

Acupuncture for the Treatment of Drug Addiction

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Accepted: 13 June 2008
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Abstract Over the last three decades there has been an increasing interest in acupuncture treatment of substance abuse around the world. Three important steps can be identified in this field. Dr. Wen of Hong Kong was the first (1972) to report that acupuncture at 4 body points and 2 ear points combined with electrical stimulation can relieve opioid withdrawal signs in the addicts. The second major step was made by Dr. M. Smith in New York, the head of the National Acupuncture Detoxification Association (NADA) of the USA, who finalized a protocol (1985), using only ear points without electrical stimulation for the treatment of drug abuse. The recent advance in this field was made by Dr. Han of the Peking University, Beijing, who characterized a protocol (2005), using electrical stimulation of identified frequencies on body points to ameliorate heroin withdrawal

signs and prevent relapse of heroin use. In this review, the efficacy of acupuncture and related techniques for the treatment of drug dependence in experimental settings and clinical practice will be reviewed, and the possible mechanisms underlying this effect be discussed.

Keywords Acupuncture · Drug addiction · Withdrawal syndrome · Relapse

Introduction

Acupuncture is an essential part of traditional Chinese medicine, performed by inserting thin solid needles to specific documented points of the body. The needle can be manipulated manually (manual acupuncture) or connecting to an electrical stimulator for “electroacupuncture” (EA). Acupuncture or EA stimulation typically elicits a composite of sensations termed *deqi*, which manifests as numbness, heaviness, distention, and soreness, believed to be a trait characteristic in achieving a therapeutic effect [1]. The practice of manual acupuncture has accumulated affluent clinical experience for thousands of years in China. It spread to Japan in the 6th century, then to Europe in the 17th century. It is now practiced in 120 countries and regions and has become an important modality for treatment throughout the world [2]. As we have known that acupuncture is most commonly used for its analgesic effects, however its medical applications are by no means limited to pain treatment. Some 35 years ago, it was serendipitously observed that acupuncture could relieve opiate withdrawal signs in the addicts [3]. This finding has been given much attention by clinicians and research scientists around the world [4–6]. Different types of protocols have been developed since then. In this review, we will briefly

Special issue article in honor of Dr. Ji-Sheng Han.

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analyze the history of development of the technique, the site of stimulation (body- or ear-points), mode of stimulation (needle insertion only, needle insertion plus manipulation, electrical stimulation via needles or via skin), parameter of electrical stimulation (frequency, pulse width and intensity), the target substance of abuse (heroin and cocaine), and the stage of drug dependence (physical or psychic dependence). In order to compare the results with pharmacological treatments, the intervention was also evaluated including the dependence liability of the acupuncture per se.

From a Serendipitous Discovery to the NADA Protocol

Although acupuncture has been used in China for thousands of years, acupuncture for the treatment of addiction in the modern era began with an incidental discovery by Wen, a neurosurgeon in Hong Kong [7]. In early November 1972, a 50-year-old man with brain concussion was admitted to the neurosurgical unit of the Kwong Wah Hospital. Knowing that the patient is an opium addict of 5 years' duration, he was given tincture of opium to relieve his withdrawal syndrome in the ward. After the cerebral concussion had improved, the patient was asked whether he would agree to do cingulotomy to relieve his drug abuse problem. He agreed. During the operation for surgery, instead of local anesthesia being injected under the scalp, acupuncture anesthesia (analgesia) was used. Four needles were inserted into the right hand (IL-4 and SI-3) and in the arm (EH-4 and TB-9), and another two needles into the right ear (brainstem and Shenmen). Stimulation with an electrical stimulator was carried out for half an hour. During stimulation, the patient voluntarily stated that his withdrawal signs had completely gone. The operation was canceled and the patient returned to the ward. In the evening, the patient had another withdrawal syndrome. Acupuncture and electrical stimulation was carried out again, and the withdrawal symptoms again disappeared. Wen and Cheung pursued this unexpected finding and conducted a series of studies examining the effect of acupuncture for heroin addiction, and concluded that acupuncture did relieve heroin withdrawal syndrome [8, 9].

