Electroacupuncture: Mechanisms and Clinical Application

George A. Ulett, Songping Han, and Ji-sheng Han

Acupuncture is an ancient Chinese method to treat diseases and relieve pain. We have conducted a series of studies to examine the mechanisms of this ancient method for pain relief. This article reviews some of our major findings. Our studies showed that acupuncture produces analgesic effect and that electroacupuncture (EA) is more effective than manual acupuncture. Furthermore, electrical stimulation via skin patch electrodes is as effective as EA. The induction and recovering profiles of acupuncture analgesia suggest the involvement of humoral factors. This notion was supported by cross-perfusion experiments in which acupuncture-induced analgesic effect was transferred from the donor rabbit to the recipient rabbit when the cerebrospinal fluid (CSF) was transferred. The prevention of EA-induced analgesia by naloxone and by antiserum against endorphins suggests that endorphins are involved. More recent work demonstrated the release of endorphins into CSF following EA. In addition, low frequency (2 Hz) and high frequency (100 Hz) of EA selectively induces the release of enkephalins and dynorphins in both experimental animals and humans. Clinical studies suggesting its effectiveness for the treatment of various types of pain, depression, anxiety, spinally induced muscle spasm, stroke, gastrointestinal disorders, and drug addiction were also discussed. Biol Psychiatry 1998;44:129–138

Key Words: Acupuncture analgesia, drug addiction, endorphins, nociception, opioids, pain, neuroelectric stimulation

Introduction–Historical

Traditional Chinese Acupuncture is a 3000-year-old folk therapy. It is based upon metaphysical concepts of "ch'i" (Qi), a supposed body energy that runs through hypothesized channels called "meridians." On these "meridians" are 365 designated acupuncture points that can be used for stimulation via needles or "moxibustion" (lighted punks of *artemis vulgaris*) to balance "yin and yang" by relieving blockages in the flow of "ch'i." Diagnosis is made by feeling for 12 organ-specific pulses located on the wrists and with cosmological interpretations including a representation of five elements: wood, water, metal, earth, and fire.

One of us (GAU) learned traditional Chinese acupuncture 30 years ago. It was found useful in treating patients with chronic pain, but the metaphysical explanations and the necessity for mystical rituals were troublesome. A few years later, in 1971, President Nixon visited China, and acupuncture became a household word in the United States. The American Medical Association was also troubled by metaphysical explanations and declared (*St. Louis Post Dispatch*, August 4, 1974) that acupuncture was "quackery." This discouraged U.S. medical schools from interest in this type of therapy. Some even called it "Oriental hypnosis."

Our laboratory in St. Louis, Missouri was then studying neurophysiological concomitants of hypnosis and received a grant from NIH to compare these two treatments (Parwatikar et al 1979; Ulett et al 1979). We were able to report that acupuncture was not hypnosis (Ulett 1983). We studied the physiological properties of acupuncture points (Brown et al 1974), and concluded with Liu (Liu et al 1975) and Gunn (1978) that useful acupuncture points were mostly motor points or areas near major nerve pathways. We published our Atlas supporting the clinical use of not 365 but rather 80 points (Ulett 1982). Studying experimental pain in human volunteers we found that although needles alone gave some pain relief, when electricity was added the modulation was 100% more effective (Saletu et al 1975). This was in keeping with our observation that Chinese surgeons added electricity to their needles when they wanted strong analgesia for surgical procedures.

Increasingly research publications (Pomeranz and Stux 1979) gave strong evidence that acupuncture could be explained on a physiological rather than metaphysical basis. In 1987 Professor Ji-sheng Han published a collection of research studies on acupuncture from his laboratory in Beijing Medical University covering a 25-year period

From the University of Missouri–Columbia, School of Medicine, St. Louis, Missouri (GAU); St. Louis University, School of Medicine, St. Louis, Missouri (SH); and Beijing Medical University, Beijing, China (JH).

Address reprint requests to George Ulett, MD, PhD, University of Missouri–Columbia, School of Medicine, 5247 Fyler Ave., Building L, St. Louis, MO 63139.

Received December 20, 1996; revised June 9, 1997; accepted July 1, 1997.

0006-3223/98/$19.00
PII S0006-3223(97)00394-6

(Han 1987). In 1990 Han demonstrated the differential release of brain neuropeptides by different frequencies of stimulation (Han and Sun 1990). He also showed that conducting polymer pads were equally as effective as needles (Wang et al 1992). Thus it was finally possible to propose a simple clinical method of acupuncture treatment, the principle of which could be taught in a single afternoon (Ulett 1992), without the requirement for hundreds of hours of lectures on Chinese metaphysics as currently mandated in 33 states. This article reviews some of Dr. Ji-sheng Han's work on the physiological mechanism of electroacupuncture-induced analgesia in the past 25 years.

Summary of Research from the Laboratory of Professor Ji-sheng Han, Beijing Medical University, Beijing, China, Establishing the Neurochemical Basis of Acupuncture Analgesia

Acupuncture Increased Pain Threshold in Human Volunteers with a Long Latency and Half-Life

The first paper demonstrating the analgesic effect of acupuncture using experimentally induced pain and quantitative methods to determine acupuncture-induced changes in pain threshold in medical student volunteers at Beijing Medical University was published in 1973 in the Chinese Medical Journal (Research Group of Acupuncture Anesthesia, Peking Medical College 1973). Pain was induced by modified potassium iontophoresis with gradually increasing anodal currents (0.1–0.3 mA/step) passing through the skin on the head, thorax, back, abdomen, and leg. The pain threshold was estimated by the current (mA) needed to produce pain. Measurements were taken every 10 min for 100 min after the insertion of the needle into the Hoku (L1-4) and Zusanli points (ST-36), which was manipulated (300 insertion/twistings per minute, manual acupuncture) for 50 min ($n = 60$). Data were expressed as average percent changes in these skin areas. Intramuscular injection of morphine (10 mg) was used as positive control, which produced an 80–90% increase in pain threshold ($p < .05$), suggesting that the method is valid (Figure 1).

