Acupuncture therapy for drug addiction

Farid Esmaeili Motlagh\textsuperscript{1,2,3}, Fatimah Ibrahim\textsuperscript{1,2*}, Rusdi Abd Rashid\textsuperscript{3}, Tahereh Seghatoleslam\textsuperscript{3,4} and Hussain Habil\textsuperscript{3}

Abstract

Acupuncture therapy has been used to treat substance abuse. This study aims to review experimental studies examining the effects of acupuncture on addiction. Research and review articles on acupuncture treatment of substance abuse published between January 2000 and September 2014 were searched using the databases ISI Web of Science Core Collection and EBSCO’s MEDLINE Complete. Clinical trial studies on the efficacy of acupuncture therapy for substance abuse were classified according to substance (cocaine, opioid, nicotine, and alcohol), and their treatment protocols, assessments, and findings were examined. A total of 119 studies were identified, of which 85 research articles addressed the efficacy of acupuncture for treating addiction. There were substantial variations in study protocols, particularly regarding treatment duration, frequency of electroacupuncture, duration of stimulation, and choice of acupoints. Contradictory results, intergroup differences, variation in sample sizes, and acupuncture placebo effects made it difficult to evaluate acupuncture effectiveness in drug addiction treatment. This review also identified a lack of rigorous study design, such as control of confounding variables by incorporating sham controls, sufficient sample sizes, reliable assessments, and adequately replicated experiments.

Background

In 1997, the National Institutes of Health accepted acupuncture as an acceptable procedure complementary to Western medicine [1]. Evidence for its therapeutic effects comes mainly from clinical practice and research into pain control, fibromyalgia, headaches, Parkinson’s disease, schizophrenia, and depression [2]. Acupuncture therapy can be administered using either manual insertion of needles or electroacupuncture (EA), a mild electrical stimulation of acupoints. Extended acupuncture methods may involve finger pressure (acupressure) and laser therapy [3].

In 1985, Dr. M. Smith finalized the National Acupuncture Detoxification Association (NADA) protocol that is currently practiced in over 250 hospitals in the United Kingdom and United States [4]. In 1996, the World Health Organization accepted acupuncture as a treatment for drug abuse [5]. The latest modification to this treatment protocol was developed in 2005 by Dr. Ji Sheng from Peking University, Beijing, China [6]. Currently, more than 700 addiction treatment centers use acupuncture as an adjunctive procedure [7].

Prominent effects of acupuncture are increases in the levels of enkephalin, epinephrine, endorphin, serotonin, norepinephrine, and dopamine in the central nervous system and plasma [8] that might mediate substance abuse. Acupuncture has been used to treat addiction for three decades [2–89]. For example, auricular acupuncture (AA) is effective in treating alcohol and drug abuse in both Europe and the United States [4].

However, several clinical trials have indicated that acupuncture was not effective in treating addiction [2,3,31,67,69,78–80]. Thus, the efficacy of the NADA protocol has been reassessed over the last decade [7]. Several factors have been studied to evaluate the efficacy of acupuncture therapy; for example, treatment protocol, choice of acupoints, duration of acupuncture, study design diversity, sample size, addiction history, and assessment techniques.

This study aims to review the published research on acupuncture therapy for substance abuse in relation to study type, authors, funding agencies, countries, agonist substances, and acupoints used for stimulation.
Experimental studies published between January 2000 and September 2014 were systematically reviewed and analyzed to try to resolve the lack of agreement about acupuncture’s efficacy for substance abuse.

**Review**

**Literature search**

A search of the ISI Web of Science Core Collection and EBSCOHost (MEDLINE Complete) databases for the period January 2000 to September 2014 was conducted to identify acupuncture clinical trials. Keywords, topics available in the databases, and titles were searched for the following terms: “acupuncture,” “electroacupuncture,” “acupoint stimulation,” “transcutaneous,” and “electrostimulation” as single words or combinations (total number of articles: 25 358). The results were refined to exclude non-English language materials. The preliminary findings of the first phase were refined by several parallel filters to identify documents relevant to acupuncture treatment of substance abuse. The operator between the filters was the “OR” command. Single, relevant words were selected for each filter and included any combination of the following: “alcohol,” “addict,” “opioid,” “heroin,” “cigarette,” “nicotine,” “tobacco,” “cocaine,” and “substance” as title, topic, keywords, or abstract text (total number of articles: 230) from both searched databases. The search results were collated and filtered to exclude proceedings papers and letters, yielding 161 studies. The abstracts of these documents were reviewed to exclude papers related to other addiction fields such as the Internet, food, or games; 119 documents comprised the refined, selected results. Three authors (FEM, RR, and TS) independently assessed studies for eligibility and crosschecked the material for study relevance. The publication selection process was shown in Fig. 1.

The articles were classified according to their specifications, including publication date, number of citations, source, authors, organization, and funding agencies. All original research papers were examined for their efficacy and method of treating different categories of addiction to agonist substances (e.g., cocaine, opioid and opiate, nicotine, alcohol, morphine). Original clinical trials that investigated the efficacy of acupuncture therapy were divided into six categories based on substance dependence (cocaine, opioid and opiate, nicotine, alcohol, morphine, and other substances) with a narrative review of their methods and results. Although morphine is an opioid, it has been assigned its own section because of the high number of publications on this topic. Heroin, methadone, and opiates are discussed in the opioid section.

The findings are discussed and compared according to type of addictive substance. There were 96 articles and 29 review papers; 83 articles were original investigations (76 of which were clinical trials of acupuncture efficacy), with 45 articles involving human beings and 38 involving animals. Figure 2 shows the percentage of all documents in each type of category. Original investigations of humans and animals were classified separately according to type of substance dependence. These articles placed more of an investigative emphasis on morphine and alcohol than on other substances.

The total number of citations for all documents was 1495 (mean = 15.83 and standard deviation = 15.27, citation range 2–87 by excluding 29 articles cited zero times or only once). The top ten most cited articles were shown in Table 1. The United States (43 articles) and China (40 articles) published almost 70 % of all articles. Among the Asian countries, China and South Korea published 59 articles, comprising 50 % of publications. Their funding agencies were also the top supporters in this field. Peking, Kyung Hee, and Daegu Haany Universities were the top three organizations, publishing 40 articles since 2000.

The published articles were associated with various research areas (Fig. 3). About 80 % of the articles focused on neuroscience and neurology, substance abuse, and integrative complementary medicine research areas. Published articles for each year were shown in Fig. 4.

Original experimental research articles were reviewed according to type of substance dependence (Fig. 2): the treatment method, subjects, objectives, and assessments of clinical trials for each group were shown in Tables 2, 3, 4, 5, 6, 7.

**Cocaine**

Avants and Margolin have evaluated the efficacy of AA for cocaine addiction treatment in four studies on human subjects. Although promising results were reported in their first study on 82 cocaine-dependent subjects [10], another study on 83 cocaine-dependent subjects found AA to be effective in reducing cocaine in only one of two trials [60]. When the original study was repeated with 620 subjects, no effect was found [61]. These researchers also conducted a study in 2005 on 40 cocaine abusers who had tested positive for the human immunodeficiency virus and were under methadone maintenance; no difference was found between the standard and reduced NADA protocols for cocaine use [59].

