



ACUPUNCTURE AND NEUROPATHIC PAIN

About neuropathic pain

Neuropathic pain results from damage to, or dysfunction of, the system that normally signals pain. The International Association for the Study of Pain (IASP 2007) defines neuropathic pain as follows: 'Pain initiated or caused by a primary lesion or dysfunction in the nervous system. Peripheral neuropathic pain occurs when the lesion or dysfunction affects the peripheral nervous system. Central pain may be retained as the term for when the lesion or dysfunction affects the central nervous system'. A review of the epidemiology of chronic pain found that there is still no accurate estimate available for the population prevalence of neuropathic pain.(Smith and Torrance 2010)

Neuropathic pain is often chronic, and can be severe and difficult to treat.(NICE 2010) The origin of neuropathic pain can be metabolic, inflammatory, infective or neoplastic, or can be due to an injury, compression or infiltration (e.g. by tumour) of peripheral nerves. Various conditions can cause neuropathic pain include diabetic neuropathy, postherpetic neuralgia and trigeminal neuralgia, pain following chemotherapy and HIV infection.

Neuropathic pain is commonly described as burning, stabbing, stinging, shooting, aching or electric shock-like in quality.(Sykes 1997; Galer 1995) The pain may be superficial or deep, intermittent or constant, and can be spontaneous or be triggered by various stimuli.

Conventional management often involves the combined use of a range of pharmacological (e.g. amitriptyline, gabapentin, opioids, NSAIDs, topical treatments such as capsaicin and lidocaine) and non-drug approaches, (e.g. transcutaneous electrical nerve stimulation, psychological treatments, and specialist procedures to stimulate, block or destroy discrete areas of the nervous system.(Sykes 1997)

References

Galer BS. Neuropathic pain of peripheral origin: advances in pharmacologic treatment. *Neurology* 1995; 45 (suppl 9): S17-25.

International Association for the Study of Pain (2007). IASP Pain terminology [online]. Available: www.iasp-pain.org/AM/Template.cfm?Section=Home&Template=/CM/HTMLDisplay.cfm&ContentID=3058#Neuropathic

National Institute for Health and Clinical Excellence, 2010. CG96 Neuropathic pain - pharmacological management: full guideline [online]. Available: <http://guidance.nice.org.uk/CG96/Guidance>

Smith BH, Torrance N (2010) Neuropathic pain. In: Croft PR, editor. *Chronic pain epidemiology: from aetiology to public health*. Oxford: Oxford University Press, in press (ISBN 9780199235766)

Sykes J et al. Difficult pain problems. *BMJ* 1997; 315: 867-9.

How acupuncture can help

This Factsheet focuses on the evidence for acupuncture in trigeminal neuralgia, chemical-induced neuropathy and neuropathy due to HIV infection. Diabetic neuropathy is discussed in the Type 2 diabetes mellitus Factsheet. There are also Factsheets on Sciatica and Cancer. Carpal tunnel syndrome and postherpetic neuralgia will be discussed in future Factsheets.

One systematic review of randomised controlled trials comparing acupuncture with carbamazepine for trigeminal neuralgia found acupuncture to be as effective as drug treatment, but to cause fewer unwanted effects.(Liu 2010) In single randomised controlled trials, electroacupuncture was found not to be effective for chronic painful neuropathy in general (Penza 2011); acupuncture was found to be more effective than cobamamide for peripheral neuropathy due to chemotherapy (Xu 2010); acupuncture plus acupoint injection was found to be more effective than carbamazepine for greater occipital neuralgia (Pan 2008); and neither acupuncture nor amitriptyline were found to be more effective than placebo for peripheral neuropathy due to HIV infection, but acupuncture was associated with reduced attrition and mortality rates(Shlay 1998; Shiflett 2011). Other non-randomised studies have found encouraging results with acupuncture for chemotherapy-induced neuropathy, HIV/AIDs-induced neuropathy, trigeminal neuralgia and peripheral neuropathy of undefined aetiology.(Donald 2011; Schrader 2007; Phillips 2004; Galantino 1999; Spacek 1998).

In summary, acupuncture seems to be at least as beneficial as the drugs it has been tested against, though in some circumstances neither may be very effective. As yet, there is insufficient research to indicate which patient groups it may be most helpful for. Acupuncture may offer additional benefits, from better sleep to reduced mortality, and probably has fewer side effects than pharmaceutical 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.

