

ACUPUNCTURE AND SUBSTANCE ABUSE

About substance abuse

In the UK, the prevalence of substance misuse is around 9 per 1,000 of the population aged 15–64 years, and around 3 per 1,000 inject drugs, in most cases opioids (NICE 2007). In 2005/6, around 181,000 people were using drug treatment services in England and Wales (Commission for Healthcare Audit and Inspection 2006). Also, research in England in 2005 estimated that 7.1 million people, or 23% of the adult population, could be categorised as hazardous or harmful alcohol users (Drummond 2005). Indeed, in England, 150,000 hospital admissions annually result from acute or chronic alcohol use, and alcohol use is implicated in 33,000 deaths each year (Academy of Medical Sciences 2004).

Dependence on drugs is a cluster of physiological, behavioural, and cognitive phenomena in which the use of a substance takes on a much higher priority for a given individual than other behaviours that once had a greater value (WHO 2007). Drugs of abuse include cannabis, opioids (opiates), CNS stimulants (cocaine, crack, amphetamines, ecstasy, crack), CNS depressants (barbiturates, benzodiazepines, alcohol), hallucinogens (LSD, psilocybin), and volatile substances (glues, gases, aerosols) (DTB 1997).

Opioid misuse and dependence are associated with a wide range of problems, such as overdose; infection with HIV, hepatitis B or hepatitis C; thrombosis; anaemia; poor nutrition; dental disease; criminal behaviour; relationship breakdown; lost productivity; unemployment; imprisonment; social exclusion; and prostitution, as well as withdrawal symptoms (Prodigy 2006; Gowing 2006; National Treatment Agency for Substance Misuse 2006). Problems associated with excessive alcohol use include hypertension, accidental injury, hand tremors, duodenal ulcers, gastrointestinal bleeding, cognitive impairments, anxiety and depression (Saunders 1990). The development of alcohol dependence appears to involve changes in brain neurotransmission (Littleton 1994; Tsai 1995).

Treatment programmes to help people with drug and alcohol problems include a range of individualised psychosocial interventions such as counselling, self-help groups, and rehabilitation programmes, in addition to medication.

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How acupuncture can help

Acupuncture is used extensively, and worldwide, in substance misuse treatment centres. This stems from the development of a simple 5-point auricular acupuncture protocol at New York's Lincoln Hospital in the 1970s, originally for drug users but subsequently extended to tobacco, alcohol and other addictive substances and behaviours. The protocol was designed to operate within Western health settings and mutual peer support systems, not as an isolated treatment.

In general, acupuncture is believed to stimulate the nervous system and cause the release of neurochemical messenger molecules. The resulting biochemical changes influence the body's homeostatic mechanisms, thus promoting physical and emotional well-being. Stimulation of certain acupuncture points has been shown to affect areas of the brain that are known to reduce sensitivity to pain and stress, as well as promoting relaxation and deactivating the analytical brain, which is responsible for anxiety and worry (Wu 1999).

Results from randomised controlled trials (Tian 2006; Berman 2001; Hyun 2010; Yeh 2009; Wu 2007) and systematic reviews (Cho 2009; Liu 2009; Gates 2006; White 2006; Jordan 2006; Mills 2005) looking at the effects of acupuncture on withdrawal symptoms and relapse rates related to alcohol, opiate, nicotine and cocaine misuse have been equivocal, mainly because of the poor quality of the research. The acupuncture provided in the trials has sometimes been inadequate, sham controls have often been inappropriate, many studies are too small and high dropout rates are common. Acupuncture has most commonly been evaluated against a sham control, which may in effect be no more than comparing two versions of acupuncture. There appears to be a discrepancy between results in experimental settings and those in normal practice, so context effects may be important (Margolin 2003). Better studies are required, especially those comparing acupuncture to usual care, and as an adjunct to usual care rather than a stand-alone intervention (See Table below).

