



# **Chronic Fatigue Syndrome**

Overview

#### Background

Chronic fatigue syndrome is characterised by severe, disabling fatigue, and other symptoms such as musculoskeletal pain, sleep disturbance, impaired concentration and headaches (Reid 2007).

The prevalence of chronic fatigue syndrome has been estimated to be from 0.007% to 2.8% in the general adult population, and from 0.006% to 3.0% in primary care, depending on the criteria used (Afari 2003). Chronic fatigue syndrome imposes substantial economic costs on society, mainly in terms of informal care costs and lost employment (McCrone 2003).

The cause of the syndrome remains poorly understood, but hypotheses include endocrine and immunological abnormalities, autonomic nervous system dysfunction, abnormal pain processing and certain infectious illnesses, such as Epstein-Barr virus and viral meningitis (Gur 2008, White 2001). People who have had a prior psychiatric disorder are nearly three times more likely to have chronic fatigue syndrome later in life than those who have not (Harvey 2008).

Prognosis is poor, with only around 5% of adults returning to pre-syndrome levels of functioning (Cairns 2005). Aims of treatment are to reduce levels of fatigue and associated symptoms, to increase levels of activity, and to improve quality of life. Conventional approaches include graded exercise therapy, cognitive behavioural therapy (CBT) and antidepressant drugs (DTB 2001).

#### **Clinical evidence**

There are consistent positive results from observational studies (Wang 2008, Huang 2008, Guo 2007), but very few randomised controlled trials as yet (Wang 2009a, 2009b; Yiu 2007; Li 2006) (see Evidence summaries). In the meantime, given the often unsatisfactory outcomes from conventional treatments, acupuncture may be a worthwhile option to consider, probably as part of a combined approach. There is evidence to support its effectiveness for some of the common symptoms – chronic pain, insomnia, depression (see other fact sheets), but for chronic fatigue syndrome as a whole there is a need for more, and higher quality, research.

#### Potential mechanisms

In general, acupuncture is believed to stimulate the nervous system and cause the release of neurotransmitters. 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 insomnia (Wu 1999).

Acupuncture may help to relieve symptoms of chronic fatigue syndrome such as musculoskeletal pain, headache, sleep problems, tiredness and depression by:

- stimulating nerves located in muscles and other tissues, which leads to release of endorphins and other neurohumoral factors, and changes the processing of pain in the brain and spinal cord (Pomeranz 1987, Zhao 2008).
- stimulating opiodergic neurons to increase the concentrations of beta-endorphin, so relieving pain (Cheng 2009).
- reducing inflammation, by promoting release of vascular and immunomodulatory factors (Kavoussi 2007, Zijlstra 2003).
- improving muscle stiffness and joint mobility by increasing local microcirculation (Komori 2009), which can reduce swelling and pain.
- reducing insomnia through increasing nocturnal endogenous melatonin secretion (Spence 2004).

### References

Afari N, Buchwald D. Chronic fatigue syndrome: a review. Am J Psychiatry 2003;160:221-36.

Cairns R, Hotopf M. A systematic review describing the prognosis of chronic fatigue syndrome. Occup Med (Oxford) 2005;55:20-31.

Gur A. Oktayoglu P. Central nervous system abnormalities in fibromyalgia and chronic fatigue syndrome: New concepts in treatment. Current Pharmaceutical Design 2008; 14: 1274-94.

Harvey SB et al. The relationship between prior psychiatric disorder and chronic fatigue: evidence from a national birth cohort study. Psychol Med 2008;38:933-40.

Reid S et al. Chronic fatigue syndrome. BMJ Clinical Evidence. Search date September 20077.

What to do about medically unexplained symptoms. DTB 2001; 39: 5-8.

White P et al. Predictions and associations of fatigue syndromes and mood disorders that occur after infectious mononucleosis. Lancet 2001;358:1946-54.

McCrone P et al. The economic cost of chronic fatigue and chronic syndrome in UK primary care. Psychological Medicine 2003; 33: 253-61.

## **Evidence** summaries

Research	Conclusion
Systematic Review	
Wang T et al. A systematic review of acupuncture and moxibustion treatment for chronic fatigue syndrome in China. American Journal of Chinese Medicine 2008; 36:1-24.	A systematic review of studies on the treatment of chronic fatigue syndrome with acupuncture and moxibustion in China. All studies concluded that acupuncture treatment is effective, with response rates ranging from 78.95% to 100%. However, the qualities of the studies were generally poor, and none of them were randomised controlled trials.
Clinical studies	
Wang JJ et al. [Randomized controlled study on influence of acupuncture for life quality of patients with chronic fatigue syndrome]. Zhongguo Zhenjiu 2009a; 29: 780-4.	A randomised controlled trial to observe effects of acupuncture on quality of life in 70 patients with chronic fatigue syndrome. Patients were allocated to treatment with 'real' acupuncture or sham acupuncture, three times a week. Individuals' own perception of their health condition and total score were significantly improved after treatment in the observation group (all P<0.05). There were no adverse effects reported. The researchers concluded that acupuncture can improve the quality of life of patients with chronic fatigue syndrome.
Wang JJ et al. [Randomized controlled clinical trials of acupuncture treatment of chronic fatigue syndrome]. [Chinese]. Chen Tzu Yen Chiu Acupuncture Research 2009b; 34: 120-4.	In the same trial, the researcher observed the effects of acupuncture on the amount of fatigue experienced by the patients. After the treatments, this had decreased significantly from baseline in both groups. Real acupuncture resulted in a greater reduction in mental fatigue than sham acupuncture, but the change in physical fatigue was similar in the two groups. <u>The researchers concluded that acupuncture</u> <u>can relieve physical and mental fatigue in patients with</u> <u>chronic fatigue syndrome.</u>
Yiu YM et al. A clinical trial of acupuncture for treating chronic fatigue syndrome in Hong Kong. Journal of Chinese Integrative Medicine 2007; 5(6): 630-3.	A randomised controlled trial to evaluate the efficacy of acupuncture in 99 patients with chronic fatigue syndrome. Patients were allocated to 'real' or sham acupuncture. Improvements in physical and mental fatigue and quality of life were seen in both groups, but the improvements in the treatment group were significantly bigger than in the control group (p<0.01 to <0.05). No adverse events occurred. <u>The</u> <u>researchers concluded that acupuncture is a safe. effective</u> <u>treatment for chronic fatigue syndrome.</u>