In 1974, Wen and Cheung's acupuncture protocol described above was introduced into the Lincoln Recovery Center in Bronx, New York. Guided by clinical observation, an acupuncture treatment protocol evolved with two modifications: (1) acupuncture was applied only at the ear, not at the body. Five needles were inserted bilaterally into the outer ear or auricle at points termed *kidney*, *liver*, *lung*, *shenmen*, and *sympathetic*. (2) Since they found that electric stimulation of the needles did not seem to increase treatment effectiveness, it was given up. The protocol was

apparently effective across different substances of abuse. In 1985, under the guidance of Dr. Michael Smith, the Director of the Detoxification Center, the National Acupuncture Detoxification Association (NADA) was formed, the five-point auricular protocol—now known widely as the “NADA protocol”—was codified. An extensive training procedure was established. Individuals who receive the 70-h NADA training are known as “acupuncture detoxification specialists” (ADS), to distinguish them from acupuncturists who have undergone multiyear training in order to perform full-body acupuncture. The NADA protocol was later adopted in many clinical settings in western countries including residential programs, acute detoxification facilities and outpatient programs [5].

The NADA Protocol Used in Treating Cocaine Addiction

As mentioned above, acupuncture was originally developed in the 1970s as a treatment for opiate withdrawal syndrome, there have been no recent studies of acupuncture for opiate addiction in the US and in Europe, due perhaps to the fact that cocaine addiction has excessively surpassed that of heroin and no effective pharmacologic treatment is available for it. The following are some results and evaluations for the effectiveness of auricular acupuncture treatment for cocaine/crack.

While the NADA protocol was primarily aimed at detoxification of drug addicts by acupuncture that seemed to facilitate compliance with a drug-free treatment program [10]. Michael Schwartz et al. [11] observed the effect of acupuncture on withdrawal syndrome in the cocaine or heroin addicts with an average length of inpatient of 1 week or three outpatient acupuncture detoxification programs with an average duration of treatment of about 4 months. The result from the programs showed the value of outpatient acupuncture detoxification programs as a component of a substance abuse treatment system, and the risk of relapse was lower in patients with access to acupuncture.

Subsequently, in a controlled study conducted at Yale Medical School [12], 82 patients addicted to cocaine and maintained on methadone were randomized to one of the following treatment conditions: auricular acupuncture (a four-point subset of the NADA protocol), needle insertion control (four needles inserted into the rim or helix of the auricle), and relaxation control (“nature” videos with relaxing music). The treatments were provided five times per week for 8 weeks. During the study, patients attended a weekly coping skills group and received standard care in the methadone program (methadone plus weekly individual counseling). The main outcome, cocaine use, was assessed

by urine samples three times per week. Treatment credibility and therapeutic alliance were also assessed. Overall, 52 of 82 patients completed the study: 13 in acupuncture condition, 17 in the needle insertion control condition; and 22 in the relaxation control. Analysis of urine screens showed that patients assigned to the NADA acupuncture condition used significantly less cocaine over the course of the study compared with each of the two control conditions. In the last week of treatment, patients receiving the NADA protocol were significantly more likely to provide three cocaine-free urine screens (54%) compared with the needle insertion control group (24%), and the relaxation group (9%). However, one interpretation of these findings was that less motivated patients dropped out of “true” acupuncture condition, but were retained in the other conditions.

The Cocaine Alternative Treatment Study (CATS) [13] was a large scale, multi-site study based on a design similar to the Yale study. In this study, 620 patients addicted to cocaine were enrolled from six treatment sites across the country; 412 of the patients were “primary” cocaine-dependent, and 208 were also opiate-dependent and maintained on methadone. Patients were randomized to the same three treatment conditions used in the previous Yale study: true acupuncture, helix needle insertion control (sham acupuncture), and relaxation control for a treatment period lasting for 8 weeks. Individual counseling was offered to patients at the primary cocaine sites, and the patients maintained on methadone received standard care as offered in their methadone program. The primary outcome measure was cocaine use as assessed by urine screens three times per week. Results showed that, unlike the previous study [14], there were no differences in outcome among any of the three treatment conditions, overall or at any of the six sites during the study or at a 3- or 6-month follow-up. In the last week of treatment, 24, 31, and 29% of patients in the true acupuncture, sham acupuncture, and relaxation control conditions, respectively, were abstinent from cocaine. This large study seemed to provide negative evidence regarding acupuncture’s efficacy for the treatment of cocaine addiction. Margolin et al. [15] reported after doing further investigation that treatment context may influence the outcome. As for the mechanism of action of the auricular acupuncture on treating cocaine addiction, there were just a few reports [16, 17], showing that stimulation of the auricular branch of the vagus nerve would cause release of endogenous opioids and other neuropeptides [18, 19].