Three studies on rats were conducted to explore the effects of bilateral stimulation at the Shenmen (HT7) points. Modulation of the central dopaminergic system by acupuncture might be effective in preventing the behavioral effects of cocaine in rats [44]. By regulating neuronal activation in the nucleus accumbens (NAC) shell, acupuncture reduced stress-induced relapse [84]. The effect of acupuncture on the inhibition of cocaine-induced locomotor activity was mediated by A-fiber...
activation of the ulnar nerve in rats [42]. See Table 2 for study details.

**Opioids and opiates**

In 2002, Montazeri investigated the efficacy of acupuncture at Hegu (LI4), Neiguan (PC6), Shenmen (HT7), Tai-chong (LR3), Zusanli (ST36), Dazhui (DU14), and Baihui (DU20) in 40 male adult heroin- or opium-addicted patients. The severity of withdrawal symptoms declined when acupuncture was used in rapid opiate detoxification [63]. Liu (2007) used functional magnetic resonance imaging to show that hypothalamus activation associated with manual acupuncture at Zusanli (ST36) was more robust in heroin addicts or opium-addicted patients. The severity of withdrawal symptoms declined when acupuncture was used in rapid opiate detoxification [63]. Liu (2007) used functional magnetic resonance imaging to show that hypothalamus activation associated with manual acupuncture at Zusanli (ST36) was more robust in heroin addicts or opium-addicted patients. The severity of withdrawal symptoms declined when acupuncture was used in rapid opiate detoxification [63].

Eligibility

Records after combination of results (n = 230)

Records screened for exclusion of letters, meetings and conference papers (n = 161)

Letters, meetings and conference papers excluded (n = 69)

Full-text articles assessed for eligibility (n = 119)

Full-text articles excluded: abstracts were reviewed to exclude any paper, which was not related to the topic. Internet and game addiction = 27, food addiction = 15 (n = 42)

Studies included in qualitative synthesis: 83 original clinical investigations on efficacy of acupuncture. (Opioid and opiate=14, cocaine=7, nicotine=9, morphine=16, alcohol=16, other substance=21) (n = 83)

Studies included in quantitative analysis of publication date, number of citations, source, authors, organization and funding agencies (n = 119)

Screening

Included
was a possible adjunctive treatment to pharmacological treatments for heroin detoxification [62]. Acupuncture at Dazhui (GV14) and Baihui (DU20) prevented brain cell apoptosis in heroin-readdicted rats, normalized neuronal ultrastructure in the ventral tegmental area of heroin relapse rats, and protected nerve cells against injury in heroin relapse rats [32, 88].

Recent studies of acupuncture's effectiveness as an adjunct therapy in methadone maintenance programs have been controversial. In 2009, Bearn demonstrated a lack of effect for adjunctive methadone maintenance treatment with AA upon withdrawal severity or craving [11]. In 2013, Pei Lin showed a lack of AA effectiveness on the number of daily consumed cigarettes, relapse rate, and withdrawal symptoms, and examined patients' satisfaction and coping with AA as an adjunct treatment to methadone maintenance treatment among Malaysian subjects [57, 58]. However, Chan et al. [22] claimed that 2 weeks of acupuncture therapy reduced the daily dose of methadone and was also associated with greater improvement in sleep latency. See Table 3 for study details.

**Nicotine**

Acupuncture stimulation at Zusanli (ST36) exerted a therapeutic effect on nicotine detoxification [21] and acupuncture at Zusanli (ST36) or Shenmen (HT7) might attenuate anxiety-like behavior following nicotine withdrawal by modulating corticotrophin-releasing factor in the amygdala [20]. Smoking withdrawal symptoms could be ameliorated by acupuncture treatment [18]. In one study, acupuncture at Shenmen (HT7) attenuated
cigarette withdrawal symptoms more than acupuncture at Shousanli (LI10) [19]. Real acupuncture (as opposed to sham acupuncture) at Shenmen (HT7) alleviated cue-induced cravings through the regulation of activity in brain regions (medial prefrontal cortex, premotor cortex, amygdala, hippocampus, and thalamus) related to craving scores in the initial abstinence phase [38].

However, one study failed to find any effect of acupuncture on cotinine serum levels, carbon monoxide exhalation, and smoking quit rate in 59 smokers [83]. It has been suggested that DRD2 gene TaqI A polymorphism was related to AA response in smoking cessation treatment [65]. Auricular transcutaneous electrical neurostimulation relieved withdrawal symptoms and decreased

### Table 1 Top 10 most cited articles from 2000 to 2014

| Title | First author | Source title | Publication year | Total citations |
|-------|--------------|--------------|-----------------|----------------|
| Acupuncture: An evidence-based review of the clinical literature | Mayer DJ | Annual Review of Medicine | 2000 | 87 |
| A randomized controlled trial of auricular acupuncture for cocaine dependence | Avants SK | Archives of Internal Medicine | 2000 | 67 |
| Acupuncture for the treatment of cocaine addiction—a randomized controlled trial | Margolin A | Journal of the American Medical Association | 2002 | 66 |
| Clinical research on acupuncture: Part I. What have reviews of the efficacy and safety of acupuncture told us so far? | Birch S | Journal of Alternative and Complementary Medicine | 2004 | 64 |
| Peripheral neuropathy: Pathogenic mechanisms and alternative therapies | Head, Kathleen A | Alternative Medicine Review | 2006 | 50 |
| Acupuncture and related interventions for smoking cessation | White AR | Cochrane Database of Systematic Reviews | 2006 | 43 |
| A large randomized placebo controlled study of auricular acupuncture for alcohol dependence | Bullock ML | Journal of Substance Abuse Treatment | 2002 | 41 |
| Peripheral electric stimulation inhibits morphine-induced place preference in rats | Wang B; Luo, F | NeuroReport | 2000 | 39 |
| Acupuncture in clinical neurology | Rabinstein AA | Neurologist | 2003 | 37 |
| Traditional Chinese medicine in treatment of opiate addiction | Shi, Jie | Acta Pharmacologica Sinica | 2006 | 34 |

![Graph](image)  
**Fig. 3** Number of research articles in each area. Neuroscience, substance abuse, and complementary medicine are ranked highest.
anxiety and stress levels during the detoxification period in a study of six smokers [15]. Auricular transcutaneous electrostimulation therapy might be an acceptable alternative therapy for smoking cessation [72]. See Table 4 for study details.

Alcohol
Conflicting results from two large randomized single-blind, placebo-controlled trials suggested that acupuncture was not effective in reducing alcohol use [16, 39]. However, promising results have been found using acupuncture as an adjunctive treatment to carbamazepine medication to reduce the severity of alcohol withdrawal symptoms [39]. In one study, AA failed to reduce the duration and severity of alcohol withdrawal symptoms [43]; another study found no advantage for laser AA in treating alcohol withdrawal [74]. However, research indicated that laser therapy helps to promote the release of endorphins in the body and decreases discomfort accompanying alcohol withdrawal [87]. It might therefore be a safe and painless beneficial adjunct treatment for alcoholism [87].