Acupuncture at Hoku point produced an increase in pain threshold with a peak increase occurring 20–40 min after the needle insertion (Figure 1). The threshold returned to the preacupuncture level 45 min after the needles were removed, with a half-life of 16.2 ± 1.9 min. This result confirmed the analgesic effect of acupuncture. There was no difference in the analgesic effect of acupuncture whether the needle was placed at the left or right hand. Furthermore, a greater increase in pain threshold was

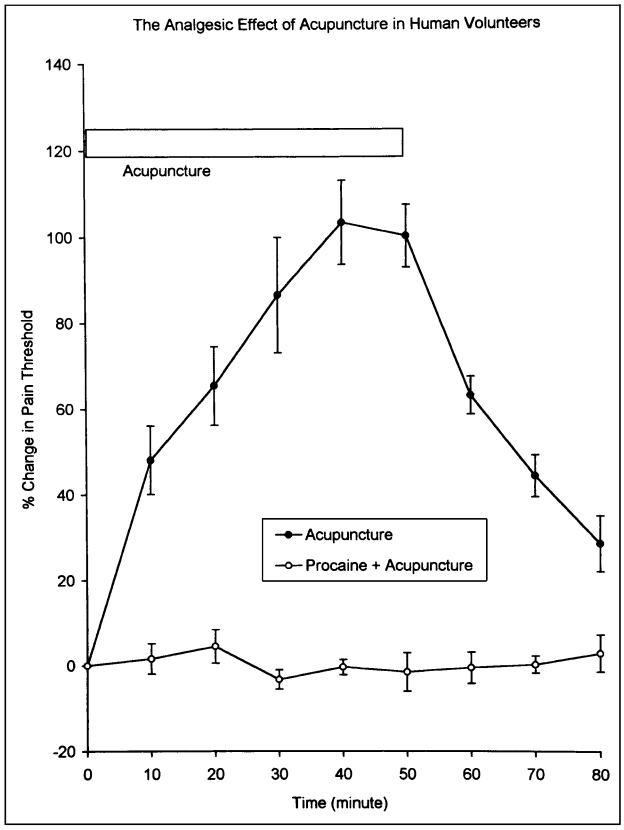

Figure 1. Effect of manual acupuncture at Hoku point on pain threshold in human volunteers.

produced when both Hoku and Zusanli points were stimulated simultaneously with acupuncture as compared with the results when either one of these two points was stimulated alone.

The analgesic effect was completely prevented by the injection of procaine into the Hoku point prior to needling. In addition, needling on the affected limbs of 12 hemiplegic and 13 paraplegic patients had no effect on pain threshold on the unaffected side, indicating the involvement of sensory nerves. The gradual increase and return in pain threshold suggest that the acupuncture-induced analgesia is mediated by humoral factors.

Rats Developing Tolerance to Electroacupuncture Analgesia Were Also Tolerant to Morphine Analgesia

Several strategies were then employed to characterize the chemical nature of the factors responsible for acupuncture analgesia. An important piece of evidence suggesting the importance of endogenous opioid substances in mediating acupuncture analgesia was derived from cross-tolerance experiments (Han et al 1981). Repeated electroacupuncture was applied to rats at Zusanli and Sanyinjiao points

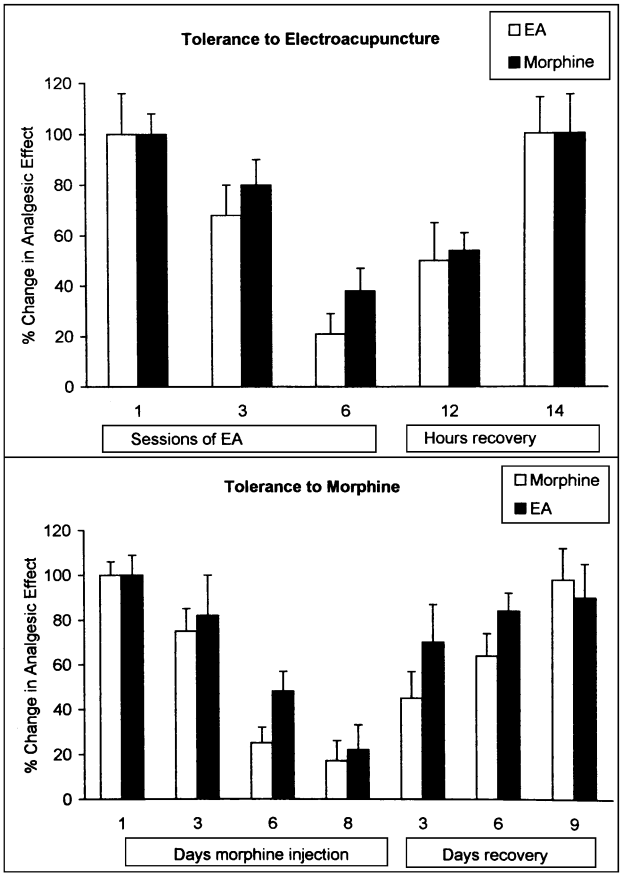

Figure 2. Repeated electroacupuncture (EA) resulted in the development of tolerance to EA and the cross-tolerance to morphine.

for six sessions using 2–15 Hz, 0.3 ms duration, 30 min for each session with 30-min intervals. The amplitude of the pulse was 1 V in the beginning of each session and increased by 1 V every 10 min, reaching 3 V as maximum. Repeated electroacupuncture resulted in tolerance, i.e., a gradual decrease of the acupuncture effect (Figure 2). In these rats, the analgesic effect of a challenging dose of morphine (6 mg/kg, IV) was also reduced correspondingly. The analgesic effect of both electroacupuncture and morphine returned to the control level at similar rates following a period of recovery ($Y = 0.78X + 22.4$, $r = .996$, $p < .01$). In addition, morphine tolerance developed in rats following chronic injection of morphine (5–50 mg/kg, three times/day for 8 days). The effect of morphine returned to the control level 9 days after the cessation of morphine treatment. A similar attenuation of electroacupuncture analgesia was also observed in these rats ($Y = 0.74X + 28.4$, $r = .938$, $p < .01$). These findings suggest that electroacupuncture analgesia and morphine analgesia share the same or similar mechanisms.