Although a review summarized by Attilio D’alberto in 2004 stated that the previous trials based on the NADA protocol could not confirm the effectiveness of acupuncture on treatment of cocaine abuse [6], the treatment of drug abuse was still kept in the record of World Health Organization

(WHO) as one of the 42 medical problems suitable for acupuncture treatment. The major putative advantages are inexpensive, simple and without side effects [20].

Acupuncture Treatment of Drug Addiction in Peking University

Why Using Acupuncture for the Treatment of Heroin Addiction?

Large scale research on acupuncture analgesia in China was triggered by the clinical application of “acupuncture anesthesia”, when a group of medical professionals started to use acupuncture for the prevention of surgically induced pain in the late 1950. In 1965, Dr. Han of the Department of Physiology, Beijing Medical University and his colleagues were involved in the study of the mechanisms underlying the acupuncture anesthesia. After about 30 years of research, it was made clear that acupuncture (both manual and electro-acupuncture) can accelerate the production and release of opioid peptides in the CNS to induce an antinociceptive effect. This effect was frequency dependent, i.e., low frequency (2 Hz) stimulation accelerated the production of enkephalin and endorphin, whereas high frequency (100 Hz) that of dynorphin [21, 22]. It was in the year of 1990 that China started to report cases of drug addiction. If acupuncture can accelerate the release of endorphins, it is natural to consider why not making use of acupuncture to relieve withdrawal syndrome of opiate addicts during drug abstinence. This thought was put into action in rats made dependent on morphine and in humans.

Acupuncture for the Relief of Withdrawal Syndrome: Rat Experiment

Rats were made dependent to morphine by repeated injections of morphine for 5 days. An injection of the opioid receptor antagonist naloxone would precipitate a serious episode of withdrawal syndrome. The original perspective was that 2 Hz would be more effective than 100 Hz in suppressing withdrawal syndrome, if the effect of EA was to accelerate the release of morphine-like opioid peptides (enkephalin and endorphin) to replace morphine, thus ameliorating abstinence syndrome. Surprisingly, the results showed that 2-Hz EA was only marginally effective in reducing withdrawal in 2 of 5 signs [23], whereas 100 Hz EA produced a dramatic suppression of all 5 withdrawal signs. In other words, 100-Hz EA was far more effective than 2-Hz EA in suppressing withdrawal syndrome [23, 24]. Literature survey revealed that dynorphin can suppress the withdrawal syndrome in heroin-dependent humans [25] and in morphine-dependent animals via the

κ -opioid receptors, and the site of action is in the spinal cord [26]. Indeed, the naloxone-precipitated withdrawal syndrome can be suppressed by spinal intrathecal administration of a κ -opioid receptor agonist U-50488, whereas the κ -opioid antagonist nor-BNI elicited a dose-dependent augmentation of naloxone-precipitated withdrawal [27]. The latter result implies that an endogenous κ -agonist, most probably dynorphin, exerts a tonic suppressive effect on morphine withdrawal syndrome at the spinal level. Recently Chu et al. observed that 100-Hz EA, while suppressing morphine withdrawal, could facilitate the recovery of the ventral tegmental area (VTA) dopaminergic cells damaged by chronic morphine treatment and up-regulate the BDNF protein level in the VTA, which implied that the detoxification effect of 100 Hz EA may be associated with the activation of endogenous BDNF [28, 29].