Acupuncture may help relieve symptoms of drug withdrawal by:

- normalising the release of dopamine in the mesolimbic system. This reduces the over-stimulating effects of abused drugs and modifies behaviours associated with addiction such as those around desire and reward. Several brain neurotransmitter systems, for example serotonin, opioid and GABA, are implicated in this (Lee 2009a, Yang 2008, Zhao 2006)
- reducing anxiety (Samuels 2008). Acupuncture can alter the brain's mood chemistry, reducing serotonin levels (Zhou 2008) and increasing endorphins (Han 2004) and neuropeptide Y levels (Lee 2009b; Cheng 2009);
- modulating postsynaptic neuronal activity in the nucleus accumbens and the striatum to reduce nicotine addiction (Chae 2004) and increasing corticotrophin-releasing factor to attenuate anxiety-like behaviour following nicotine withdrawal (Chae 2008);

About traditional acupuncture

Acupuncture is a tried and tested system of traditional medicine, which has been used in China and other eastern cultures for thousands of years to restore, promote and maintain good health. Its benefits are now widely acknowledged all over the world and in the past decade traditional acupuncture has begun to feature more prominently in mainstream healthcare in the UK. In conjunction with needling, the practitioner may use techniques such as moxibustion, cupping, massage or electro-acupuncture. They may also suggest dietary or lifestyle changes.

Traditional acupuncture takes a holistic approach to health and regards illness as a sign that the body is out of balance. The exact pattern and degree of imbalance is unique to each individual. The traditional acupuncturist's skill lies in identifying the precise nature of the underlying disharmony and selecting the most effective treatment. The choice of acupuncture points will be specific to each patient's needs. Traditional acupuncture can also be used as a preventive measure to strengthen the constitution and promote general well-being.

An increasing weight of evidence from Western scientific research (see overleaf) is demonstrating the effectiveness of acupuncture for treating a wide variety of conditions. From a biomedical viewpoint, acupuncture is believed to stimulate the nervous system, influencing the production of the body's communication substances - hormones and neurotransmitters. The resulting biochemical changes activate the body's self-regulating homeostatic systems, stimulating its natural healing abilities and promoting physical and emotional well-being.

About the British Acupuncture Council

With over 3000 members, the British Acupuncture Council (BAcC) is the UK's largest professional body for traditional acupuncturists. Membership of the BAcC guarantees excellence in training, safe practice and professional conduct. To find a qualified traditional acupuncturist, contact the BAcC on 020 8735 0400 or visit www.acupuncture.org.uk