Acupuncture-Induced Analgesic Effect Can Be Transferred to Another Rabbit When Cerebrospinal Fluid Is Transferred

Neurochemical factors responsible for acupuncture analgesia may be produced in, and released from the central nervous system (CNS). If this is true then infusion of the CSF taken from an animal that has undergone acupuncture into a naive animal might produce a significant increase of the pain threshold in the recipient animal. This hypothesis was tested in a cross-perfusion/infusion experiment (Research Group of Acupuncture Anesthesia, Peking Medical College 1974). Finger acupuncture by pressing Quenlun point (on the top of the Achilles tendon) of the rabbit for 30 min produced a dramatic analgesic effect. This was determined by the changes in avoidance response latency during a noxious stimulation produced by radiant heat from an incandescent lamp (12 V, 50 W in 8.75-mm cine-projector). The lateral ventricle of the rabbit was perfused with artificial CSF at a rate of 10–15 μL/min during acupuncture. The CSF from the donor rabbit (0.3–0.5 mL) was then infused into the lateral ventricle of a naive recipient rabbit. A rather marked nociceptive effect was observed in the recipient rabbit (Figure 3). Perfusion or infusion of the ventricle with control artificial CSF had no significant effect on avoidance response latency in donor or recipient rabbits. These results clearly demonstrated that the acupuncture-induced analgesia is mediated by substances that are released from the CNS.

Microinjection of Opioid Receptor Antagonist (Naloxone) into Selected Brain Regions Attenuated the Analgesic Effect of Morphine or Acupuncture

To examine the biochemical and anatomical characteristics of the receptors responsible for acupuncture analgesia, an opioid receptor antagonist was introduced into selected brain regions by the microinjection technique in an attempt to prevent the acupuncture-induced analgesia (Zhou et al 1981). Intravenous injection of morphine (4 mg/kg) or finger acupuncture (Kuenlun point, 10 min) produced a significant analgesic effect in rabbits, as shown by the increase of the avoidance response latency. Naloxone, an opioid receptor antagonist, was microinjected into the following nuclei: accumbens, amygdala, habenula, or periaqueductal gray (PAG), at a rate of 0.25 μL/min for 20 min either unilaterally or bilaterally. Microinjection of naloxone into any one of these four nuclei significantly attenuated the analgesic effect induced by morphine or acupuncture (Figure 4). These results suggest that the analgesic effect of morphine and acupuncture is mediated by opioid receptors in these brain areas. Results obtained from experiments using chemical blockade, and from studies using lesion methods, further suggest that acupunc-

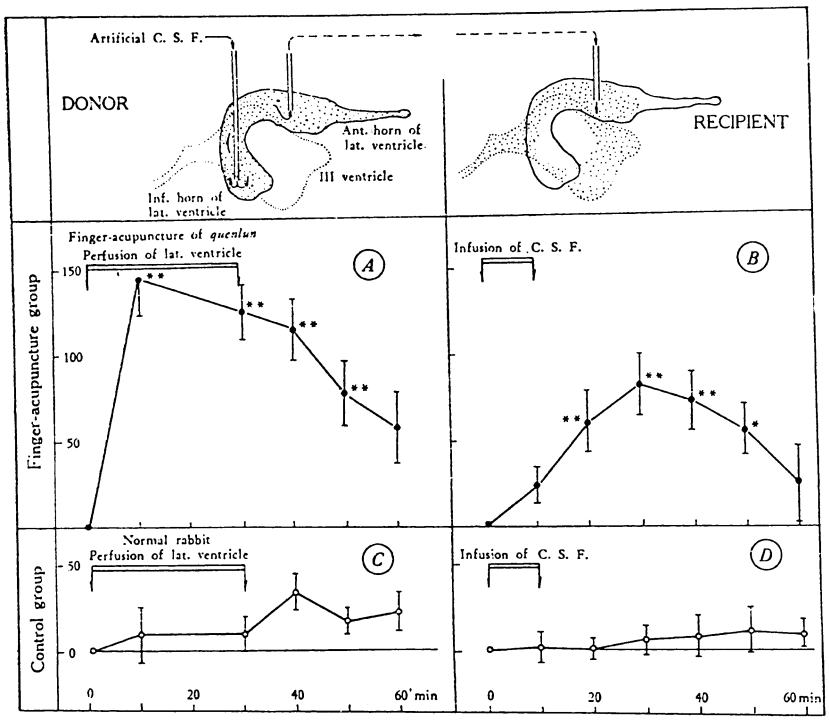

Figure 3. The analgesic action of acupuncture can be transferred between rabbits by the transfer of CSF.

