncture on anaesthesia: a search for optimal design. *Anaesthesia* 58, 928–929 (2003).

41 Barker R, Kober A, Hoerauf K *et al.* Out-of-hospital auricular acupressure in elder patients with hip fracture: a randomized double-blinded trial. *Acad. Emerg. Med.* 13, 19–23 (2006).

42 Alimi D, Rubino C, Pichard-Leandri E, Fermand-Brule S, Dubreuil-Lemaire ML, Hill C. Analgesic effect of auricular acupuncture for cancer pain: a randomized, blinded, controlled trial. *J. Clin. Oncol.* 21, 4120–4126 (2003).

43 Trumpler F, Oez S, Stahli P, Brenner HD, Juni P. Acupuncture for alcohol withdrawal: a randomized controlled trial. *Alcohol* 38, 369–375 (2003).

44 Shiraishi T, Onoe M, Kojima TA *et al.* Effects of bilateral auricular acupuncture stimulation on body weight in healthy volunteers and mildly obese patients. *Exp. Biol. Med. (Maywood)* 228, 1201–1207 (2003).

45 Alimi D, Rubino C, Leandri EP, Brule SF. Analgesic effects of auricular acupuncture for cancer pain. *J. Pain Symptom Manage.* 19, 81–82 (2000).

46 Ben H, Zhu Y. The effect of electro-acupuncture at auricular and body acupoints on the curve changes of the pressure-volume of urinary bladder and the electric activity of pelvic nerves of rat. *Zhen Ci Yan Jiu* 20, 51–54 (1995).

47 Romoli M, Allais G, Airola G, Benedetto C. Ear acupunture in the control of migraine pain: selecting the right acupoints by the "needle-contact test". *Neurol. Sci.* 26, 158–161 (2005).

48 Ceccherelli F, Tortora P, Nassimbeni C, Casale R, Gagliardi G, Giron G. The therapeutic efficacy of somatic acupuncture is not increased by auriculotherapy: a randomised, blind control study in cervical myofascial pain. *Complement. Ther. Med.* 14, 47–52 (2006).

49 Green S, Buchbinder R, Hetrick S. Acupuncture for shoulder pain. *Cochrane Database Syst. Rev.* CD005319 (2005).

50 Wen HL, Ng YH, Ho WK *et al.* Acupuncture in narcotic withdrawal: a preliminary report on biochemical changes in the blood and urine of heroin addicts. *Bull. Narc.* 30, 31–39 (1978).

51 Wen HL, Ho WK, Ling N, Mehal ZD, Ng YH. Immunoassayable beta-endorphin level in the plasma and CSF of heroin addicted and normal subjects before and after electroacupuncture. *Am. J. Chin. Med.* 8, 154–159 (1980).

52 Wen S, Cao Q, Zhai N *et al.* Effect of electroacupuncture on the enzymes of microvasculature and CA fluorescence in acute myocardial ischemia. *Zhen Ci Yan Jiu* 18, 223–227 (1993).

53 Smith MO. An acupuncture programme for the treatment of drug addicted persons. *Bull. Narc.* 1, 35–41 (1988).

54 D'Alberto A. Auricular acupuncture in the treatment of cocaine/crack abuse: a review of the efficacy, the use of the National Acupuncture Detoxification Association protocol, and the selection of sham points. *J. Altern. Complement. Med.* 10, 985–1000 (2004).

55 Gates S, Smith LA, Foxcroft DR. Auricular acupuncture for cocaine dependence. *Cochrane Database Syst. Rev.* CD005192 (2006).

56 Margolin A, Kleber HD, Avants SK *et al.* Acupuncture for the treatment of cocaine addiction: a randomized controlled trial. *JAMA* 287, 55–63 (2002).

57 Bullock ML, Culliton PD, Olander RT. Controlled trial of acupuncture for severe recidivist alcoholism. *Lancet* 1, 1435–1439 (1989).

58 Bullock ML, Kiresuk TJ, Sherman RE *et al.* A large randomized placebo controlled study of auricular acupuncture for alcohol dependence. *J. Sub. Abuse Treat.* 22, 71–77 (2002).