Acupuncture at Zusanli (ST36) or Sanyinjiao (SP6) modulated postsynaptic neural activation in the striatum.
### Table 2 Original investigations of acupuncture therapy effects in cocaine-dependent subjects

| Publication year; first author | Objectives | Subjects | Stimulated acupoints (acupuncture type, acupoints, frequency) | Assessments | Outcomes |
|-------------------------------|------------|----------|---------------------------------------------------------------|-------------|----------|
| 2000 Avants [10]              | To evaluate the AA efficacy in cocaine addiction treatment compared to needle-insertion and no-needle relaxation control conditions | 82 Cocaine-dependent, methadone-maintained patients | Auricular acupuncture at 4 NADA points (sympathetic, lung, liver, and Shenmen (HT7)), 5 times a week for 8 weeks | Urine toxicology screens 3-times-weekly | Acupuncture showed positive results compared to control groups for treatment of cocaine dependence |
| 2002 Margolin [60]            | To Compare two cocaine addiction clinical trials of AA to explore consistency of treatment effects | 165 Cocaine-dependent, methadone-maintained patients (Study 1, n = 82; Study 2, n = 83) | Auricular acupuncture at 4 NADA points (sympathetic, lung, liver, and Shenmen (HT7)), 5 times a week for 8 weeks | Urine toxicology screens 3-times-weekly, retention in treatment, treatment attendance, treatment credibility, therapeutic alliance, and acute effects | The results of two groups were controversial and no conclusion could be made regarding the effectiveness of AA |
| 2002 Margolin [61]            | To evaluate the AA efficacy in cocaine addiction treatment | 620 Cocaine-dependent methadone-maintained patients. 412 Cocaine only and 208 opiates + cocaine | Auricular acupuncture at 4 NADA points (sympathetic, lung, liver, and Shenmen (HT7)), 5 times a week for 8 weeks | Urine toxicology during treatment and at the 3- and 6-month post randomization follow-up, and retention in treatment | Acupuncture was not more effective than a needle insertion or relaxation control in reducing cocaine use |
| 2005 Margolin [59]            | To evaluate effects of acupuncture and spirituality, therapy in the treatment of HIV-positive drug users | 40 HIV-seropositive, cocaine-dependent, methadone-maintained patients | Auricular acupuncture at 5 NADA points, 5 times weekly for 8 weeks | Urine toxicology twice weekly, depression and anxiety at pre- and post-treatment | Acupuncture and a spirituality-focused psychotherapy was effective in reducing the cocaine use |
| 2009 Lee and Bombi [44]       | To investigate the effects of acupuncture on the repeated cocaine-induced neuronal and behavioral sensitization alternations | 32 Male Sprague-Dawley rats, n = 15 acupuncture | Acupuncture bilaterally at Shenmen (HT7) for 1 min | Cocaine-induced locomotor activity and the expression of tyrosine hydroxylase (TH) in the brain | Acupuncture was effective for inhibiting the behavioral effects of cocaine by possible modulation of the central dopaminergic system |
| 2012 Yoon [84]               | To investigate the effects of acupuncture on cocaine-seeking and the expression of c-Fos and the transcription factor cAMP response element-binding protein (CREB) | 24 Male Sprague-Dawley rats, n = 6 EA | Acupuncture at Shenmen (HT7) as study and Yangxi (LI5) as control for 1 min | Cocaine-seeking behavior, surface expression, and phosphorylated CREB (pCREB) activation in the NAc shell | Acupuncture attenuated stress-induced relapse by regulating neuronal activation in the NAc shell |
| 2013 Kim and Seol Ah [42]     | To explore the peripheral mechanisms underlying acupuncture treatment for drug addiction | 12 Male Sprague-Dawley rats | Acupuncture at Shenmen (HT7) as study and Yangxi (LI5) as control for 1 min | Suppression of cocaine-induced locomotor activity | Acupuncture inhibited the cocaine-induced locomotor activity |

Acupoints in NADA protocol are located at: sympathetic: in the deltoid fossa at the junction of the infra-antihelix crus and the medial order of the helix, lung: in the center of the cavum concha, liver: located in the posterior to upper portion of the helix crus, kidney: in the cleft between the upper plateaus, and the helix
| Publication year, first author | Objectives | Subjects | Stimulated acupoints. (acupuncture type, acupoints, frequency) | Assessments | Outcomes |
|-------------------------------|------------|----------|---------------------------------------------------------------|-------------|----------|
| Montazeri, Kamran [63] 2002  | To identify the effects of body acupuncture on rapid opiate detoxification | 40 Opioid addicts during ROD by naloxone, n = 20 acupuncture | Bilaterally acupuncture at Hegu (LI4), Neiguan (PC6), Shenmen (HT7), Taichong (LR3), Zusanli (ST36), Baihui (DU20) and Dazhui (DU14) 30 min for 3 days | Severity of withdrawal reaction (Clinical Institute Narcotic Assessment (CINA) score) | Acupuncture reduced the severity of withdrawal symptoms associated with rapid opiate detoxification |
| Liu [55] 2007 | To investigate the activation in the hypothalamus associated with acupuncture stimulation | Six healthy men and six heroin addicts | Acupuncture at Zusanli (ST36) with rotation for 11 min | fMRI, Cortisol level and psychophysical responses, including the deqi sensation, anxiety, and sharp pain | Acupuncture caused activation of the hypothalamus among addicts |
| Bearn [11] 2009 | To investigate AA effects as an adjunct to MMT upon withdrawal severity or craving | 83 Opioid users under MMT | Acupuncture at 5 points of cartilage ridge area in the ear, 30–40 min for 14 days | Daily measures of withdrawal severity and craving using the short opiate withdrawal scale and an eight-item craving questionnaire | AA had no effect upon withdrawal severity or craving when provided as an adjunct to a standard methadone detoxification treatment |
| Meade [62] 2010 | To evaluate the effectiveness of TEAS as an adjunctive treatment for inpatients receiving opioid detoxification | 48 Men and women under detoxification with buprenorphine-naloxone | 2 and 100 Hz TEAS at Hegu (LI4) and Neiguan (PC6), 30 min daily for 4 days | The addiction severity index, opioid withdrawal scale, brief pain inventory, the Pittsburgh sleep quality index, physical and mental health status by the medical outcomes survey | TEAS was effective in using drugs and improving the pain interference and physical health |
| Xia [81] 2011 | To investigate the rewarding effect of EA | 68 Male Sprague–Dawley rats | 2 Hz EA at Neiguan (PC6) and Zusanli (ST36), 30 min for 5 days | Conditioned place preference (CPP) | EA was capable of inducing CPP in the rat via the activation of the endogenous opioid-, cannabinoid- and dopamine-systems |
| Jiang [37] 2011 | To compare the changes of cognitive attention-related brain function before and after EA | Ten Heroin addicts and ten healthy subjects | 2 Hz bilateral EA at Neiguan (PC6) and Zusanli (ST36) | ERP at 64 electrode spots before and after EA intervention task on the positive emotional clue (PEG), negative emotional clues (NEG), and heroin-related clue (HRC). The P200 amplitude components on (Fz, Cz, and Pz) | Electroacupuncture effectively inhibited the attention bias to heroin |
| Cai [17] 2012 | To understand the influence of heroin cue exposure on brain activation | 12 Heroin addicts and 12 healthy subjects | non-twirled acupuncture and twirled acupuncture at bilateral Zusanli (ST36) for 1 min | fMRI during heroin cue exposure | Acupuncture can rapidly suppress the activation of specific brain regions related to craving as an intervention for drug craving |
| Liu [56] 2012 | To investigate the beneficial effects of EA on heroin-seeking behavior | 40 Male Sprague–Dawley rats, n = 10 EA | 2 Hz EA at Zusanli (ST36) and Sanyinjiao (SP6), once a day for 14 days during heroin abstinence | Contextual and discrete cue-induced reinstatement of active responses. Fos-positive nuclei detection in the nucleus accumbens (NAcc) core and shell | Acupuncture was effective in preventing relapse to drug addiction |
| Publication year, first author | Objectives | Subjects | Stimulated acupoints. (acupuncture type, acupoints, frequency) | Assessments | Outcomes |
|-------------------------------|------------|----------|---------------------------------------------------------------|--------------|----------|
| 2013 Hu [33]                  | To investigate the effects of EA on the extinction of heroin-seeking behavior | 18 Male Sprague–Dawley rats, n = 6 EA | 2 Hz EA at Zusanli (ST36) and Sanyinjiao (SP6), once a day for 7 days | The extinction response of heroin-associated cues and applied immunohistochemistry to detect FosB-positive nuclei in the nucleus accumbens core | Acupuncture enhanced extinction learning when combined with extinction therapy for the treatment of heroin addiction |
| 2013 Lua, Pei Lin [57]        | To find the effects of AA in number of consumed daily cigarettes, relapse rate, and withdrawal symptoms | 40 MMT, 29 MMT + AA human subjects | Auricular acupuncture at 5 points NADA points, 3 times a week | Malay HOQOLBREF, withdrawal symptoms | Acupuncture adjunct to MMT was beneficial in managing addiction behaviors |
| 2013 Lua, Pei Lin [58]        | To examine the patients’ satisfaction and coping with AA as an adjunct treatment to MMT | 40 MMT, 29 MMT + AA human subjects | Auricular acupuncture at 5 points NADA points, 3 times a week | Patient satisfaction with pharmaceutical care questionnaire (PSPCQ) and Malay brief COPE-27 | Acupuncture adjunct to MMT did not influence patient satisfaction and their coping ways |
| 2014 Chan [22]               | To examine the effectiveness of acupuncture for heroin addicts on methadone maintenance | 60 Heroin addicts in MMP | EA at Hegu (LI4), Zusanli (ST36) and Shenmen (P17), twice a week for 4 weeks | Daily consumption of methadone, variations in the 36-item Short Form Health Survey-36 (SF-36) and the Pittsburgh Sleep Quality Index (P50) scores, and heroin craving | Acupuncture adjunct to MMT was useful in reducing the daily dose of methadone and great improvement in sleep latency at follow-up |
| 2014 Hou [32]                | To observe cell apoptosis in the hippocampus and frontal lobe of heroin readdicted rats by electron microscopy | 40 Wistar rats during the detoxification by methadone | Acupuncture at Baihui (GV20) and Daohui (GV14), 30 min for 5 successive days | Morphology of nerve cells, Bax expression and Bcl-2 expression in the frontal cortex and hippocampus | Acupuncture was effective in preventing brain cell apoptosis in heroin readdicted rats |
| 2014 Zhang [88]              | To verify the relationship between acupuncture, neurotrophic factor expression and brain cell structural changes | 32 Wistar rats, n = 16 acupuncture | Acupuncture at Baihui (GV20) and Daohui (DV14) for 30 min, once a day for five consecutive days | The neuronal ultrastructure of the ventral tegmental area, brain-derived and glial cell line-derived neurotrophic factor expression in the ventral tegmental area | Acupuncture protected brain neurons against injury in rats with heroin relapse |