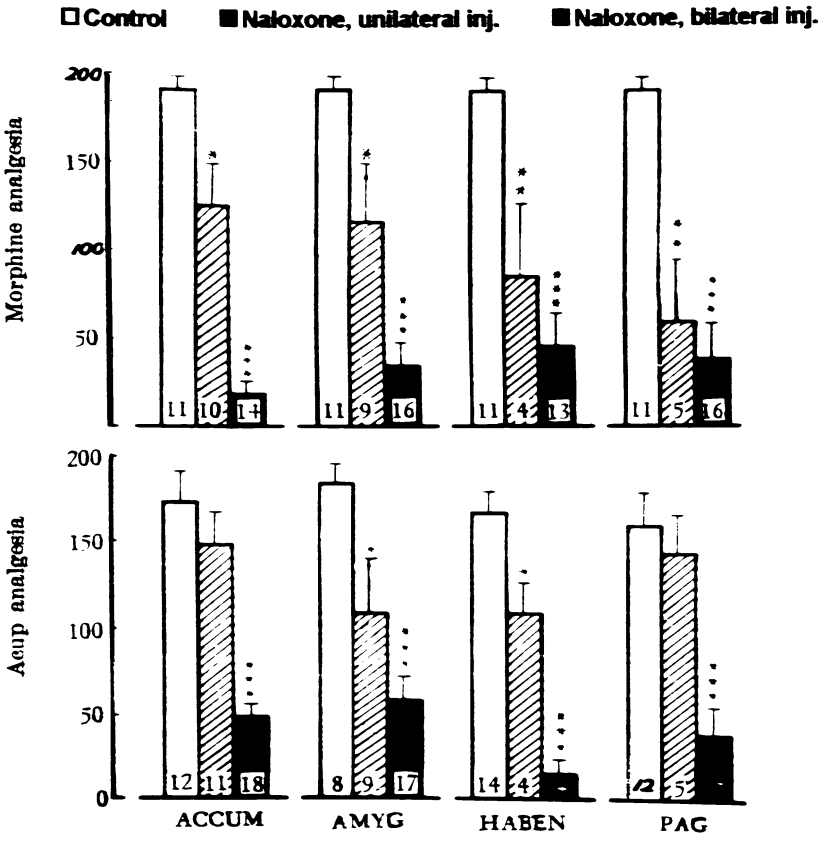

Figure 4. Microinjection of naloxone into certain brain nuclei attenuates morphine analgesia and acupuncture analgesia. Acup, acupuncture; inj., injection; ACCUM, accumbens; AMYG, amygdala; HABEN, habenula.

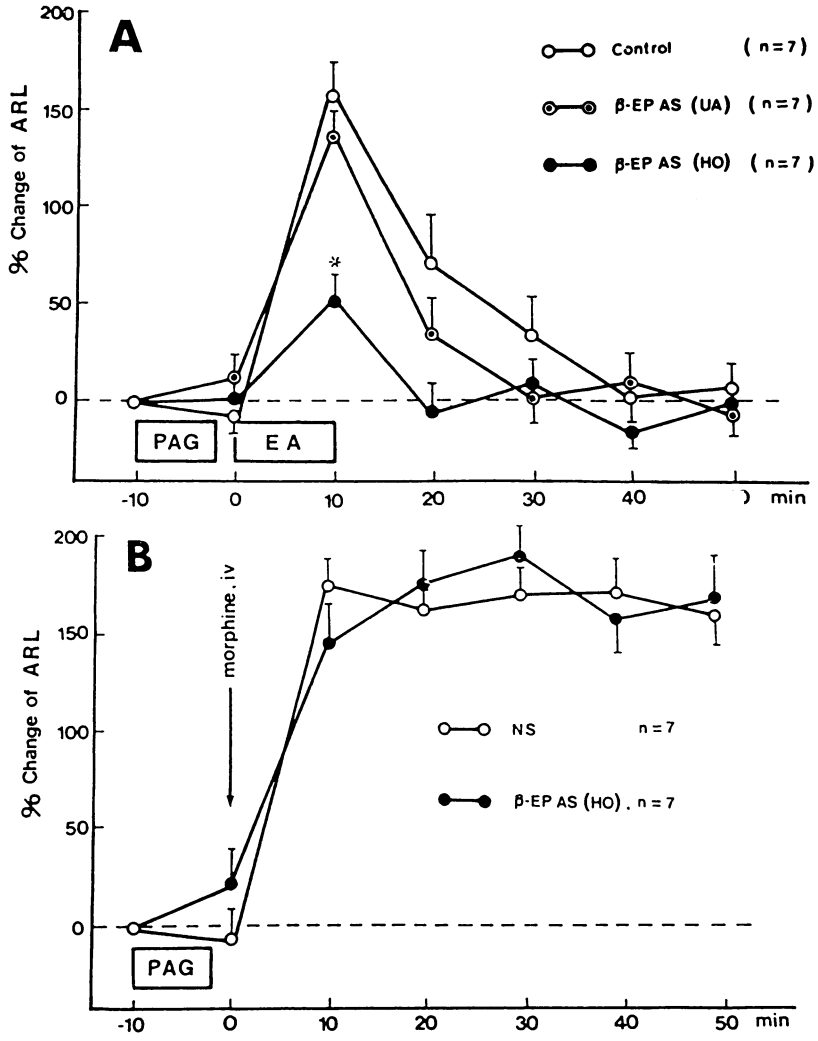

Figure 5. Microinjection of antiserum against beta-endorphin into the periaqueductal gray attenuates acupuncture analgesia but not morphin analgesia. β-EP, β-endorphin; AS, antiserum; NS, normal saline.

ture analgesia and morphine analgesia may require a neural connection among these nuclei using endorphins as transmitters.