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The evidence

Research	Conclusion
Systematic reviews (SRs)	
Cho SH, Whang WW. Acupuncture for alcohol dependence: A systematic review. <i>Alcoholism: Clinical and Experimental Research</i> 2009; 33: 1305-13.	A systematic review that assessed the results of randomised controlled trials of acupuncture for alcohol dependence (up to June 2008). Eleven studies, including a total of 1,110 individual cases, were included, only 2 of which reported all quality criteria satisfactorily. Three of 4 trials comparing acupuncture with sham treatments reported that there was no difference in craving between groups. Among 4 trials comparing acupuncture and no acupuncture with conventional therapies, 3 reported significant reductions in cravings with acupuncture. Only 3 trials reported on acupuncture-related adverse events, which were mostly minimal. <u>The reviewers concluded that the results were equivocal, and that the poor methodological quality and limited number of the trials did not allow any conclusions to be drawn about the efficacy of acupuncture for treatment of alcohol dependence.</u>
Liu TT et al. A meta-analysis of acupuncture combined with opioid receptor agonists for treatment of opiate-withdrawal symptoms. <i>Cell Mol Neurobiol</i> 2009; 29: 449-54.	A review and meta-analysis of acupuncture's utility for treating opioid detoxification, addressing the efficacy of acupuncture when combined with allopathic therapies. It included randomised controlled trials that compared acupuncture plus opioid agonist treatment with opioid agonists alone for treating symptoms of opioid withdrawal. The outcome measures assessed were withdrawal-symptoms score, relapse rate, side effects, and medication dosage. Withdrawal-symptom scores were lower in combined treatment trials than in agonist-alone trials on withdrawal days 1, 7, 9, and 10. Combined treatment also produced lower reported rates of side effects and appeared to lower the required dose of opioid agonist. There was no significant difference on relapse rate after 6 months. <u>The reviewers concluded that acupuncture combined with opioid agonists can effectively be used to manage the withdrawal symptoms, but highlighted that the poor quality of the methodology of some included trials was a limitation of this meta-analysis.</u>
Gates S et al. Auricular acupuncture for cocaine dependence. <i>Cochrane Database of Systematic Reviews</i> 2006, Issue 1. Art. No.: CD005192. DOI: 10.1002/14651858.CD005192.pub2.	A systematic review that assessed whether auricular acupuncture is an effective treatment for cocaine dependence, and to investigate whether its effectiveness is influenced by the treatment regimen. It included 7 randomised controlled trials (with a total of 1,433 participants) comparing auricular acupuncture with sham acupuncture or no treatment. All were of generally low methodological quality. No differences were found between acupuncture and sham acupuncture (RR 1.05, 95% CI 0.89 to 1.23) or between acupuncture and no acupuncture (RR 1.06, 95% CI 0.90 to 1.26) for any measure of cocaine or other drug use. However, the number of participants included in meta-analyses was low, and power was limited. <u>The reviewers concluded that there was no evidence that auricular acupuncture is effective for the treatment of cocaine dependence.</u>
White AR, Rampes H, Campbell J. Acupuncture and related interventions for smoking cessation. <i>Cochrane Database of Systematic Reviews</i> 2006, Issue 1. Art. No.: CD000009. DOI:	A systematic review that assessed the effectiveness of acupuncture and the related interventions of acupressure, laser therapy and electrostimulation, in smoking cessation in comparison with no intervention, sham treatment, or other interventions. A total of 24 randomised controlled trials were included. <u>The only comparison for which there were sufficient studies to combine</u>

10.1002/14651858.CD000009.pub2. meaningfully was acupuncture with sham acupuncture, which found ~~real~~ acupuncture was more effective in the short-term (odds ratio 1.36, 95% CI 1.07 to 1.72) However, this result was strongly influenced by one individual positive study. The benefit did not last in the long-term. There was no consistent evidence that acupuncture is superior to no treatment, and no evidence that the effect of acupuncture was better or worse than that of other anti-smoking interventions. The reviewers concluded that there was no consistent evidence that acupuncture, acupressure, laser therapy or electrostimulation are effective for smoking cessation, but methodological problems meant that no firm conclusions can be drawn.

Jordan JB. Acupuncture treatment for opiate addiction: A systematic review. *Journal of Substance Abuse Treatment* 2006; 30: 309-14. A systematic review that looked at the efficacy of acupuncture as treatment for opiate addiction. Supportive evidence was found often to come from uncontrolled non-blinded methodologies. When well-designed clinical trials (randomised, controlled, single-blind methodologies) were used, there was no significant evidence for acupuncture being a more effective treatment than controls.

Mills EJ et al. Efficacy of acupuncture for cocaine dependence: A systematic review and meta-analysis. *Harm Reduction Journal* 2005; 2: Article Number: 4. A systematic review involving 9 randomised controlled trials of acupuncture for the treatment of cocaine addiction, comparing it with sham or other control in a total of 1,747 participants. The pooled odds ratio estimating the effect of acupuncture on cocaine abstinence at the last reported time-point was 0.76 (95% CI, 0.45 to 1.27, p=0.30). Most trials were hampered by large loss to follow up. The reviewers concluded that their systematic review and meta-analysis did not support the use of acupuncture for the treatment of cocaine dependence.

Margolin A. Acupuncture for substance abuse. *Curr Psychiatry Rep.* 2003 Oct;5(5):333-9. Acupuncture trials in addictions frequently have been conducted without preliminary dose-ranging studies to establish efficacious doses of the experimental treatment, use needle insertion controls of unknown degrees of activity, and present no rationale for the type or intensity of concurrently offered psychotherapy. It was concluded that it is premature to put forth recommendations for or against acupuncture for the treatment of addiction based on evidence from extant studies.