Acupoints in NADA protocol are located at: (sympathetic in the deltoid fossa at the junction of the infra-antihelix crus and the medial order of the helix, lung in the center of the cavum concha, liver located in the posterior to upper portion of the helix crus, kidney in the cleft between the upper plateau, and the helix)
### Table 4 Original investigations of acupuncture therapy effects in nicotine-dependent subjects

| Publication year; first author | Objectives | Subjects | Stimulated acupoints (acupuncture type, acupoints, frequency) | Assessments | Outcomes |
|-------------------------------|------------|----------|-------------------------------------------------------------|-------------|----------|
| 2004 Chae [21] | To investigate the acupuncture effects on the functional alterations of the mesolimbic dopaminergic systems | 35 Male Sprague-Dawley rats | Acupuncture at Zusanli (ST36), Shenmen (HT7), or Taiyuan (LU9) for 4 days | Nicotine-induced FLI in the striatum and the nucleus accumbens | acupuncture had a therapeutic effect on nicotine addiction |
| 2005 Park [65] | To examine whether the DRD2 Taq1 A polymorphism is associated with the response to acupuncture | 231 Healthy Korean male smokers | AA at lung, throat, Shimen (HT7), and endocrine points for 96 ± 3 times for a week | Cigarette consumption, the desire to smoke, and Genomic DNA extracted from blood samples | acupuncture was effective to influence the DRD2 Taq1 A polymorphism |
| 2008 Chae [20] | To investigate the effect of acupuncture on anxiety-like behavior and corticotrophin-releasing factor (CRF) and neuropeptide Y (NPY) mRNA expression in the amygdala during nicotine withdrawal | 38 Male Sprague-Dawley rats, n = 18 acupuncture | Acupuncture at Zusanli (ST36), Shenmen (HT7), 30 s for 3 days | The anxiogenic response by using an elevated plus maze, CRF and NPY mRNA levels by using reverse transcription polymerase chain reaction (RT-PCR) analysis | acupuncture attenuated anxiety-like behavior following nicotine withdrawal |
| 2008 Bonnette [15] | To explore the effects of ATENS in combination with addiction education, behavioral training and coaching | 6 Smokers | Acupuncture at 5 NADA protocol or 1-3 points, 5 times a week for 8 weeks | In-depth interviews for withdrawal symptoms, anxiety and stress levels | auriculotherapy relieved withdrawal symptoms and reduced anxiety and stress levels during the detoxification |
| 2009 Yeh [83] | To evaluate the effects of a 6-week acupuncture stimulation program for quitting | 59 Smokers | Acupuncture at Shenmen (HT7), lung, stomach, mouth and endocrine and Tim me for 20 min, once a week for 6 weeks | Demographic factors, serum cotinine, carbon monoxide exhalation, daily tobacco consumption, and quit smoking rate of participants before and after the 6-week intervention | acupuncture showed no statistically significant effect on quitting smoking |
| 2010 Thanavarro [72] | To explore the efficacy of ATENS as an adjunctive treatment to intensive individual counseling on smoking cessation | 29 Subjects | Auricular transcutaneous electrostimulation therapy at 10 areas on the pinna | The “Fagerstrom Test for Nicotine Dependence,” the “What Are Your Triggers Test” and the “Why Do I Smoke Quiz” | individual counseling may produce smoking cessation rates comparable to counseling with pharmacotherapy |
| 2010 Chae [18] | To investigate the effect of acupuncture on the selective attention to smoking-related visual cues | 29 Smokers | Acupuncture, Shenmen (HT7), (NA) | The attentional bias and cigarette withdrawal scale | acupuncture ameliorated the smoking withdrawal symptoms as well as the selective attention to smoking-related visual cues |
| 2011 Chae [19] | To investigate effects of acupuncture on ameliorating cigarette withdrawal symptoms | 29 Smokers, n = 15 acupuncture | Acupuncture at Shenmen (HT7) or Shousanli (LI10), 20 min for 3 days | The cigarette withdrawal scale (CWS), comparing the low-frequency/high-frequency (HF/LF) ratio in the HRV of the RA and SA groups | acupuncture ameliorated withdrawal symptoms and smoking cues-induced autonomic responses |
| 2013 Kang [38] | To investigate acupuncture effects on ameliorating cravings induced by smoking-related visual cues | 25 Male smokers | Acupuncture at Shenmen (HT7) for 1 min | fMRl and craving scores to smoking-related visual cues were assessed before and after RA or sham treatment | acupuncture alleviated cue-induced craving through the regulation of activity in brain regions involved in attention, motivation, and reward |