Acupuncture for the Relief of Withdrawal Syndrome: Human Observation

Encouraged by the results obtained in rats, acupuncture was used in heroin addicts for detoxification. A technical problem was that in drug addicts subjected to withdrawal, they were very much irritated and inconvenient for precise needle insertion. Moreover, the needle inserted into the point was sometimes broken by excessive agitation. The metallic needle was thus replaced by self-sticky electrodes placed at the skin over the acupoint. Experimental data showed that this transcutaneous acupoint electrical stimulation was at least as effective as, if not more effective than, EA [30]. The device used for this purpose was named Han's acupoint nerve stimulator (HANS).

Immediate Effect Induced by Single HANS Treatment

For acupoint stimulation, one pair of skin electrodes (29 × 29 mm) was placed on the Hegu point (LI-4, at the dorsum of the hand) and the other at the palmar side on Laogong point (P-8, opposite to LI-4), to complete an electric circuit. Another pair of electrodes were placed on Neiguan (P-6, located at the palmar side of the forearm, 2 inches proximal to the palmar groove, between the tendons of the palmaris longus and flexor carpi radialis) and Waiguan (TE-5, on the dorsal surface of the forearm opposite the P-6) point to complete a circuit (Fig. 1). These points are known to calming down the heart rate according to the theories of traditional Chinese medicine. A “dense-and-disperse, DD” mode of stimulation was administered, in which 2-Hz stimulation alternated automatically with 100-Hz stimulation, each lasting for 3 s. This mode of stimulation could release all four kinds of opioid peptides in the central nervous system (CNS) [31], producing a maximal opioidergic effect. The control group received the

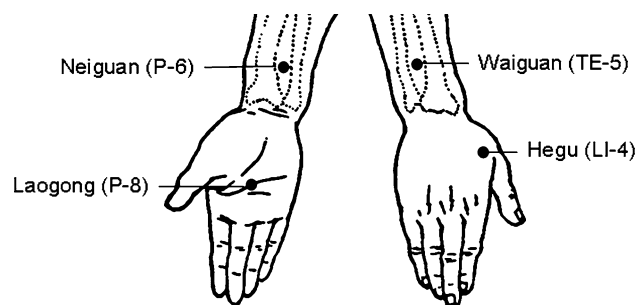


Fig. 1 Sketch map indicating the location of acupoints: LI-4 (at the dorsum of the hand on the thenar eminence) and P-6 (at the palmar side of the forearm, 2 inches proximal to the palmar groove, between the tendons of the palmaris longus and flexor carpi radialis) for the application of HANS stimulation

same treatment of placing the skin electrodes on site, except that the electrodes were disconnected from the electric circuitry. One of the most prominent signs of withdrawal was tachycardia. The average heart rate of the patients in opioid withdrawal was 109 beats per minute (BPM) before treatment. The DD mode stimulation produced an immediate suppression of the tachycardia within 5–10 min, reaching 90 BPM at the end of 30 min. While the effect is statistically very significant, even though it is short lasting, and return to its original level in another 30 min [32].

Cumulative Effect of Multiple Treatments with HANS [32]

In another study, the same treatment was given 30 min a day for 10 consecutive days. Heart rate was measured with an electrocardiogram before (PRE) and immediately after (POST) the HANS stimulation. The difference between the PRE and the POST of the same day indicated the immediate effect, while the decay of the PRE over the whole period of observation showed the long lasting effect. It took 4 days for the heart rate to return to the baseline level. In the control group receiving mock HANS, heart rate did not come down to a level of 100 BPM until 8 days after the starting of the “treatment”. The results suggest that repeated daily HANS treatment is effective in reducing the tachycardia of heroin withdrawal syndrome, with an effective order of DD > 100 Hz > 2 Hz.

Another objective parameter for measuring the severity of heroin withdrawal is the body weight. The heroin addicts recruited in this study were 17–35 years old, their average body weight was 49–51 kg. In the control group receiving mock HANS, body weight remained unchanged in the 10 day observation period, whereas in the HANS treated groups, a net increase of 5 kg was recorded. This increase of body weight (approximately 10%) is apparently due to the reduction of the withdrawal syndrome, leading to an increase of food and water intake.