Clinical trials

General substance misuse

Tian X, Krishnan S. Efficacy of auricular acupressure as an adjuvant therapy in substance abuse treatment: a pilot study. *Altern Ther Health Med* 2006; 12: 66-9. A randomised placebo-controlled trial that examined the efficacy of auricular acupressure in addition to usual care in substance abuse treatment. Participants reported an average lifetime use of drug of choice of 14 years. The acupressure (real or placebo) treatment was offered once a week for 6 consecutive weeks. The Hopkins Symptom Checklist (SCL-20) Depression Scale (the primary outcome measure) was administered before and after treatment to assess changes in emotional distress. Brief Substance Craving Scale was used at baseline and weekly for 6 weeks to assess changes in craving. Both specific and placebo acupressure groups showed a significant reduction in craving at the end of treatment, with the specific acupressure group having a greater and more steady reduction in craving. Both specific acupressure and usual-care-only groups demonstrated a significant reduction in emotional stress. The researchers concluded that, overall, there was a positive response to the specific auricular acupressure treatment on psychological distress, craving, and drug/alcohol use measures.

Berman A.H. Auricular acupuncture A randomised controlled 18-month study that investigated the

as an auxiliary treatment for substance abusers a controlled study of the NADA-Acudetox protocol in two Swedish prisons. *Deutsche Zeitschrift für Akupunktur* 2001; 44: 51.

physical and psychological effects of auricular acupuncture treatment (14 sessions over 4 weeks) in 145 substance abusers in prison. Effects were measured before and after the treatment program with self report Visual Analogue Scales, psychiatric assessment according to the Symptom Checklist-90, personal interviews and prison officers assessment of individual inmates. Substance abuse was measured with urine tests. Significant positive changes in both the experimental (specific addiction protocol points) and control groups (non-specific ear points) occurred in levels of muscle tension, drug craving and physical well-being, as well as in worry, psychological well-being and psychiatric status. Participants who received at least ten treatments experienced the treatment effects as calming and giving a sense of harmony. Most of these participants also indicated significant improvement in the quality of their sleep. The prison officers perceived participants in the study as more content, more cooperative and more active than non-participating prison inmates. Urine tests showed that study participants had significantly fewer positive urine tests compared with non-participating inmates. The researchers concluded that one major finding was that auricular acupuncture is a simple technique for creating positive physical and psychological effects in the prison environment.

Nicotine studies since SRs

Hyun MK et al. Body acupuncture for nicotine withdrawal symptoms: A randomized placebo-controlled trial. *Evidence-based Complementary and Alternative Medicine* 2010; 7: 233-8.

A randomised controlled trial that evaluated whether improvements in nicotine withdrawal symptoms, depression and anxiety are greater for body (real) acupuncture than for sham acupuncture. Eighty people were allocated to six sessions of either real or sham acupuncture for 2 weeks. The primary outcome measure was withdrawal symptoms measured by the Minnesota Nicotine Withdrawal Score, and the secondary measures were scores on the Beck Depression Inventory (BDI) and Beck Anxiety Inventory (BAI). Nicotine withdrawal symptoms did not differ significantly between the real and sham acupuncture groups immediately after the treatment or at the 2-week follow-up. Both groups also showed similar improvements in BDI and BAI scores. The researchers concluded that their results showed that the real acupuncture treatment tested was no more effective than sham acupuncture at reducing nicotine withdrawal symptoms, depression and anxiety for smoking cessation.

Yeh ML et al. A six-week acupoint stimulation intervention for quitting smoking. *American Journal of Chinese Medicine* 2009; 37: 829-36.