Acupoints in NADA protocol are located at (sympathetic: in the deltid fossa at the junction of the infra-antihelix crus and the medial order of the helix, lung: in the center of the cavum concha, liver: located in the posterior to upper portion of the helix crus, kidney: in the cleft between the upper plateau, and the helix)
Table 5  Original investigations of acupuncture therapy effects in alcohol-dependent subjects

| Publication year; first author | Objectives | Subjects | Stimulated acupoints (acupuncture type, acupoints, frequency) | Assessments | Outcomes |
|-------------------------------|------------|----------|---------------------------------------------------------------|-------------|----------|
| 2001 Yoshimoto [86]           | To investigate the effect of EA on changes in alcohol-drinking behavior in rats challenged with restriction and immobilization stress | 8–12 Male Sprague–Dawley rats | 1 Hz and 100 Hz EA at Zusanli (ST 36) and Shenshu (BL 23) for 10 min, twice a week for 1–3 weeks | Time-access alcohol-drinking behavior, brain dopamine (DA) level | Acupuncture at Zusanli (ST 36) was more effective for reducing the increased alcohol-drinking behavior |
| 2002 Bullock [16]             | To report the clinical data on the efficacy of acupuncture for alcohol dependence | 503 Alcoholics | AA at Shenmen (HT7), lung, sympathetic, and liver for 40 min, 6 days a week for 3 weeks | Alcohol use, depression, anxiety, functional status, and preference for therapy | Acupuncture was not found to be effective in reduction of alcohol use alone |
| 2002 Karst [39]               | To investigate the acupuncture effects on alcohol withdrawal therapy with carbamazepine | 34 Alcoholics | AA at Sympathetic, Shenmen (HT7), kidney, liver, lung, Baihui (GV20), extra1, and He Gu (LI4), daily for 10 days | Clinical Institute Withdrawal Assessment (CIWA-Ar-scale) | Acupuncture as an adjunctive treatment to carbamazepine medication shows promise for the treatment of alcohol withdrawal symptoms |
| 2003 Trumpler [74]           | To compare auricular laser and needle acupuncture with sham laser stimulation in reducing the duration of alcohol withdrawal | 48 alcoholics undergoing alcohol withdrawal with clomethiazole n = 17 laser, n = 15 needle | AA (2-10 out of 24 points) for 30-45 min, laser AA at 24 points (1 min for each point), 3 days | The duration of withdrawal symptoms (nurse-rated scale), duration of sedative prescription | Acupuncture showed no relevant benefit for alcohol withdrawal |
| 2004 Zalewska-Kazubska [87] | To intensify AA method by additional biostimulation of the whole organism | 53 Alcoholics under daily helium–neon laser for neck biostimulation | Laser AA at concha points for 4 periods of ten times applied every 2nd day | The Beck Depression Inventory-Fast Screen (BDI-FS), beta-endorphin plasma concentration by using the radioimmunoassay (RIA) | Laser therapy was useful as an adjunct treatment for alcoholism |
| 2005 Kim [40]                | To investigate the effects of acupuncture on alcohol withdrawal syndrome (AWS) and Fos-like immunoreactivity (FLI) in the striatum and the nucleus accumbens (NAC) of rats | 24 Male Sprague–Dawley rats | Acupuncture at Zusanli (ST36) and Sanyinjiao (SP6) for 3 days | Alcohol withdrawal syndrome (AWS) and Fos-like immunoreactivity (FLI) in the striatum and the nucleus accumbens (NAC) | Acupuncture was useful in the treatment of alcoholism by modulating post-synaptic neural activation in the striatum and NAC |
| 2006 Yoshimoto [85]          | To investigate the neuropharmacological mechanisms of oriental acupuncture | 24 Male Sprague–Dawley rats, n = 16 acupuncture | unilateral or bilateral acupuncture at Shenshu (BIU23) acupoint, 60 min | Dopamine (DA) and serotonin (5-HT) contents of the microdialysates in the ACC | Acupuncture was effective for treatment of emotional disorders and laconism by increasing and prolonging the activity of serotonergic neurons |
| 2006 Zhao [89]               | To investigate the effects of acupuncture on chronic ethanol-induced changes in extracellular dopamine levels in the nucleus accumbens shell | 35 Male Sprague–Dawley rats, n = 21 sham or real acupuncture | Bilateral acupuncture at Shenmen (HT7) point or Neiguan (PC6) or tail for 1 min | Extracellular dopamine levels in the nucleus accumbens shell (using in vivo microdialysis in unanesthetized rats) | Acupuncture at HT7 was effective to normalize the release of dopamine in the mesolimbic system following chronic ethanol treatment |
| Publication year; first author | Objectives | Subjects | Stimulated acupoints (acupuncture type, acupoints, frequency) | Assessments | Outcomes |
|-------------------------------|------------|----------|---------------------------------------------------------------|-------------|----------|
| 2007 Kunz [43]               | To compare auricular needle acupuncture with aromatherapy in reducing the duration and severity of symptoms of alcohol withdrawal with carbamazepine, oxcarbazepine, and benzodiazepines | 74 alcoholics, n = 36 acupuncture, n = 38 aromatherapy | AA at 5 NADA points, 45 min for 5 days | Alcohol-withdrawal syndrome (AWS scale), subjective visual analog scale of craving and the Self-Assessment Manikin (SAM) | acupuncture was not more effective than the control therapy on alcohol withdrawal symptoms |
| 2008 Overstreet [64]         | To investigate the EA effects for reducing voluntary alcohol intake in alcohol-preferring rats | 18 inbred alcohol-preferring P rats (IP), n = 9 EA | 2 and 100 Hz EA at Zusanli (ST36) and Sanyinjiao (SP6) for 30 min | Alcohol intake | Acupuncture affected on alcohol intake in the alcohol-dependent IP rats |
| 2009 Dos Santos [28]         | To investigate the effects of EA on locomotor sensitization induced by ethanol in mice | 12 Male Swiss mice | 2 Hz EA at Zusanli (ST36) and/or Neiguan (PC6) for 10 min | The locomotor activity, the expression of homer1A mRNA assessed by PCR | EA modulated homer1A expression and glutamateergic plasticity |
| 2010 Yang [82]               | To investigate the effects of HT7 acupuncture on VTA GABA neuron excitability, ethanol inhibition of VTA GABA neuron firing rate, and ethanol self-administration | 32 Male Wistar rats | 2 Hz EA at Shenmen (HT7) or Neiguan (PC6) for 1 min | Ethanol-Reinforced Responding, VTA GABA Neuron Activity, VTA GABA Neuron Firing Rate | acupuncture reduced ethanol suppression of VTA GABA neuron firing rate, and reduced ethanol self-administration without affecting sucrose consumption |
| 2011 Li [50]                 | To demonstrate that SD rats escalated their ethanol intake and subsequently developed ethanol dependence under the IE procedure | 26 Male Sprague-Dawley rats | 2 and 100 Hz EA at Zusanli (ST36) for 20 min | Intake of and preference for ethanol | EA treatments decreased the intake of and preference for ethanol, without resulting in a rebound increase in ethanol intake when the EA treatments were terminated |
| 2012 Li [49]                 | To test the hypothesis that EA suppression on alcohol consumption may be mediated by transcription factors, such as FosB/ΔFosB protein in reward-related brain regions | 33 Male Sprague-Dawley rats | 2 and 100 Hz EA at Zusanli (ST36), 30 min for 6 days | The expression of FosB/ΔFosB in several reward-related brain regions using immunohistochemistry | EA treatment effectively reduced ethanol consumption and preference in rats by down-regulation of FosB/ΔFosB in reward-related brain regions |
| 2012 Escosteguy-Neto [29]    | To investigate EA effects during ethanol withdrawal on CB1R immunoreactivity | 12 Male Swiss mice | 2 and 100 Hz EA at Zusanli (ST36)/Neiguan (PC6) or Dazhui (DU14)/Baihui (DU20), 10 min for 4 days | CB1R in the prefrontal cortex, striatum, hippocampus, amygdala and ventral tegmental area | EA inhibited CB1 R upregulation which depended on acupoints association and frequency of stimulation |
| 2012 Fallopa [30]            | To investigate whether EA reverses locomotor sensitization induced by ethanol is parallel to ERK signaling | 12 Male Swiss mice | 2 and 100 Hz EA at Zusanli (ST36)/Neiguan (PC6) or Dazhui (DU14)/Baihui (DU20), 10 min for 4 days | pERK immune-histochemistry | EA increased CB1R in the prefrontal cortex, striatum, hippocampus, amygdala and ventral tegmental area |