To obtain a quantitative estimate of the effect of HANS, the following protocol was established in another clinical setup, with a total observation period of 14 days [33]: (a) HANS of 2/100 Hz, 30 min per session, was used 3–4 times a day on the first 2 days, then 2–3 times a day on days 3–7, and twice a day on days 8 to 14. (b) A four-channel HANS device was used instead of two channel device. The acupoints used were Hegu/Laogong (LI-4/P-8) for left (or right) hand, Neiguan/Waiguang (P-6/TE-5) for right (or left) arm, and Xingjian/Sanyinjiao (LV-2/SP-6) for both legs. (c) The intensity of stimulation was twice threshold (4–6 mA being the threshold value [T]) for the first 2 days, and 2.5 to 3.0 T thereafter. (d) Buprenorphine (Buprenex) i.m. was ordered *p.r.n.* Twenty eight heroin addict were randomly divided into 2 groups, receiving buprenorphine only, or HANS plus buprenorphine. In the buprenorphine-only group, the total dose of buprenorphine requested in 14 days averaged to 12.91 ± 1.34 mg, whereas that of the HANS-plus-buprenorphine group averaged only to 1.01 ± 0.09 mg, which was consumed only in the first 5 days. In other words, the total amount of buprenorphine used in the HANS group was only 7.8% of that needed in the pure buprenorphine group showing a reduction of more than 90%. This can be taken as a quantitative estimate of the effect of HANS for opioid detoxification. Similar observations were made in another group of heroin-addicts using methadone [34] instead of buprenorphine. The total dose of methadone used in the control group averaged to 202 ± 15 mg, whereas that in the HANS-plus-methadone group was only 50.5 ± 8.2 mg, with a 75% reduction ($p < 0.001$).

Acupuncture for Suppression of Psychic Dependence: Animal Studies

It is well-known that drug addiction is a chronic, recurrent condition with high rate of relapse even after prolonged drug-free periods. According to statistics from different sources, the relapse rate can be as high as 95–99%. Therefore the final goal for treating drug addiction is not just detoxification (relieving or curing the withdrawal syndrome), but to relieve craving (psychic dependence) and to remove the compulsive behavior of drug seeking and taking after the detoxification. There are several animal models [35] that can be used to study the problem of craving and relapse to drugs of abuse. Conditioned place preference (CPP) is one of the frequently used models. In a two-chamber or three-chamber experimental apparatus, the drug (unconditioned stimulus) is injected to the animal in one of the chambers, and normal saline to the other chamber. After repeated training, the rat will choose to stay longer on the drug-associated side than in a chamber associated with normal saline. The ratio between the time

spent in the drug-associated and the saline associated side can be taken as an index for the degree of “craving”. Using this model, experiments were conducted to test whether acupuncture can suppress the expression of morphine-induced CPP. Wang et al. [36] first observed the effect of EA at 2, 100, or 2/100 Hz (DD) for 30 min, with intensity increasing stepwise from 1 mA to 2 mA and to 3 mA within 30 min, on morphine CPP expression in rats. The result showed that the CPP was significantly suppressed by EA of 2 and 2/100 Hz, but not of 100 Hz. Three control groups of rats received one of the following: (a) restraining in the holder for 30 min, (b) holder restraining plus needle insertion without electrical stimulation, or (c) intermittent electrical stimulation on the feet (foot shock). None of the three control groups showed any suppression of the CPP. The results suggest that it is the low-frequency component of the EA that suppressed the CPP expression. Since the effect of 2 Hz EA can be completely reversed by the opioid receptor antagonist naloxone at a small dose of 1 mg/kg, which is sufficient to block the opioid μ - and δ -, but not the κ - receptors, it seems evident that the effect of EA is mediated by endogenously released μ - and δ -opioid agonists, most likely endorphins and enkephalins, to ease “craving” for exogenous opioids (in this case, the morphine). Another issue deserving attention is that the effect of EA can still be revealed 12 h after the episode of EA, suggesting that this effect lasts longer than acupuncture-induced analgesia [21], which usually disappears within 60 min after the end of stimulation.