Microinjection of Antiserum against β-Endorphin into the Periaqueductal Gray Attenuated the Analgesic Effect of Electroacupuncture But Not That of Morphine

At least three kinds of endorphins and their receptors have been found in the CNS. Results from studies using naloxone indicate the involvement of opioid receptors but do not discriminate as to which types of endorphins are involved. Specific antiserum raised against a certain type of endorphin can neutralize and prevent the action of that endorphin. Antiserum that recognizes (HO) or does not recognize (UA) rabbit β-endorphin was injected bilaterally at a volume of 4 μL into the rabbit PAG through chronically implanted cannulae (Xie et al 1983). Changes in avoidance response latency (ARL) were determined before and after electroacupuncture at points Zusanli and Quenlun for 10 min (Figure 5A) or after the intravenous injection of morphine (Figure 5B). The antinociceptive effect of electroacupuncture, but not of morphine, was attenuated by "HO" antiserum. In contrast, neither saline nor "UA" affected the analgesic effect of electroacupuncture or morphine. These results suggest that morphine produces an analgesic effect by direct activation of opioid receptors in the PAG, whereas the effect of electroacupuncture is mediated by β-endorphin.

Enkephalins and Dynorphins Are Selectively Released into the Cerebrospinal Fluid by Electroacupuncture of Low and High Frequencies, Respectively

Different endorphins have different distribution patterns and biological functions in the CNS. It would have great

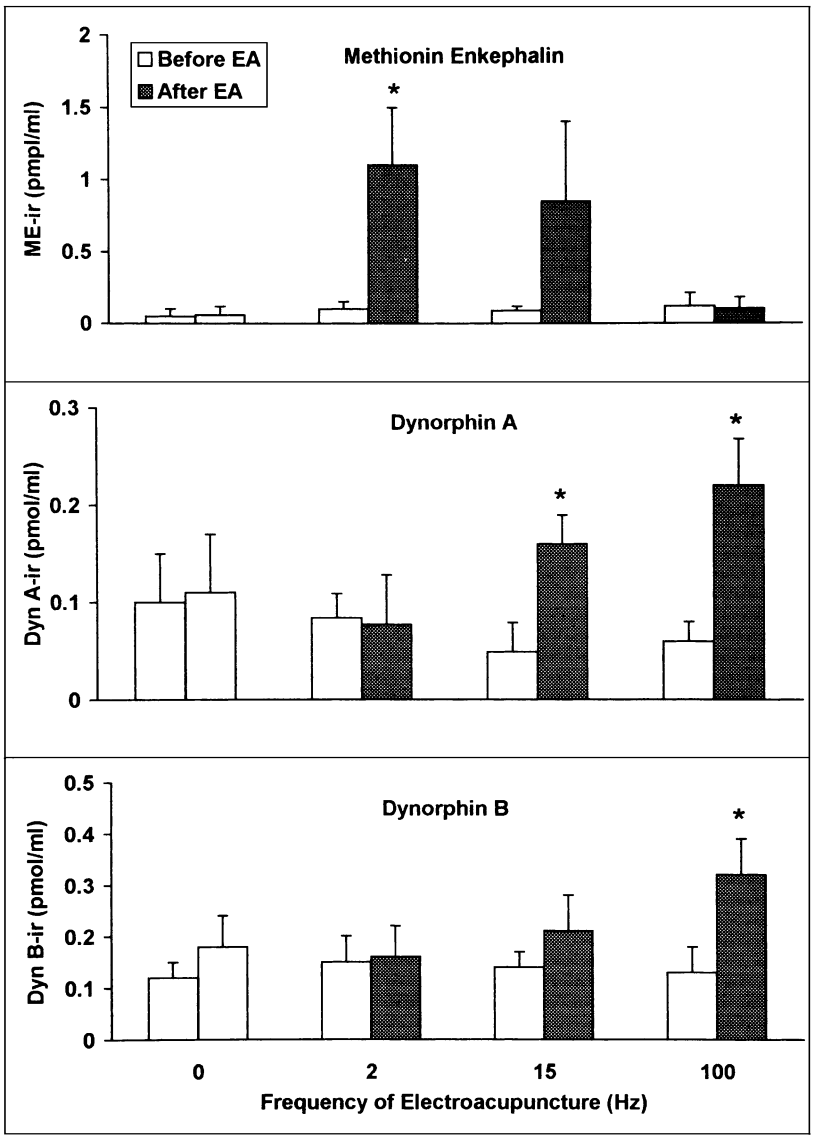

Figure 6. Acupuncture of low and high frequencies releases different types of endogenous opioids from the CNS. ME, methionin enkephalin; Dyn, dynorphin.

clinical advantage if one could selectively stimulate the release of a certain type of endorphin without affecting others. The selectivity of acupuncture on endorphin release was examined using EA of different frequencies (Fei et al 1986). The spinal subarachnoid space of the rat was perfused with artificial CSF before and after electroacupuncture at Zusanli and Sanyinjiao points using 2, 15, or 100 Hz. CSF was collected for measurement of methionin enkephalin, dynorphin A, or dynorphin B using radioimmunoassay. Methionin enkephalin and dynorphins were selectively released into the CSF by electroacupuncture of low and high frequencies, respectively (Figure 6). Similar results were also obtained from studies in humans.

Electroacupuncture Produced Corresponding Increases in Pain Threshold and β-Endorphin Immunoreactivity in the Rat Brain

Electroacupuncture also increases the tissue content of endorphins (Chen et al 1983). Rats were divided into three groups according to the degree of analgesia produced by electroacupuncture (15 Hz, 3 V for 30 min). The electroacupuncture-induced increase in tail flick latency was less than 20%, between 21–70%, and over 70% in these groups respectively. The brain was removed after electroacupuncture for measurement of cerebral β-endorphin immunoreactivity (β-endorphin-ir) with radioimmunoassay. The results show no changes in β-endorphin-ir in rats with low