Acupoints in NADA protocol are located at: sympathetic: in the deltoïd fossa at the junction of the infra-antihelix crus and the medial order of the helix, lung: in the center of the cavum concha, liver: located in the posterior to upper portion of the helix crus, kidney: in the cleft between the upper plateau, and the helix.
and NAc in rats [89]. Acupuncture at Shenmen (HT7) normalized dopamine release in the mesolimbic system [89], modulated mesolimbic dopamine release, and suppressed the reinforcing effects of ethanol [82]. Activation of the endogenous opiate system might be responsible for Zusanli (ST36) and Sanyinjiao (SP6) stimulation effects on alcohol intake in alcohol-dependent rats [64].

EA applied at Zusanli (ST36) was more effective than EA at Shenshu (BL23) at normalizing alcohol-drinking behavior in rats [86]; the activity of serotonergic neurons in the reward system pathway of the brain might be increased and prolonged by acupuncture [85]. EA at the combination Zusanli (ST36) and Neiguan (PC6) (but not at either point alone) prevented sensitization of the mesocorticolimbic pathway induced by ethanol in mice and modulated both the expression of the protein homer1A and glutamatergic plasticity [28]. EA (2 Hz) at Zusanli (ST36) could reduce voluntary intake of ethanol, but not sucrose, in rats [50] and 100 Hz EA treatment at Zusanli (ST36) effectively reduces preference for ethanol and its consumption in rats [49]. In one study, 2 Hz EA at Zusanli (ST36) and Neiguan (PC6) or 100 Hz EA at Dazhui (DU14) and Baihui (DU20) inhibited CB1R upregulation in ethanol-withdrawn mice [29]. The behavioral effects of 2 Hz EA at Dazhui (DU14) and Baihui (DU20), but not 100 Hz EA at Zusanli (ST36) and Neiguan (PC6), depended on extracellular signal-regulated kinase signaling [30]. See Table 5 for study details.

Morphine

Compared with 100 Hz, 2 Hz peripheral electric stimulation (PES) at Zusanli (ST36) and Sanyinjiao (SP6) inhibited the expression of morphine-induced conditioned place preference (CPP) (see [52] for information on CPP) via activation of opioid receptors [75]. One study found that the release and synthesis of enkephalin in the NAc was accelerated by 2 Hz stimulation of Zusanli (ST36) and Sanyinjiao (SP6) [53]. In addition, EA suppression of opiate addiction might involve the release of endogenous μ-, δ-, and κ-opioid agonists in the NAc shell [52] and might activate the cannabinoid, endogenous opioid, and dopamine systems to induce CPP in rats [81]. PES (100 Hz) at Zusanli (ST36) and Sanyinjiao (SP6) activated the suprasegmental δ- and κ-opioid receptors in the central nervous system, which cause the anticroaving effects of PES in rats [70]. It was also found that the expression of preproenkephalin and preprodynorphin mRNAs in the NAc was mediated by 2 Hz or 100 Hz PES, with the release of endogenous μ-, δ-, and κ-opioid agonists to suppress morphine-induced CPP [71]. Stimulation at Zusanli (ST36) and Sanyinjiao (SP6) (100 Hz) for 30 min normalized the activity of ventral tegmental area dopamine neurons [34], downregulated p-cAMP response element binding, and accelerated dynorphin synthesis in the spinal cord [76].

Some research suggests that 2 Hz EA is a potential complementary therapy for improving immune dysfunction in opiate addicts [51] and that 2 Hz or 100 Hz EA facilitates the recovery of male sexual behavior in rats during morphine withdrawal [27]. Thirty minutes of EA of 2 Hz or 100 Hz at Zusanli (ST36) and Sanyinjiao (SP6) reversed the morphological alterations induced by chronic morphine administration [25]. In addition, by increasing NREM sleep, REM sleep, and total sleep time, EA could be a potential treatment for sleep disturbance during morphine withdrawal [48].

EA at Shenshu (BL23) attenuated the expression of the proto-oncogene c-Fos in the central nucleus of the amygdala [54]. Acupuncture at Shenmen (HT7) inhibited neurochemical and behavioral sensitization to morphine by decreasing dopamine release in the NAc [41]. Acupuncture at Shenmen (HT7) significantly suppressed morphine-induced increase in locomotor activity and Fos expression in the NAc and striatum [45]. Acupuncture at Yanggu (SI5) can reduce the reinstatement of morphine-seeking behaviors by mediating the gamma-aminobutyric acid receptor system [46, 47]. See Table 6 for study details.

Other substances

Studies of methamphetamine, cannabis, illicit/psychoactive drugs, and polydrug users are shown in Table 7. Twelve studies used the NADA 5-point protocol and AA as their treatment method. The findings indicated that people dependent on drugs preferred acupuncture treatment [9], which was associated with a decrease in psychological distress [12] and an increase in confidence [14], but showed no efficacy for drug consumption and withdrawal symptoms [9, 12–14]. However, the conflicting nature of the research findings remains a controversial issue. Although there was evidence against the effectiveness of acupuncture in drug addiction treatment [7, 35, 36], recent studies have shown an effect for AA [23, 24, 26, 68, 73] and transcutaneous electric acupoint stimulation [66] per se or as adjunct treatments. Issues of safety and placebo effects suggest the need for further research [26, 35, 36, 66]. See Table 7 for study details.