In practical life, craving and relapse can be easily induced by stress or by a very small dose of opioids. This phenomenon can be reproduced in animals using the CPP model. Wang et al. [36] reported that morphine-induced CPP disappeared after a 9-day extinction period. The extinguished CPP could be easily reinstated by foot shock stress, or by a small dose of morphine or amphetamine. Again, the reinstated CPP could be reversed by 2 or 2/100-Hz EA in a naloxone-preventable manner [37]. It is worth mentioning that while both drug priming and foot shock stress can reactivate morphine CPP, the underlying mechanisms may be different. The drug-priming-induced reactivation can be totally blocked by the destruction of the mesolimbic dopamine system, including the VTA and the shell part of the nucleus accumbens, while the foot-shock-induced reactivation of CPP depends on the integrity of the central nucleus of amygdala [37].

It was interesting to find that while single session of 100 Hz EA was ineffective to block morphine CPP [36], multiple treatments of 100 Hz EA (once a day for 3 days) became effective [38]. This effect can be blocked by the δ - and κ -, but not the μ opioid antagonists. Both 2 and 100 Hz EA (once a day for 3 days) could also inhibit the CPP reinstated by drug priming [39].

In a further study, Chen et al. [40] confirmed that the efficacy of EA to suppress morphine induced CPP depends not only on the frequency of EA (2 Hz better than 100 Hz), but also on the total session of EA being administered (5 times > 3 times > single session). This may be related with the degree of activation of the genes encoding opioid peptides. By measuring the mRNA level of preproenkephalin (PPE) and prodynorphin (PPD) in Nucleus Accumbens of morphine CCP rats, it was found that 2 and 100 Hz EA can selectively elevate the level of PPE- and PPD-mRNA, respectively [39].

Acupuncture for Suppression of Psychic Dependence: Human Studies [41]

In a clinical trial using HANS for the suppression of opiate craving in humans, a total of 117 heroin-addicts who had completed the process of detoxification for more than 1 month, were recruited. They were randomly and evenly assigned into 4 groups. Three groups received HANS treatment of different frequencies (2, 100, or 2/100 Hz). Self-sticking skin electrodes were placed on four acupoints: Hegu and Laogong (palmar side of the Hegu point) in the left (or right) hand to complete a circuit, and Neiguan and Weiguan in the opposite arm to complete a circuit. The control group was processed as in the previous groups except that the intensity was minimal (15 Hz, threshold stimulation for 3 min, and then switched to 1 mA thereafter) to serve as a mock HANS control. Visual analogue scale (VAS) was used to assess the degree of craving. There was a very slow decline of the VAS in the mock HANS control group in a period of 1 month. A dramatic decline of the degree of craving was observed in the groups receiving 2 and 2/100-Hz electric stimulation, but not in the group receiving 100-Hz stimulation. In summary, the results observed in humans were in line with the findings obtained in the rat: low-frequency HANS is more effective than high-frequency HANS in suppressing the morphine-induced CPP [41].

Meanwhile, Hainan province in south China, a local rehabilitation center under the auspices of the Peking University Neuroscience Research Institute was established. The staffs kept in close contact with all the previous drug-addicts discharged from the detoxification center. They could get HANS treatment from the rehabilitation center for free and ad libitum. As an alternative, they could buy a unit of the device at an affordable cost and apply HANS at home under the staff's continuing supervision. A follow-up study was conducted on a group of 56 subjects who used HANS at home. Using monthly urine test as an outcome criterion, the relapse rates at third, sixth, ninth, and twelfth months were 50.0, 71.4, 80.4, and 83.9%, respectively. Those showing negative urine tests for 12 or

24 consecutive months were given a naloxone test (0.4 mg subcutaneously \times 2 at 15-min interval) to further confirm their heroin-free status. Compared with the 94% relapse rate at 6 months and more than 98% relapse rate at 1 year in the majority of reports on heroin addiction (without methadone maintenance) [42], an 83.9% relapse rate (16.1% success rate) at 1 year in the present investigation is encouraging [43].

Similar studies [44] were performed in treatment centers located in Zhanjiang county, Guangdong province and in Shanghai, the 1-year success rate was between 20% and 30% respectively, depending on the degree of follow-up psychological and medical care offered to the patients. Obviously, EA or HANS has been emerged as a highly hopeful foreground on the treatment for opioid addiction. A well designed, multicenter clinical trial is warranted in the future. Whether HANS is effective in reducing the craving for other drugs of abuse, such as cocaine, and other substance of abuse, such as alcohol and cigarette smoking, deserves further investigation.