A randomised controlled trial that compared the effects of 6-weeks of acupuncture for quitting smoking in 59 smokers with sham acupuncture. Before and after the six-week intervention, the participants completed questionnaires and offered blood samples to provide data on demographic factors, serum cotinine, carbon monoxide exhalation, daily tobacco consumption, and the quit smoking rate before and after the 6 weeks. After the intervention, there were no significant differences in the serum level of cotinine and carbon monoxide exhalation between the two groups. The quit rate in the experimental group was 13.3% (vs. 13.7% in the sham group), and daily tobacco consumption was 10 cigarettes in the experimental group (vs. 11.21 in the sham group). The researchers concluded that there were no statistically significant differences between acupuncture and sham acupuncture for quitting smoking.

Wu TP. A randomized controlled clinical trial of auricular acupuncture in smoking cessation. *Journal of the Chinese Medical Association* 2007; 70: 331-8.

A randomised controlled trial that compared auricular acupuncture with sham acupuncture for smoking cessation in 131 adults. The participants were followed monthly for 6 months after stopping the acupuncture treatment. At the end of treatment, cigarette consumption had significantly decreased in both groups, but only the treatment group also showed an effect on the nicotine withdrawal symptom score. There was no significant difference in

smoking cessation rate between the treatment group (27.1%) and the control group (20.3%) at the end of treatment or at the end of follow-up (16.6% and 12.1%, respectively). The researchers concluded that auricular acupuncture did not have a better efficacy in smoking cessation than sham acupuncture.

Research on mechanisms for acupuncture in general

Cheng CH et al. Endogenous Opiates in the Nucleus Tractus Solitarius Mediate Electroacupuncture-induced Sleep Activities in Rats. *Evid Based Complement Alternat Med* 2009 Sep 3. [Epub ahead of print]

An animal study that investigated the involvement of the nucleus tractus solitarius opioidergic system in electroacupuncture-induced alterations in sleep, the findings of which suggested that mechanisms of sleep enhancement may be mediated, in part, by cholinergic activation, stimulation of the opioidergic neurons to increase the concentrations of beta-endorphin and the involvement of the μ -opioid receptors.

Lee B et al. Effects of acupuncture on chronic corticosterone-induced depression-like behavior and expression of neuropeptide Y in the rats. *Neuroscience Letters* 2009b; 453: 151-6.

In animal studies, acupuncture has been found to significantly reduce anxiety-like behaviour, and increase brain levels of neuropeptide Y, the brain levels of which appear to correlate with reported anxiety.

Zhou Q et al. The effect of electro-acupuncture on the imbalance between monoamine neurotransmitters and GABA in the CNS of rats with chronic emotional stress-induced anxiety. *Int J Clin Acupunct* 2008 ;17: 79-84.

A study of the regulatory effect of electro-acupuncture on the imbalance between monoamine neurotransmitters and GABA in the central nervous system of rats with chronic emotional stress-induced anxiety. The levels of serotonin, noradrenaline and dopamine fell significantly, while GABA levels were significantly higher in the rats given acupuncture ($P < 0.05$, or $P < 0.0$). The researchers concluded that the anti-anxiety effect of electro-acupuncture may relate to its regulation of the imbalance of neurotransmitters.

Samuels N et al. Acupuncture for psychiatric illness: a literature review. *Behav Med* 2008; 34: 55-64.

A literature review of acupuncture for psychiatric illness, which presents research that found acupuncture to increase central nervous system hormones, including ACTH, beta-endorphins, serotonin, and noradrenaline.

Han JS. Acupuncture and endorphins. *Neurosci Lett* 2004; 361: 258-61.

A literature review of studies relating to the release of endorphins by acupuncture.

Wu MT et al. Central nervous pathway for acupuncture stimulation: localization of processing with functional MR imaging of the brain--preliminary experience. *Radiology* 1999 ;212: 133-41.

An experimental study using fMRI to characterise the central nervous system pathway for acupuncture stimulation, which found that acupuncture activates structures of descending antinociceptive pathway and deactivates areas mediating pain modulation.

Specific research into mechanisms in drug misuse

Lee B et al. Acupuncture attenuates cocaine-induced expression of behavioral sensitization in rats: Possible involvement of the dopaminergic system in the ventral tegmental area. *Neuroscience Letters* 2009a; 449: 128-32.