Conclusion

AA and NADA protocols failed to show a strong therapeutic effect for cocaine, nicotine, and alcohol addiction treatment. However, some studies discussed here
Table 6  Original investigations of acupuncture therapy effects in morphine-dependent subjects

| Publication year; first author | Objectives | Subjects | Stimulated acupoints (acupuncture type, acupoints, frequency) | Assessments | Outcomes |
|-------------------------------|------------|----------|-------------------------------------------------------------|-------------|----------|
| 2000 Wang [75]               | To observe the effect of peripheral electric stimulation (PES) on morphine-induced Conditioned place preference CPP | 57/82 Male Sprague–Dawley rats | 2 and 100 Hz PES at Zusanli (ST36) and Sanyinjiao (SP6) for 30 min | Conditioned place preference | 2 Hz PES could specifically inhibit the expression of morphine-induced CPP |
| 2003 Shi [70]                | To examine the effect of 100 Hz peripheral electric stimulation (PES) on the expression of morphine-induced CPP | 48 Male Sprague–Dawley rats | 100 Hz PES at Zusanli (ST36) and Sanyinjiao (SP6), 30 min a day for 3 days | Conditioned place preference | Repeated 100 Hz PES had anti-craving effects by activating supra-segmental δ- and κ-opioid receptors |
| 2004 Shi [71]                | To elucidate if preproenkephalin (PPE) and preprodynorphin (PPD) mRNAs in the nucleus accumbens (NAc) play a role in PES suppressing morphine-induced CPP | 48 Male Sprague–Dawley rats | 2 and 100 Hz PES at Zusanli (ST36) and Sanyinjiao (SP6), 30 min a day for 3 days | Conditioned place preference | PES suppressed both the expression of morphine-induced CPP and the reinstatement of extinguished CPP |
| 2004 Cui [27]                | To investigate the effect of EA on the sexual behavior of male rats undergoing morphine withdrawal | 41 Male Sprague–Dawley rats | 2 and 100 Hz EA at Zusanli (ST36) and Sanyinjiao (SP6), 30 min a day for 7 days | Total serum testosterone (TST) concentrations | EA facilitated the recovery of male sexual behavior and increased TST concentrations |
| 2005 Kim [41]                | To investigate the effect of acupuncture on repeated morphine-induced changes in extracellular dopamine levels | 31 Male Sprague–Dawley rats | Acupuncture at Shenmen (HT7) for 1 min | Dopamine release in the nucleus accumbens and behavioral hyperactivity | Acupuncture decreased both dopamine release in the nucleus accumbens and behavioral hyperactivity |
| 2005 Liu [54]                | To evaluate the effect of EA on morphine withdrawal signs and c-Fos expression of the amygdala | 21 Male Sprague–Dawley rats | 100 Hz EA at Shenshu (BL23) for 30 min | Corticosterone levels and behavioral responses during EA stimulation | EA significantly reduced the signs of morphine withdrawal |
| 2008 Chu [25]                | To observe the effect of EA on chronic morphine-induced neuronal morphological changes in the ventral tegmental area (VTA) | 12 Male Sprague–Dawley rats | 2 and 100 Hz EA at Zusanli (ST36) and Sanyinjiao (SP6), 30 min for 3 days | The rough endoplasmic reticulum, membrane configuration of the nucleus and mitochondria, and structure of myelin sheath | EA reversed the morphological alterations induced by chronic morphine administration |
| 2009 Hu [34]                | To examine alterations in the firing rate of Dopamine neurons in 100 Hz EA treatment | 40 Male Sprague–Dawley rats | 100 Hz EA at Zusanli (ST36) and Sanyinjiao (SP6), 30 min for 10 days | Conditioned place preference | EA was effective for the treatment of opiate addiction by normalizing the activity of VTA DA neurons |
| 2010 Liang [53]              | To find the role of enkephalin in the nucleus accumbens mediating the effects of EA | 218 Male Sprague–Dawley rats | 2 Hz EA at Zusanli (ST36) and Sanyinjiao (SP6), 30 min for 1–3 days | Conditioned place preference | EA up-regulated the mRNA level of preproenkephalin in the NAc |
| 2010 Lee [45]                | To investigate the effect of acupuncture on morphine-induced behavioral sensitization and the neuronal changes in NAc and striatum | 14 Male Sprague–Dawley rats | Acupuncture at Shenmen (HT7), 1 min for 3 days | Morphine-induced changes of locomotor activity and Fos expression | Acupuncture suppressed the morphine-induced increases in the locomotor activity and Fos expression in the NAc and striatum |
| Publication year; first author | Objectives | Subjects | Stimulated acupoints (acupuncture type, acupoints, frequency) | Assessments | Outcomes |
|-------------------------------|------------|----------|---------------------------------------------------------------|-------------|----------|
| 2011 Li [48]                  | To observe whether EA could modulate the immune status of morphine dependence and withdrawal mice | 40 Male BALB/c mice | 2 Hz EA at Zusanli (ST36) and Sanyinjiao (SP6), 30 min for 5 days | Splenic T Lymphocyte Proliferation, IL-2 Production, CD4<sup>+</sup>/CD8<sup>+</sup> Ratio | EA raised IL-2 and normalized chronic morphine exposure-induced immune dysfunctions |
| 2011 Li [51]                  | To investigate the effect of 2 and 100 Hz EA of the sleep disturbance during morphine withdrawal | 15 Male Sprague–Dawley rats | 2 and 100 Hz EA at Zusanli (ST36) and Sanyinjiao (SP6), 30 min twice a day for 3 days | Electroencephalogram and electromyogram | EA decreased NREM/REM and total sleep time, while the sleep latency prolonged significantly during acute morphine withdrawal |
| 2011 Wang [76]               | To find the optimum protocol for EA effective for alleviating withdrawal syndrome | 40 Male Sprague–Dawley rats | 100 Hz EA at Zusanli (ST36) and Sanyinjiao (SP6) for 30 min | Conditioned place preference | EA down-regulated p-CREB and accelerated of dynorphin synthesis in spinal cord |
| 2011 Xia [81]                 | To investigate whether EA by itself will produce some rewarding effect | 44 Male Sprague–Dawley rats | 2 Hz EA at Zusanli (ST36) and Sanyinjiao (SP6) for 30 min | Conditioned place preference | EA was capable of inducing CPP in the rat via the activation of the endogenous opioid-, cannabinoid- and dopamine-systems |
| 2012 Lee [47]                | To investigate the role of acupuncture in the reinstatement of morphine seeking | 15 Male Sprague–Dawley rats | Acupuncture, Yanggu (SI5) or Yangxi (LI5) for 1 min | Morphine reinstatement | acupuncture attenuated the reinstatement of morphine seeking behavior by blocking the GABA receptor antagonists |
| 2013 Lee [46]                | To investigate whether acupuncture could suppress the reinstatement of morphine-seeking behavior | 28 Male Sprague–Dawley rats | Acupuncture, Yanggu (SI5) or Yangxi (LI5) or Zusanli (ST36) for 1 min | Morphine-seeking behavior | acupuncture suppressed morphine injection perfectly |