Some Technical Comments

Ear Acupuncture Versus Body Acupuncture

Although the ear is not included in the area of distribution of the classical 14 meridian system of the ancient Chinese medicine, it is certainly worthwhile to try ear acupuncture in medical practice. However, there is at least no evidence to limit the site of acupuncture only at the ear, and not at the body sites. In fact, the original protocol [3] of Wen used 4 body points and 2 ear points for treatment. In the United States, a person received 70 h of NADA ear protocol training obtained a mid-level title of "acu-detox specialist" allowed only to administer the ear protocol [5]. It would be difficult for them to treat other complaints with conventional body acupuncture. In fact, the vast possibility of using body acupuncture should not be neglected.

Needle Staying Versus Mechanical or Electrical Stimulation

The original protocol of Wen used acupuncture combined with electrical stimulation [3], now called EA, whereas the NADA protocol preferred to leave the needle in place without further stimulation. It is true that the ear concha, composed of cartilage and skin, is very sensitive to pain even when the needle is remained untouched. However, an early study conducted in 1973 in Shanghai had revealed that in order to produce a significant analgesic effect, manual manipulation or electrical stimulation applied on the needle is indispensable [45].

Acupuncture and EA Versus Transcutaneous Electrical Stimulation

A series of study showed that the manipulation of the needle triggers a train of nerve impulses transmitted along the afferent nerve to the CNS. Injection of local anesthetics deep into the acupoint or along the nerve trunk would block the effect of acupuncture [46]. If nerve activation accounts for the transmission of the acupuncture signals, then similar effect should be produced whether the nerve impulses are generated (1) by manipulation of the needle, (2) by electrical stimulation via the needle, or (3) by electrodes placed on the skin over the point that force the current to pass through the same underlying tissue and producing a sense of *deqi*. In a rat experiment the analgesic effect of EA and transcutaneous nerve stimulation was compared and found that there was no significant difference between them, whether on the efficacy of antinociception or on the underlying mechanisms [30].

Compared to manual needling, EA or HANS has the advantage of easy to master with high reproducibility. To take an example, it is now evident that the frequency is a very important and precise parameter of the electrical stimulation: high frequency (100 Hz) stimulation is best for reducing the physical dependence, low frequency (2 Hz) for the psychic dependence, and DD for both in opioid addicts. Another example is that while 2 Hz EA is more effective than 100 Hz EA to suppress morphine-induced CPP in the rat, the reverse is true when EA is used to suppress cocaine-induced CPP [47]. Compared to EA, it may take years to master the sophisticated technique of manual needling, according to Traditional Chinese Medicine.

Compared to EA, the advantages of using the transcutaneous stimulation for the treatment of drug addiction are at least two fold: (1) treatments can be performed at home by the patient under the auspice of the physician thus saving time and effort to be treated in the hospital; (2) the possibility of cross infection through needles is reduced from minimal to zero (Table 1).

How Frequently Should Acupuncture be Used for the Treatment of Drug Dependence?

Although the use of single session of EA or HANS is effective in reducing opiate withdrawal, it is recommended to use 3 times a day in the first 5 days, 2 times a day in the next 5 days and at least once a day for the rest of the time for a total of 2 weeks. The session applied immediately before sleep is critical since this would facilitate a good sleep [48].

Treatment for Physical Versus Psychic Dependence

The effect of acupuncture for reducing withdrawal syndrome is easy to observe and straight forward as was described by Wen in his first incidental experience [3]. The most important advantage of HANS resides on its ability to suppress craving hence to reduce the chance of relapse, since there is so far no effective means to prevent relapse without introducing another drug of addition, such as methadone. The drug addicts always confess that they have no confidence on themselves. What is important to them is not the past, nor the future, but the present. They often asked the question of “Can you solve my problem without taking the drug?” Once they feel that acupuncture or HANS can resolve, or partially resolve their problem in 30 min without taking an addictive drug, they will start to develop confidence. After several episodes of effective protection, the confidence and loyalties to this non-pharmacological treatment becomes increasingly evident, and the compliance to acupuncture is built up quickly. In other words they start to seek help not from outside, but from within their own brain (increased release of endorphins). This is one of the most important psychological perspectives for the treatment of drug abuse with acupuncture.