59 Margolin A. Acupuncture for substance abuse. *Curr. Psychiatry Rep.* 5, 333–339 (2003).

60 Margolin A, Kleber HD, Avants SK *et al.* Acupuncture for the treatment of cocaine addiction: a randomized controlled trial. *JAMA* 87, 55–63 (2002).

61 White AR, Rampes H, Ernst E. Acupuncture for smoking cessation. *Cochrane Database Syst. Rev.* CD000009 (2002).

62 Kang HC, Shin KK, Kim KK, Youn BB. The effects of the acupuncture treatment for smoking cessation in high school student smokers. *Yonsei Med. J.* 46, 206–212 (2005).

63 Li L, Wang ZY. Clinical therapeutic effects of body acupuncture and ear acupuncture on juvenile simple obesity and effects on metabolism of blood lipids. *Zhongguo Zhen Jiu* 26, 173–176 (2006).

64 Cabyoglu MT, Ergene N, Tan U. The treatment of obesity by acupuncture. *Int. J. Neurosci.* 116, 165–175 (2006).

65 Richards D, Marley J. Stimulation of auricular acupuncture points in weight loss. *Aust. Fam. Physician* 27(Suppl. 2), S73–S77 (1998).

66 Lacey JM, Tershakovec AM, Foster GD. Acupuncture for the treatment of obesity: a review of the evidence. *Int. J. Obes. Relat. Metab. Disord.* 27, 419–427 (2003).

67 Sator-Katzenschlager SM, Wölfler MM, Kozek-Langenecker SA *et al*. Auricular electro-acupuncture as an additional perioperative analgesic method during oocyte aspiration in *in-vitro*-fertilization treatment. *Hum. Reprod.* 21, 1–7 (2006).

•• **Auricular electroacupuncture significantly reduces pain intensity and analgesic consumption of remifentanil during oocyte aspiration in IVF treatment.**

68 Michalek-Sauberer A, Heinzl H, Sator-Katzenschlager SM, Monov G, Knolle E, Kress H-G. Perioperative auricular electroacupuncture has no effect on pain and analgesic consumption after third molar tooth extraction. *Anesth. Analg.* (2006) (In Press).

• **After dental surgery, auricular electroacupuncture failed to reduce pain and analgesic consumption.**

69 Sator-Katzenschlager SM, Szeles JC, Scharbert G *et al*. Electrical stimulation of auricular acupuncture points is more effective than conventional manual auricular acupuncture in chronic cervical pain: a pilot study. *Anesth. Analg.* 97, 1469–1473 (2003).

•• **First study to demonstrate that continuous electrical stimulation of auricular acupuncture points improves the treatment of chronic cervical pain in an outpatient population.**

70 Sator-Katzenschlager SM, Scharbert G, Kozek-Langenecker SA *et al*. The short- and long-term benefit in chronic low back pain through adjuvant electrical versus manual auricular acupuncture. *Anesth. Analg.* 98, 1359–1364 (2004).

•• **Continuous electrical stimulation of auricular acupuncture points significantly decreased pain intensity and improved psychological well-being, activity and sleep in chronic low back pain patients.**

71 Aapro MS, Molassiotis A, Olver I. Anticipatory nausea and vomiting. *Support Care Cancer* 13, 117–121 (2005).

Affiliations

• *Sabine M Sator-Katzenschlager, MD*
Ao. Univ.-Prof.
Department of Anesthesiology and Intensive Care Medicine (B)
Medical University of Vienna, Waehringer Guertel 18–20, A-1090 Vienna, Austria
Tel.: +43 140 400 4144
Fax: +43 140 400 4165
sabine.sator-katzenschlager@meduniwien.ac.at

• *Andrea Michalek-Sauberer, MD*
Department of Anesthesiology and Intensive Care Medicine (B)
Medical University of Vienna, Waehringer Guertel 18–20, A-1090 Vienna, Austria
Tel.: +43 140 400 4144
Fax: +43 140 400 4165
andrea.michalek-sauberer@meduniwien.ac.at