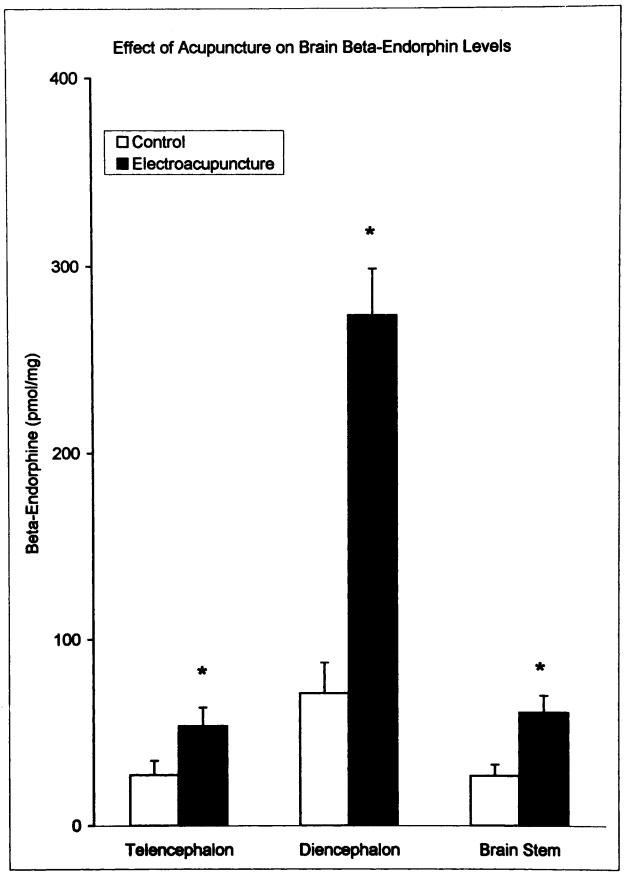

Figure 7. Acupuncture produces concomitant increases in pain threshold and brain beta-endorphin levels (*: $p < .05$ comparing with control groups).

analgesic effect and a dramatic increase in β-endorphin-ir in rats with high analgesic effect (Figure 7). There was a strong correlation between electroacupuncture-induced analgesia and β-endorphin-ir in brain tissue.

Electroacupuncture Is More Effective Than Manual Acupuncture and Transcutaneous Electric Nerve Stimulation (TENS) Is as Effective as Electroacupuncture

A series of studies was conducted in rats to compare the analgesic effect induced by three types of stimulation: manual acupuncture, electroacupuncture, and TENS (Wang et al 1992). The analgesic effect of electroacupuncture was greater than manual acupuncture, whereas electroacupuncture and TENS produced similar analgesic effect (Figure 8). High degrees of correlation were found between the analgesic effect produced by electroacupuncture and TENS in individual rats when low (2 Hz, $r = .68$, $p < .01$), intermediate (15 Hz, $r = .72$, $p < .01$), or high (100 Hz, $r = .76$, $p < .01$) frequencies were used.

Clinical Applications of Neuroelectroacupuncture

The development of a scientific neuroelectrical acupuncture has made it possible to consider a wide variety of clinical applications that have been demonstrated and now stand ready for replication and double-blind studies. These include the following:

Pain

Traditionally acupuncture has been widely used as a treatment for various types of acute and chronic pain. A 70% rate of success for pain elimination or modulation has been reported clinically in patients with low back strain, arthritis, myofascial discomfort, migraine, and other painful disorders (Ulett 1989; Ng et al 1992; Thomas and Lundberg 1994; Anderson et al 1976).

Depression

The successful treatment of major depression has been demonstrated in China to require twice daily, 30-min periods of electrostimulation (Han 1986; Lou et al 1990). Medical insurance reimbursement does not presently cover such treatments in U.S. hospitals. Our experience therefore has been limited to weekly office treatments for less severe depression. This less intense schedule, however, has permitted a decrease, and in some cases, an elimination of the need for antidepressant medication.

Addiction

Wen (Wen and Cheung 1973) first demonstrated the use of ear acupuncture for addiction by placing a needle in the concha, an area innervated by the vagus nerve. Metaphysical theories of "auriculotherapy" claim 168 body points on the ear connecting to various body locations. It is more likely that there is only one physiologically active point in the ear, the conchal area innervated by the vagus nerve. Wen stressed the necessity of electrical stimulation of the concha in his treatment for heroin addiction, and such electrical stimulation has been used by others (Katims et al 1992). The necessity for electrical stimulation has been overlooked by U.S. addictionologists, who instead follow the fanciful theories of "auriculotherapy" with unstimulated needles. A recent study suggests such procedures may well be placebo treatments (Wells et al 1995).

Han (Han et al 1994) reported the use of transcutaneous stimulation of acupuncture points with a Han's acupoint and nerve stimulator (HANS) at identified frequencies for the treatment of heroin addicts. The alternating high (100 Hz) and low (2 Hz) frequency stimulation produced the most significant improvement on the opioid withdrawal

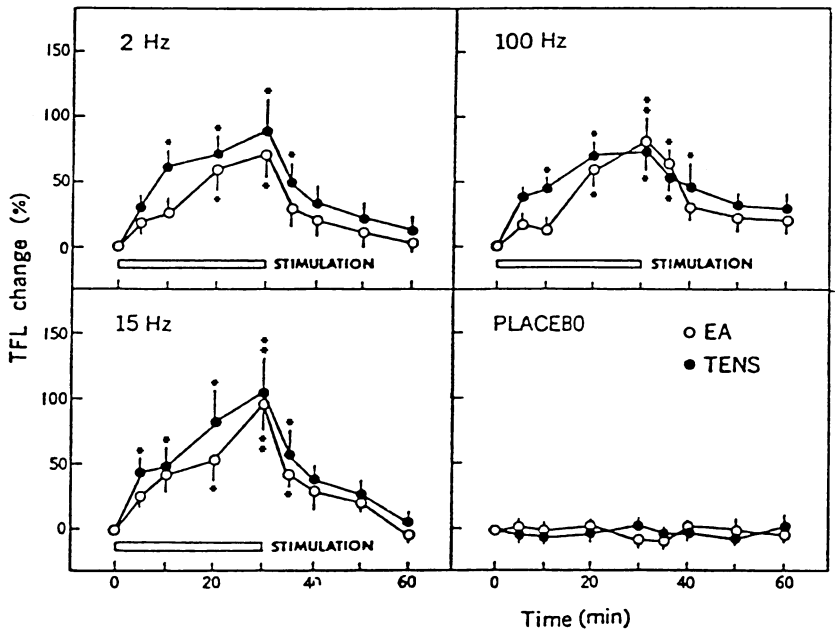

Figure 8. Electroacupuncture (EA) and transcutaneous electric nerve stimulation (TENS) at acupoints produce similar analgesic effects. TFL, tail flick lantency.