Unexpected Physiologic Changes that Help to Build up Psychological Confidence

Two unexpected changes in the body function were found. One is the disappearance of injection marks within 2 weeks of HANS treatment [33], and the other is the recovery of

Table 1 Technical settings for acupuncture treatment of drug abuse

Protocol	Site of stim. Body/Ear	Mode of stim. Needle/ES	Dependence Physical/Psychic	Drug of abuse Heroin/Cocaine
Wen et al. [3]	4/2	N/ES	+/-	+/-
Smith et al. [5]	-/5	N/-	+/-	+/+
Han et al. [43]	4-8/-	N or Skin/ES	+/+	+/-

Numbers indicate number of needles used

N: needle insertion; Skin: skin electrode pad; ES: electrical stimulation

the depressed sexual function [49]. These changes provided with positive psychological impact and confidence, and would certainly be helpful in the establishment of their normal life, thus delaying the occurrence of relapse to drug. The underlying mechanisms for the above mentioned efficacies of HANS have not yet been clarified.

Does EA or HANS per se Induce Dependence?

If EA can accelerate the release of endogenous endorphins to relieve craving, a natural question would be “Does EA itself produce dependence?” Chen et al. [40] used CPP model to clarify this question. Twenty eight rats were randomly divided into 2 groups. The EA group was confined in the holder for EA stimulation for 30 min and then immediately put into one of the chambers for 45 min. The control group was treated in the same way except with no electrical stimulation administered to the needles and put into another chamber. The treatment was executed in 4 consecutive days. In the fifth day, the rats were put into the midway chamber to test their preference between the two chambers. Most of the rats stay longer time in the chamber paired with EA ($p < 0.05$), indicating that they seem to like the experience of EA. However, to the best of our knowledge, there is no single report showing dependence to EA or HANS. Therefore the risk of producing dependence to EA or HANS appears to be minority.

We known that CPP involves the mechanisms of learning and memory. Theoretically a blockade of the expression of CPP may be caused by the deterioration of the memory. To assess whether EA could affect learning and memory, Chen et al. [40] performed the Morris water maze (MWM) experiment to observe the effect of EA on the consolidation of spatial memory. EA was administered after the completion of MWM training for 7 days. On day 8–12 the rats were given EA or restraint once a day for 5 days, with the blank control group leaving in the home cage in the same time period. Results showed that in the control group and restraint group, there was a marked prolongation of the escape latency, implying a natural fading of memory with time. In the EA group, no significant change was observed as compared to the pre-EA value, suggesting that EA not only produces no dysfunction or worsening of memory, rather, causes a strengthening of memory maintenance or consolidation.

Conclusions

Science is rapidly progressing, so should be the idea and technology of acupuncture. The identification of “specific” points on the ear is a discovery of the 20th century [50]. The use of needles made of stainless steel rather than

silver, and the application of electric stimulation in lieu of manual needling is natural to modern physicians. The principle of acupuncture treatment of drug abuse is based more on the evidence obtained from clinical observation as well as basic research in animals and humans. Meanwhile the ancient rules of the traditional acupuncture should certainly be considered seriously.

In order to best serve the drug addicts seeking for painless drug abstinence, the following should be considered in setting up criteria for the protocols for acupuncture treatment: effectiveness, standardization and reproducibility, low-cost, time-saving, least side effects and complete drug abstinence achievement. The HANS protocol introduced by the Neuroscience Research Institute at Peking University could be considered as one of the choices when a large scale, multi-center research program is planned in the future.

Acknowledgements This study was supported by the National Basic Research Program (G1999054000, 2003CB515407) and National Natural Science Foundation (30170814, 30370466 and 30770690) of China and NIH (P01 AT 002038), USA. We sincerely thank Professor JS Han for his critical review and in-depth comments in preparation of this manuscript.

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