An animal study that investigated the effects of acupuncture on the repeated cocaine-induced neuronal and behavioural sensitisation alterations. Male SD rats were given repeated injections of cocaine hydrochloride for 10 days, followed by one challenge injection on the 4th day after the last daily injection. Cocaine challenge produced a large increase in the locomotor activity and the expression of tyrosine hydroxylase (TH) in the ventral tegmental area (VTA). acupuncture at the acupoint HT7 significantly inhibited the increase of locomotor activity as well as TH expression in the VTA. The results show that the inhibitory effects of acupuncture on cocaine-induced expression of behavioural sensitization were closely associated with the reduction of dopamine biosynthesis

and the postsynaptic neuronal activity.

Yang CH et al. A possible mechanism underlying the effectiveness of acupuncture in the treatment of drug addiction. Evid Based Complement Alternat Med. 2008 Sep;5(3):257-66.

A critical review of the evidence on basic mechanisms of acupuncture, some of which suggests that it can play an important role in reducing the reinforcing effects of abused drugs. The neurochemical and behavioural evidence showed that acupuncture's role in suppressing the reinforcing effects of abused drugs takes place by modulating mesolimbic dopamine neurons. Also, several brain neurotransmitter systems such as serotonin, opioid and amino acids including GABA have been implicated in the modulation of dopamine release by acupuncture. These results provided clear evidence for the biological effects of acupuncture that ultimately may help us to understand how it can be used to treat abused drugs.

Chae Y et al. Effect of acupuncture on anxiety-like behavior during nicotine withdrawal and relevant mechanisms. *Neuroscience Letters* 2008; 430: 98-102.

An animal study that investigated the effect of acupuncture on anxiety-like behaviour and corticotrophin-releasing factor (CRF) and neuropeptide Y (NPY) mRNA expression in the amygdala during nicotine withdrawal. Rats were given repeated nicotine injections or saline for 7 days. Acupuncture was given during withdrawal. Rats undergoing nicotine withdrawal were less likely to explore the open arms of a plus maze compared with the saline-treated controls. The percentage of open arm entries in the HT7 acupuncture group, but not in the ST36 acupuncture group, was significantly increased compared with the nicotine withdrawal group. Consistent with this behaviour, CRF mRNA levels in that group were increased compared with the control group. NPY mRNA levels were not different among the groups.

Zhao RJ et al. Acupuncture normalizes the release of accumbal dopamine during the withdrawal period and after the ethanol challenge in chronic ethanol-treated rats. *Neuroscience Letters* 2006; 395: 28-32.

An animal study that investigated the effects of acupuncture on chronic ethanol-induced changes in extracellular dopamine levels in the nucleus accumbens shell (using in vivo microdialysis in unanaesthetized rats). Male Sprague-Dawley rats were treated with 3 g/kg/day of ethanol (20%, w/v) or saline by intraperitoneal injection for 21 days. Following 72 h of ethanol withdrawal, acupuncture was given. Acupuncture at the specific acupoint HT7, but not at control points (PC6 or tail) significantly prevented both a decrease of extracellular dopamine levels in the nucleus accumbens during ethanol withdrawal and an increase in accumbal dopamine levels induced by the ethanol challenge.

Chae Y et al. Acupuncture attenuates repeated nicotine-induced behavioral sensitization and c-Fos expression in the nucleus accumbens and striatum of the rat. *Neuroscience Letters* 2004; 358: 87-90.

An animal study that examined the effect of acupuncture on nicotine-induced behavioural locomotor activity and c-fos expression in the nucleus accumbens and striatum utilizing the immunocytochemical detection of the Fos protein. The rats were given repeated daily nicotine injections (0.4 mg/kg s.c., twice daily for 7 days) followed by one challenging injection on the 4th day after the last daily injection. Acupuncture significantly attenuated expected increase in nicotine-induced locomotor activity and Fos-like-immunoreactivity in the nucleus accumbens and striatum to subsequent nicotine challenge, changes that were not seen in the control group.

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