syndrome. A clinical study on more than 500 heroin addicts shows that the treatment with HANS significantly decreased heart rate and palpitation and produced a euphorialike sensation and warm feeling. It also produced a significant hypnotic effect and an increase in the body weight (Wu et al 1995). Following this lead, we have used electrical stimulation of the dorsal interosseous muscle for treating a variety of addictions (Ulett and Nichols 1996).

Cerebrovascular Accidents and Their Sequelae

Recent reports suggest that early intervention following a stroke may assist with earlier rehabilitation and decrease nursing home stay by 50% (Johansson et al 1993; Magnusson et al 1994). Studies by Han (Han et al 1994) suggest that specific frequencies of stimulation may be effective for the treatment of spinal spasticity. Although these preliminary reports appear promising, replication of these studies in the U.S. is needed.

Gastrointestinal Disorders

In traditional Chinese medicine, stimulation of the point Zusanli (tibialis anticus motor point) has long been advocated for the treatment of both diarrhea and constipation. Such normalization of colon function could theoretically be explained by impulses reaching the lumber plexus. The effects of such stimulation have been reported both in animals and humans (Li et al 1992; Jin et al 1992). In the light of research emphasizing the importance of specific frequencies of stimulation, it could well be that different frequencies at the same point could have different clinical effects.

Anxiety

Acupuncture has long been associated with a homeostatic (yin/yang), regulation, or calming effect. This may be explained in light of the research reported above indicating that electroacupuncture releases opioid neuropeptides in the central nervous system. We have reported using Pavlovian conditioning techniques combined with electroacupuncture to train patients for the self-release of endorphins (Ulett 1996).

Conclusions

Centuries old, metaphysically interpreted traditional Chinese acupuncture is widely practiced in the United States. It involves a belief that a mysterious energy “ch’i” travels over hypothetical channels called “meridians.” It is believed that “acupuncture points” on these “meridians” can act as places where needle stimulation can serve to release blockages of “ch’i,” which are thought to be the cause of illnesses.

Research findings have made such fanciful metaphysical theories obsolete. Our own studies, published reports from research laboratories around the world, and particularly the work performed in the Beijing Medical University by Han and his group, have resulted in the development of a new scientifically based neuroelectric

acupuncture. This is demonstrated to be a simple procedure, the principle of which can be learned in a few hours and often does not even require the use of needles. Clinical reports of successful treatment of patients with a variety of symptoms and illnesses give this method high credibility. A basis has now been developed for further physiological investigations and controlled clinical studies. Such increasing evidence for a scientific neuroelectric acupuncture will gain its acceptance as a useful and effective procedure to be taught in U.S. medical schools.

Acupuncture has a great potential of being used for various medical purposes. For example, we and others have shown that the doses of anesthetics and postoperational analgesics can be significantly reduced when a HANS is used during a surgical procedure (acupuncture-assisted analgesia). This can result in a reduced risk of complications associated with the operation and the duration of hospital stay. In another example, instead of using daily application of methadone or other potent and long-lasting opioid receptor agonists in the treatment of heroin addiction, HANS stimulates the suppressed endorphinergic neurons in the CNS to attenuate the heroin withdrawal syndrome and to restore the function of these neurons. The important next step in acupuncture research is to have a better understanding of the neurochemical mechanism of acupuncture in order that the therapeutic effectiveness of acupuncture can be further increased. Also scientifically conducted clinical research is needed to examine the effectiveness of acupuncture for each disease or symptom that has been claimed to be treatable by acupuncture. Once the effectiveness is demonstrated, a standardized procedure of electroacupuncture including the site, frequency, intensity, duration, and intervals of stimulation can be recommended for treating each disease.

This work is supported by the National Institute of Drug Abuse, USA, DA 03983, and by the National Natural Science Foundation of China.

References

Anderson SA, Hansson G, Holmgren E, Renberg O (1976): Evaluation of the pain suppressive effect of different frequencies of peripheral electrical stimulation in chronic pain conditions. *Acta Orthop Scand* 47:149–159.

Brown M, Ulett G, Stern J (1974): Acupuncture loci and techniques for location. *Am J Chin Med* 2:67–74.

Chen QS, Xie CW, Tang J, Han JS (1983): Effect of electroacupuncture on the content of immunoreactive beta-endorphin in rats brain regions. *Kexue Tonga* 28:312–319.

Fei H, Xie GX, Han JS (1986): Differential release of met-enkephalin and dynorphin in spinal cord by electroacupuncture of different frequencies. *Kexue Tongbo* 31:1512–1515.

Gunn CC (1978): Motor points and motor lines. *Am J Acupunct* 6:55–58.

Han JS (1986): Electroacupuncture: An alternative to antidepressants for treating affective diseases? *J Neurosci* 29:79–92.

Han JS (1987): *The Neurochemical Basis of Pain Relief by Acupuncture.* Beijing: Chinese Medical Science and Technology Press, 1987.

Han JS, Sun SL (1990): Differential release of enkephalin and dynorphin by low and high frequency electroacupuncture in the central nervous system. *Acupunct Sci Int J* 1:19–27.