Research has shown that acupuncture treatment may specifically help to relieve neuropathic pain by:

- Reducing hypersensitivity induced by spinal nerve ligation, an effect dependent on the opioid system (Cidral-Filho 2011);
- Inhibiting paclitaxel-induced allodynia/hyperalgesia through spinal opioid receptors (Meng 2011);
- Influencing the neurotrophic factor signalling system, which is important in neuropathic pain (Dong 2006).
- Acting on areas of the brain 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 (Hui 2010; Hui 2009);
- Increasing the release of adenosine, which has antinociceptive properties (Goldman 2010);

- Improving muscle stiffness and joint mobility by increasing local microcirculation (Komori 2009), which aids dispersal of swelling;
- Reducing inflammation, by promoting release of vascular and immunomodulatory factors (Kavoussi 2007);

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 wellbeing.

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 wellbeing.

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	
Liu H et al. A systematic review on acupuncture for trigeminal neuralgia. <i>Altern Ther Health Med</i> 2010; 16: 30-5.	A systematic review that assessed the efficacy of acupuncture treatment for trigeminal neuralgia. Twelve randomised controlled studies involving a total of 920 people were included that compared acupuncture with carbamazepine. Four trials reported that acupuncture was superior to carbamazepine, and the remaining eight studies showed no difference between the treatment and control groups. Adverse effects with acupuncture, which were reported in three studies, were mild. The reviewers concluded that the evidence suggests that acupuncture is of a similar efficacy to carbamazepine, but results in fewer adverse effects in treatment of trigeminal neuralgia.
Randomised controlled trials	
Penza P et al. Electroacupuncture Is Not Effective in Chronic Painful Neuropathies. <i>Pain Med.</i> 2011 Sep 14. doi: 10.1111/j.1526-4637.2011.01230.x.	A double-blind randomised placebo-controlled trial that investigated the analgesic efficacy of electroacupuncture (EA) in 16 patients with chronic painful neuropathy. EA was compared to pseudo-EA (placebo). Only one patient per group (EA and pseudo-EA) reported 50% of pain relief at the end of each treatment compared with pain intensity at baseline. Pain intensity did not differ between EA and pseudo-EA. The researchers concluded that their results do not support the use of EA in this population of painful neuropathy patients.
Xu WR et al. Clinical randomized controlled study on acupuncture for treatment of peripheral neuropathy induced by chemotherapeutic drugs. [Article in Chinese] <i>Zhongguo Zhen Jiu</i> 2010; 30: 457-60.	A randomised controlled trial that looked at effective treatments for peripheral neuropathy induced by chemotherapeutic drugs. A total of 64 patients with peripheral neuropathy induced by paclitaxel or oxaliplatin were randomly allocated to acupuncture or intramuscular injection of cobamamide. The neurotoxicity of two groups was compared using a questionnaire before and after treatment. The total effective rate for sensory nerve disorder in the acupuncture group was 66.7% compared to 40.0% in medication group ($p < 0.05$). The researchers concluded that acupuncture is more effective than cobamamide for treatment of peripheral neuropathy induced by chemotherapeutic drugs.
Pan C, Tan G. Forty-two cases of greater occipital neuralgia treated by acupuncture plus acupoint-injection. <i>J Tradit Chin Med</i> 2008; 28: 175-7.	A randomised controlled study that assessed the therapeutic effects of acupuncture plus acupoint-injection on greater occipital neuralgia in 84 patients. Acupuncture plus acupoint-injection was compared with oral carbamazepine. The total effective rate was 92.8% in the treatment group and 71.4% in the control group. The difference in the total effective rate was significant ($p < 0.05$) between the two groups. The researchers concluded that acupuncture plus acupoint-injection is effective for greater occipital neuralgia and better than the

carbamazepine.

Shlay JC et al. Acupuncture and amitriptyline for pain due to HIV-related peripheral neuropathy: a randomized controlled trial. Terry Bein Community Programs for Clinical Research on AIDS. JAMA 1998; 280: 1590-5.

A randomised controlled trial that evaluated the efficacy of a standardised acupuncture regimen (SAR) and amitriptyline hydrochloride for the relief of pain due to HIV-related peripheral neuropathy in 250 patients. All treatment groups showed a reduction in mean pain scores at 6 and 14 weeks compared with baseline values, but there was no significant difference between the placebo, acupuncture or amitriptyline groups. The researchers concluded that neither acupuncture nor amitriptyline was more effective than placebo in relieving pain caused by HIV-related peripheral neuropathy.

Shiflett SC, Schwartz GE. Effects of acupuncture in reducing attrition and mortality in HIV-Infected men with peripheral neuropathy. Explore (NY). 2011; 7: 148-54.

A reassessment of research assessing acupuncture versus amitriptyline for peripheral neuropathy in 114 HIV-infected patients study. The results were inconclusive for pain measures, but acupuncture had a strong and positive effect on attrition and mortality. Overall, acupuncture was associated with lower attrition rate (27.6% vs. 44.6%, $p=0.058$), and a zero mortality rate (0% vs. 12.5%, $p=0.047$) than amitriptyline. This protective effect of acupuncture was most pronounced among patients with poorest physical functioning at the beginning of the study (0% vs. 23.8%, $p=0.047$). The researchers concluded that acupuncture was clearly effective in reducing attrition and mortality in men with HIV and peripheral neuropathy, but that results for pain relief were mixed.