Research	Conclusion
Clinical studies	
Li Y et al. The therapeutic effects of electrical acupuncture and auricular- plaster in 32 cases of chronic fatigue syndrome. Journal of Traditional Chinese Medicine 2006; 26(3): 163-4.	A randomised controlled trial to compare the therapeutic effects of electroacupuncture and auricular-plaster therapy against oral hydrocortisone in 64 patients with chronic fatigue syndrome (CFS). The total effective rates were 93.75% in the acupuncture group and 75.00% in the control group, with a statistically significant difference between the two groups (P<0.05). The researchers concluded that electroacupuncture and auricular-plaster therapy may show a better anti-fatigue effect than that of hydrocortisone.
Huang Y et al. Clinical observation on the effects of Bo's abdominal acupuncture in 40 cases of chronic fatigue syndrome. Journal of Traditional Chinese Medicine 2008; 28(4): 264-6.	An observational study on the effect of acupuncture in 40 patients with chronic fatigue syndrome. Treatment was given once a day for 2 weeks, and scores for symptoms and fatigue were compared before and after treatment. After treatment, scores for symptoms, mental condition and neural feeling associated with fatigue were significantly reduced (P<0.01-0.05). The researchers concluded that acupuncture has a good general effect on the complex symptoms of chronic fatigue syndrome, especially on lassitude, anorexia, insomnia, amnesia, diarrhoea, and general pain.
Guo J. Chronic fatigue syndrome treated by acupuncture and moxibustion in combination with psychological approaches in 310 cases. Journal of Traditional Chinese Medicine 2007; 27(2): 92-5.	An observational study on the clinical therapeutic effect of acupuncture and moxibustion combined with a psychological approach on chronic fatigue syndrome in 310 patients. In all, 275 patients (88.7%) were clinically cured, 28 cases (9%) improved, and 7 cases (2.3%) did not get better. <u>The researchers concluded that acupuncture plus moxibustion combined with a psychological approach is an effective therapy for chronic fatigue syndrome.</u>
Physiology studies (animals and humans)	
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]	Animal study investigating the involvement of the NTS 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 opiodergic neurons to increase the concentrations of beta-endorphin and the involvement of the $\mu$ -opioid receptors.
Komori M et al. Microcirculatory responses to acupuncture stimulation and phototherapy. Anesth Analg 2009; 108(2): 635-40	Experimental study on rabbits, in which acupuncture stimulation was directly observed to increase diameter and blood flow velocity of peripheral arterioles, enhancing local microcirculation.

Research	Conclusion
Physiology studies (animals and humans)	
Zhao ZQ. Neural mechanism underlying acupuncture analgesia. Prog Neurobiol 2008; 85(4): 355-75.	Review article that discusses the various peripheral and central nervous system components of acupuncture anaesthesia in detail.
Kavoussi B, Ross BE. The neuroimmune basis of anti- inflammatory acupuncture. Integr Cancer Ther 2007; 6(3): 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.
Spence et al. Acupuncture increases nocturnal melatonin secretion and reduces ilnsomnia and anxiety: a preliminary report. J Neuropsych Clin Neurosciences 2004; 16: 19-28.	Study in 18 anxious adults with insomnia that found a significant (p = 0.002) nocturnal increase in endogenous melatonin secretion after 5 weeks of acupuncture, as well as significant improvements in polysomnographic measures of sleep onset latency (p = 0.003), arousal index (p = 0.001), total sleep time (p = 0.001), and sleep efficiency (p = 0.002).
Zijlstra FJ et al. Anti- inflammatory actions of acupuncture. Mediators Inflamm 2003; 12(2): 59-69.	Review article that suggests a hypothesis for anti- inflammatory action of acupuncture: Insertion of acupuncture needles initially stimulates production of beta-endorphins, CGRP and substance P, leading to further stimulation of cytokines and NO. While high levels of CGRP have been shown to be pro-inflammatory, CGRP in low concentrations exerts potent anti-inflammatory actions. Therefore, a frequently applied 'low-dose' treatment of acupuncture could provoke a sustained release of CGRP with anti-inflammatory activity, without stimulation of pro-inflammatory cells.
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.	Experimental study using fMRI to characterise the central nervous system pathway for acupuncture stimulation, which found that acupuncture activates structures of descending antinocioceptive pathway and deactivates areas mediating pain modulation.

Research	Conclusion
Physiology studies (animals and humans)	
Pomeranz B. Scientific basis of acupuncture. In: Stux G, Pomeranz B, eds. Acupuncture Textbook and Atlas. Heidelberg: Springer- Verlag; 1987: 1-18.	Needle activation of A delta and C afferent nerve fibres in muscle sends signals to the spinal cord, where dynorphin and enkephalins are released. Afferent pathways continue to the midbrain, triggering excitatory and inhibitory mediators in spinal cord. Ensuing release of serotonin and norepinephrine onto the spinal cord leads to pain transmission being inhibited both pre- and postsynaptically in the spinothalamic tract. Finally, these signals reach the hypothalamus and pituitary, triggering release of adrenocorticotropic hormones and beta- endorphin.