Han JS, Li SJ, Tang J (1981): Tolerance to electroacupuncture and its cross tolerance to morphine. *Neuropharmacology* 20:593–596.

Han JS, Chen XH, Yuan Y, Yan SC (1994a): Transcutaneous electrical nerve stimulation for treatment of spinal spasticity. *Chin Med J* 107:5–11.

Han JS, Wu LZ, Cui CL (1994b): Heroin addicts treated with transcutaneous electrical nerve stimulation of identified frequencies. *Regul Pept* 54:115–116.

Jin H, Zhou L, Lee K, Chang T, Chey W (1992): The inhibition by electrical acupuncture on gastric acid secretion is mediated via endorphin and somatostatin in dogs. *Clin Res* 40:167A.

Johansson K, Lindgren I, Widner H, Wiklund I, Johansson BB (1993): Can sensory stimulation improve the functional outcome in stroke patients? *Neurology* 43:2189–2192.

Katims JJ, Ng L, Lowinson JH (1992): Acupuncture and transcutaneous electrical nerve stimulation: Afferent nerve stimulation (ANS) in the treatment of addiction. In: Lowinson J, editor. *Substance Abuse: A Comprehensive Textbook,* 2nd ed. Baltimore: Williams and Wilkins, 1992, pp 574–583.

Li Y, Tougas G, Chiverton S, Hunt R (1992): The effect of acupuncture on gastrointestinal function and disorders. *Am J Gastroenterol* 87:1372–1381.

Liu KY, Varela M, Oswald R (1975): The correspondence between acupuncture points and motor points. *Am J Chin Med* 3:347–358.

Lou HC, Shen YC, Zhou D, Jia KY (1990): A comparative study of the treatment of depression by electro-acupuncture. *Acupunct Sci Int J* 1:20–26.

Magnusson M, Johansson K, Johansson B (1994): Sensory stimulation with electroacupuncture promotes normalization of postural control after stroke. *Stroke J Cereb Circ* 25:1176–1180.

Ng L, Katims JJ, Lee M (1992): Acupuncture: A neuromodulation technique for pain control. In: Aronoff G, editor. *Evaluation and Treatment of Chronic Pain,* 2nd ed. Baltimore, Williams and Wilkins, 1992, pp 291–298.

Parwatikar S, Brown M, Stern J, Ulett G, Sletten I (1979): Acupuncture, hypnosis and experimental pain: I. Study with volunteers. Acupuncture and electrotherapeutics. *Res Int J* 3:161–190.

Pomeranz B, Stux G (eds) (1979): *Scientific Basis of Acupuncture.* New York: Springer Verlag.

Research Group of Acupuncture Anesthesia, Peking Medical College (1973): The effect of acupuncture on the human skin pain threshold. *Chin Med J* 3:151–157.

Research Group of Acupuncture Anesthesia, Peking Medical College (1974): The role of some neurotransmitters of brain in finger-acupuncture analgesia. *Scientia Sinica* 17:112–130.

Saletu B, Saletu M, Brown M, Stern J, Sletten I, Ulett G (1975): Hypnosis and acupuncture analgesia: A neurophysiological reality? *Neuropsychobiology* 1:218–242.

Thomas M, Lundberg T (1994): Importance of modes of acupuncture in the treatment of chronic nociceptive low back pain. *Acta Anaesthesiol Scand* 38:63–69.

Ulett G (1982): *Principles and Practice of Physiologic Acupuncture.* St. Louis, MO: Warren H. Green, 1982.

Ulett G (1983): Acupuncture is not hypnosis: Physiological studies. *Am J Acupunct* 11:5–13.

Ulett G (1989): Acupuncture. In: Tollison C, Kriegel M, editors. *Interdisciplinary Rehabilitation of Low Back Pain.* Baltimore: Williams and Wilkins, 1989, pp 85–100.

Ulett G (1992): *Beyond Yin and Yang: How Acupuncture Really Works.* St. Louis, MO: Warren H. Green, 1992.

Ulett G (1996): Conditioned healing with electroacupuncture. *Alternative Ther* 2:56–60.

Ulett G, Nichols J (1996): *The Endorphin Connection.* Gleve, Australia: Wild and Woolley, 1996.

Ulett G, Parwatikar S, Stern J, Brown M (1979): Acupuncture, hypnosis and experimental pain: II. Study with patients. Acupuncture and electrotherapeutics. *Res Int J* 3:191–201.

Wang J, Mao L, Han JS (1992a): Antinociceptive effects induced by electroacupuncture and transcutaneous electrical nerve stimulation in the rat. *Int J Neurosci* 65:117–129.

Wang JQ, Mao L, Han JS (1992b): Comparison of the antinociceptive effects induced by electroacupuncture and transcutaneous electrical nerve stimulation in the rat. *Int J Neurosci* 65:117–129.

Wells E, Jackson R, Diaz R, Stanton V (1995): Acupuncture as an adjunct to methadone treatment services. *Am J Addict* 4:198–214.

Wen H, Cheung S (1973): Treatment of drug addiction by acupuncture and electrical stimulation. *Asian J Med* 9:138–141.

Wu LZ, Cui CL, Han JS (1995): Han's acupoint nerve stimulator (HANS) for the treatment of opiate withdrawal syndrome. *Chin J Pain Med* 1:30–38.

Xie GX, Han JS, Hollt V (1983): Electroacupuncture analgesia blocked by microinjection of anti-beta-endorphin antiserum into periaqueductal gray of the rabbit. *Int J Neurosci* 18:287–292.

Zhou ZF, Du MY, Wu WY, Jiang Y, Han JS (1981): Effect of intracerebral microinjection of naloxone on acupuncture- and morphine-analgesia in the rabbit. *Scientia Sinica* 24:1166–1178.