Other clinical studies

Donald GK et al. Evaluation of acupuncture in the management of chemotherapy-induced peripheral neuropathy. Acupunct Med. 2011; 29: 230-3.

An observation study that clinically evaluated the effectiveness of acupuncture in the management of 18 patients with chemotherapy-induced peripheral neuropathy (PN). In all, 82% ($n=14$) of patients reported an improvement in symptoms following their course of acupuncture; one patient with advanced disease died during the 6 weeks. Some patients derived additional benefits from the treatment, including a reduction in analgesic use and improved sleeping patterns. The researchers concluded that, although these results are encouraging, they are uncontrolled.

Schröder S et al. Acupuncture treatment improves nerve conduction in peripheral neuropathy. Eur J Neurol 2007; 14: 276-81.

A pilot study to evaluate the therapeutic effect of acupuncture on peripheral neuropathy as measured by changes in nerve conduction and assessment of subjective symptoms. Forty seven patients with neuropathy of undefined aetiology were enrolled: 21 were treated with acupuncture therapy according to classical Chinese Medicine, while 26 received best medical care but no specific treatment for neuropathy. Sixteen patients (76%) in the acupuncture group improved symptomatically and objectively, while only four patients in the control group (15%) did so. Three patients in the acupuncture group (14%) showed no change and two patients an aggravation (10%), whereas in the control group seven showed no change (27%) and 15 an aggravation (58%). The researchers concluded that their results suggest there is a positive effect of acupuncture on peripheral neuropathy of undefined aetiology as measured by objective parameters.

<p>Phillips KD et al. Effect of acupuncture administered in a group setting on pain and subjective peripheral neuropathy in persons with human immunodeficiency virus disease. <i>J Altern Complement Med</i> 2004; 10: 449-55.</p>	<p>A study that assessed acupuncture treatment for pain and symptoms of peripheral neuropathy in 21 patients with HIV infection. Comparison of the pretreatment and post-treatment Pain Rating Scale results indicated a significant reduction in present pain ($p=0.0002$), least and most pain in the last 24 hours ($p<0.0001$ and $p=0.0004$, respectively) and the total pain summary score ($p<0.0001$). Scores for pain/aching/burning, pins and needles, and numbness in the hands and feet were reduced ($p=0.0065$), as well as the total summary score ($p=0.0001$). The researchers concluded that subjective pain and symptoms of peripheral neuropathy were reduced during the period of individual acupuncture therapy.</p>
<p>Galantino ML et al. Use of noninvasive electroacupuncture for the treatment of HIV-related peripheral neuropathy: a pilot study. <i>J Altern Complement Med</i> 1999; 5: 135-42.</p>	<p>A prospective study that tested the hypothesis that low-voltage non-invasive electroacupuncture will improve the condition of 11 patients with neuropathic HIV/AIDS. Complete data was obtained from only 7 patients, and there was improvement in the condition of all of them. They felt much better and reported feelings of increased physical strength and a significant overall improvement in functional activities ($p=0.02$). The researchers concluded that their results support the hypothesis that low-voltage electroacupuncture will improve the condition of the neuropathic HIV/AIDS patient.</p>
<p>Spacek A et al. Acupuncture and ganglionic local opioid analgesia in trigeminal neuralgia. [Article in German] <i>Wien Med Wochenschr</i> 1998; 148: 447-9.</p>	<p>A retrospective analysis of data from 39 patients with trigeminal neuralgia. In all, 17 patients had received carbamazepine and acupuncture therapy (group A), 11 had had carbamazepine and GLOA + acupuncture (group B), and 11 had received carbamazepine and GLOA without acupuncture (group C). All subjects had taken carbamazepine for at least 4 weeks. Of the groups who received acupuncture as an additive, 8 of the subjects in group A, and 5 of the subjects in group B were pain free, but only 2 of the subjects of group C (no acupuncture). The results for patients with marked pain reduction were similar. The researchers concluded that their results showed that the combined use of acupuncture and carbamazepine with or without GLOA achieves an additional therapeutic effect in the treatment of trigeminal neuralgia, and that the addition of acupuncture seems to have a superior effect to the addition of GLOA.</p>