Acupoints in NADA protocol are located at (sympathetic: in the deltoid fossa at the junction of the infra-antihelix crus and the medial order of the helix, lung: in the center of the cavum concha, liver: located in the posterior to upper portion of the helix crus, kidney: in the cleft between the upper plateau, and the helix)
Table 7  Original investigations of acupuncture therapy effects in poly-drug and other substance abusers (NA not available)

| Publication year; first author | Objectives | Subjects | Stimulated acupoints (acupuncture type, acupoints, frequency) | Assessments | Outcomes |
|-------------------------------|------------|----------|---------------------------------------------------------------|-------------|----------|
| 2000 Russell [68]             | To compare the behavior of addicts in a treatment center with archived information from no-acupuncture (NA) patients | 86 Patients (Methamphetamine was the primary drug of choice for 44) | AA at 5 NADA points, 45 min for 9 weeks | Program retention, new arrests incurred, drug-positive urinalysis results, and number of days needed to progress from entry level to secondary level treatment | Acupuncture improved program retention up to 30 days among methamphetamine-addicted patients |
| 2000 Song Bernstein [14]     | To explore the meaning of substance abusers’ experience while receiving acupuncture as a part of the treatment for substance dependence | 8 Human Subjects | AA, (NA), once a week | Interviews, researcher’s field notes, and demographic data obtained from the participants’ medical records | Acupuncture caused anticipation of pain, apprehension concerning a new experience, mood elevation, inability to describe the experience, physical sensation, relaxation, and improved sleep |
| 2004 Berman [13]             | To compare the experimental NADA-Acudetox protocol with a non-specific helix control protocol in a randomized trial | 174 Inmates | Auricular acupuncture at 5 NADA points, 40 min for 4 weeks | A simple drug use questionnaire; the Acupuncture Treatment Assessment Scale (ATAS), a Swedish research version of the Symptom Check List 90 | Acupuncture had no significant efficiency over the placebo |
| 2005 Janssen [36]            | To examine the utility of acupuncture treatment in reducing substance use in the marginalized, transient population | 261 Humans | AA at 5 NADA points for 40 min | Questionnaire, Drug use symptomatology, severity of withdrawal symptoms | Acupuncture caused reduction in overall use of substances and decrease in intensity of withdrawal symptoms |
| 2006 Tian [73]              | To examine the efficacy of AA in addition to usual care in substance abuse treatment | 17 Humans | AA at 5-points NADA, once a week for 6 consecutive weeks | The Hopkins Symptom Checklist (SCL-20) depression scale, brief substance craving scale | there was a positive response to the specific auricular acupressure treatment on psychological distress, craving and drug/alcohol use measures |
| 2007 Courbasson and Christine [26] | To evaluate the benefits of adding AA to a 21-day outpatient structured psychoeducational treatment program | 185 Women with concurrent substance use problems, anxiety, and depression | AA at 5 points NADA for 45 min, 3 times a week | Physiological cravings for substances, depression, and anxiety | Acupuncture as an adjunct therapy to a comprehensive psychosocial treatment was effective and more viable treatment alternative to anxiolytics |
| Publication Year | First Author | Objectives | Subjects | Stimulated Acupoints (Acupuncture Type, Acupoints, Frequency) | Assessments | Outcomes |
|-----------------|--------------|------------|----------|-------------------------------------------------------------|-------------|---------|
| 2009            | Ashton [9]   | To describe the characteristics of clients choosing AA or counseling to treat dependence at a UK self-referral center | 162 Humans, n = 36 acupuncture, n = 126 counselling | AA at 5-points NADA, 45 min, once a week for 11 weeks | Psychometric variables (anxiety, depression, dependence severity, readiness to change), and alcohol and drug consumption | Acupuncture was preferred by clients and follow up assessments showed a significant decrease in psychological distress and reduction of alcohol consumption |
| 2014, 2010      | Chang and Bei-Hung [23, 24] | Examine the effects of acupuncture and related response (RR) on reducing craving | 23 Acupuncture, 23 RR, 21 controls (homeless military veterans) | AA at 5-points NADA, 45 min twice a week | Degree of craving and anxiety levels | Acupuncture and the relaxation reduced craving and anxiety levels |
| 2011            | Black, S. [7] | To test the hypothesis if AA reduces the anxiety associated with withdrawal from psychoactive drugs. | 101 Patients recruited from an addiction treatment service | AA at 5-points NADA 45 min for 3 days | Anxiety state by using a pretest–posttest treatment design | The NADA protocol was not more effective than sham or treatment setting control in reducing anxiety |
| 2012            | Janssen [35] | To test the ability of maternal acupuncture treatment among mothers who use illicit drugs to reduce the frequency and severity of withdrawal symptoms among their newborns | 50 Women using acupuncture, 39 women standard care | AA at 5-points NADA for 45 min | Days of neonatal morphine treatment for symptoms of neonatal withdrawal. Neonatal outcomes included admission to a neonatal ICU and transfer to foster care | Length of treatment for neonatal abstinence syndrome showed no efficiency of acupuncture |
| 2012            | Penetar [66] | To investigate the effects of TEAS on drug addiction | 9 Cocaine-dependent, 11 Cannabis-dependent | 2 and 100 Hz at Neiguan (PC6)/Waiguan (TH5) and Hegu (LI4)/Laogong (PC8) stimulation, Twice-daily 30-minute sessions of for 3.5 days | Drug use and drug cravings, cue-induced craving EEG evaluation, and P300 ERP | TEAS did not reduce drug use or drug cravings, or alter the ERP peak voltage or latency but modulated several self reported measures of mood and anxiety |
| 2014            | Bergdah [12] | To describe patients' experiences of receiving AA during protracted withdrawal | 15 Human subjects | AA at 5-points NADA 40 min, twice a week for 5 weeks | Interview | AA reinforced sense of relaxation and well-being, peacefulness and harmony, and new behaviors |

Acupoints in NADA protocol are located at (sympathetic: in the deltid fossa at the junction of the infra-antihelix crus and the medial order of the helix, lung: in the center of the cavum concha, liver: located in the posterior to upper portion of the helix crus, kidney: in the cleft between the upper plateau, and the helix)
indicate that acupuncture at Shenmen (HT7), Zusanli (ST36), and Sanyinjiao (SP6) acupoints can affect drug-induced physiological activities.

Authors' contributions
FEM, FL, RAR, and TS designed and conceived the study. FEM, RR, TS, FL, and RAR carried out the article searches. FEM performed the statistical analysis. FEM and TS wrote the manuscript. FL, RAR, and HH revised the manuscript. All authors read and approved the final manuscript.

Author details
1 Department of Biomedical Engineering, Faculty of Engineering, University of Malaya, 50603 Kuala Lumpur, Malaysia. 2 Centre for Innovation in Medical Engineering, Faculty of Engineering, University of Malaya, 50603 Kuala Lumpur, Malaysia. 3 Centre of Addiction Sciences, University of Malaya, 21st Floor, Wisma Research and Development, Jalan Pantai Baru, 59200 Kuala Lumpur, Malaysia. 4 Shahid Beheshti University of Medical Sciences, Tehran, Iran.

Acknowledgements
We would like to acknowledge and thank the University of Malaya and Ministry of Higher Education for providing High Impact Research Grant, account codes E000007-20001 to fund this project.

Competing interests
The authors declare that they have no competing interests.

Received: 12 September 2014   Accepted: 29 March 2016

Published online: 05 April 2016

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