Possible mechanisms of acupuncture

<p>Cidral-Filho FJ et al. Manual acupuncture inhibits mechanical hypersensitivity induced by spinal nerve ligation in rats. <i>Neuroscience</i> 2011; 193: 370-6.</p>	<p>A study in rats that found acupuncture stimulation was able to reduce mechanical hypersensitivity with treatment beginning in both acute and sub-chronic phases of SNL-induced neuropathy. The effect was blocked by naloxone, and was similar to the effect with gabapentin. The researchers concluded that their results demonstrated that manual acupuncture reduces hypersensitivity induced by the spinal nerve ligation, and the effect is dependent on the opioid system and comparable with the one obtained with gabapentin.</p>
<p>Meng X et al. The effects of opioid receptor antagonists on electroacupuncture-produced anti-allodynia/hyperalgesia in rats with</p>	<p>A study using rats that found electroacupuncture (EA) to significantly inhibit paclitaxel-induced allodynia/hyperalgesia through spinal opioid receptors. The researchers concluded that EA may be a useful complementary treatment for</p>

<p>paclitaxel-evoked peripheral neuropathy. <i>Brain Res.</i> 2011 Sep 26;1414:58-65.</p>	<p>neuropathic pain patients.</p>
<p>Goldman N et al. Adenosine A1 receptors mediate local anti-nociceptive effects of acupuncture. <i>Nat Neurosci</i> 2010; May 30.</p>	<p>A study showing that the neuromodulator adenosine, which has anti-nociceptive properties, was released during acupuncture in mice, and that its anti-nociceptive actions required adenosine A1 receptor expression. Direct injection of an adenosine A1 receptor agonist replicated the analgesic effect of acupuncture. Inhibition of enzymes involved in adenosine degradation potentiated the acupuncture-elicited increase in adenosine, as well as its anti-nociceptive effect. The researchers concluded that their observations indicate that adenosine mediates the effects of acupuncture and that interfering with adenosine metabolism may prolong the clinical benefit of acupuncture.</p>
<p>Hui KK et al. Acupuncture, the limbic system, and the anticorrelated networks of the brain. <i>Auton Neurosci</i> 2010; 157: 81-90.</p>	<p>Studies have shown that acupuncture stimulation, when associated with sensations comprising deqi, evokes deactivation of a limbic-paralimbic-neocortical network, as well as activation of somatosensory brain regions. These networks closely match the default mode network and the anti-correlated task-positive network. The effect of acupuncture on the brain is integrated at multiple levels, down to the brainstem and cerebellum and appears to go beyond either simple placebo or somatosensory needling effects. Needling needs to be done carefully, as very strong or painful sensations can attenuate or even reverse the desired effects. Their results suggest that acupuncture mobilises the functionally anti-correlated networks of the brain to mediate its actions, and that the effect is dependent on the psychophysical response. They discuss potential clinical application to disease states including chronic pain, major depression, schizophrenia, autism, and Alzheimer's disease.</p>
<p>Hui K.K.-S. The salient characteristics of the central effects of acupuncture needling: limbic-paralimbic-neocortical network modulation. <i>Human Brain Mapping</i> 2009; 30: 1196-206.</p>	<p>This study assessed the results of fMRI on 10 healthy adults during manual acupuncture at 3 acupuncture points and a sham point on the dorsum of the foot. Although certain differences were seen between real and sham points, the hemodynamic and psychophysical responses were generally similar for all 4 points. Acupuncture produced extensive deactivation of the limbic-paralimbic-neocortical system. Clusters of deactivated regions were seen in the medial prefrontal cortex, the temporal lobe and the posterior medial cortex. The sensorimotor cortices, thalamus and occasional paralimbic structures such as the insula and anterior middle cingulate cortex showed activation. The researchers concluded that their results provided additional evidence that acupuncture modulates the limbic-paralimbic-neocortical network. They hypothesised that acupuncture may mediate its analgesic, anti-anxiety, and other therapeutic effects via this intrinsic neural circuit that plays a central role in the affective and cognitive dimensions of pain.</p>
<p>Komori M et al. Microcirculatory responses to acupuncture stimulation and phototherapy. <i>Anesth Analg</i> 2009;</p>	<p>Experimental study on rabbits in which acupuncture stimulation was directly observed to increase diameter and blood flow velocity of peripheral arterioles, enhancing local</p>

108: 635-40.	microcirculation.
Kavoussi B, Ross BE. The neuroimmune basis of anti-inflammatory acupuncture. Integr Cancer Ther 2007; 6: 251-7.	Review article that suggests the anti-inflammatory actions of traditional and electro-acupuncture are mediated by efferent vagus nerve activation and inflammatory macrophage deactivation.
Dong Z-Q et al. Down-regulation of GFRalpha-1 expression by antisense oligodeoxynucleotide attenuates electroacupuncture analgesia on heat hyperalgesia in a rat model of neuropathic pain. Brain Research Bulletin 2006; 69: 30-6.	An animal study that found the endogenous glial cell line-derived neurotrophic factor signalling system (important in neuropathic pain) is involved in the effects of electroacupuncture analgesia on neuropathic pain in rats.

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