

ACUPUNCTURE AND STRESS

About stress

Up to half a million people in the UK experience work-related stress every year, which often results in illness.(Health and Safety Executive 2011) Other factors that affect stress levels include alcohol, smoking, exams, pregnancy, divorce, moving, death in family, lifestyle, drugs, poor nutrition and unemployment.

The signs of stress can vary from one individual to the next.(NHS Choices 2011) They may manifest physically as an illness, tiredness or lethargy, or as symptoms such as sore, tight muscles, dull skin, lank hair, or erratic sleep patterns. Mental stress can result in depression, mood swings, anger, frustration, confusion, paranoid behaviour, jealousy or withdrawal.

Conventional treatments include medication such as anti-anxiety drugs, cognitive behavioural therapy and relaxation techniques.(NHS Choices 2011)

References

Health and Safety Executive, 2011. Stress-related and psychological illness [online]. Available: <http://www.hse.gov.uk/statistics/causdis/stress/scale.htm>

NHS Choices, 2011. Stress Management [online]. Available: <http://www.nhs.uk/livewell/stressmanagement/Pages/Stressmanagementhome.aspx>

How acupuncture can help

Stress is a common complaint cited by acupuncture patients, with a variety of possible associated symptoms. The most prevalent of these is anxiety, for which there is information about acupuncture treatment in the Anxiety Fact Sheet. There are also factsheets on other conditions that are affected by stress, such as back pain, chronic pain, depression, headache, insomnia, irritable bowel syndrome, menopausal symptoms, migraines, premenstrual syndrome and urinary incontinence.

Aside from such associated conditions, there is little clinical research on stress per se. One small randomised controlled trial (RCT) suggested that acupuncture might be successful in treating the symptoms of chronic stress (Huang 2011). Another three RCTs have investigated acupuncture in very specialised situations: a) as an adjunct to anaesthesia, it was found to help keep haemodynamics stable and reduce the stress response during laparoscopic cholecystectomy (Wu 2011); b) it did not reduce salivary cortisol concentrations (and so may not be able to reduce emotional stress) in female dysphonic speakers (Kwong 2010); c) acute acupuncture appeared to control excessive sympathetic excitation during mental stress in patients with advanced heart failure (Middlekauff 2002). A crossover study with healthy individuals subjected to stress testing found acupuncture at a point indicated for stress was more effective than a control point (Fassoulaki 2003). Several uncontrolled studies have looked at various

aspects of stress and the effects of acupuncture. One found that it might be effective in attenuating psychological distress, as well as increasing cellular immunity (Pavao 2011). In another, acupuncture was associated with less stress around embryo transfer and improved pregnancy rates in women having IVF (Balk 2010). In a small pilot study, the use of one particular acupuncture point led to marked reductions in stress (Chan 2002).

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 benefit anxiety disorders and symptoms of anxiety by:

- 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);
- Improving stress induced memory impairment and an increasing AchE reactivity in the hippocampus (Kim 2011);
- Reducing serum levels of corticosterone and the number of tyrosine hydroxylase-immunoreactive cells (Park 2010);
- Regulating levels of neurotransmitters (or their modulators) and hormones such as serotonin, noradrenaline, dopamine, GABA, neuropeptide Y and ACTH; hence altering the brain's mood chemistry to help to combat negative affective states (Lee 2009; Cheng 2009; Zhou 2008);
- Stimulating production of endogenous opioids that affect the autonomic nervous system (Arranz 2007). Stress activates the sympathetic nervous system, while acupuncture can activate the opposing parasympathetic nervous system, which initiates the relaxation response;
- Reversing pathological changes in levels of inflammatory cytokines that are associated with stress reactions (Arranz 2007);
- Reducing inflammation, by promoting release of vascular and immunomodulatory factors (Kavoussi 2007, Zijlstra 2003);
- Reversing stress-induced changes in behaviour and biochemistry (Kim 2009).

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The evidence

Research	Conclusion
Randomised controlled trials	
<p>Wu Y et al. Effect of acupuncture-assisted anesthesia on stress response during laparoscopic cholecystectomy in aged patients. [Article in Chinese] <i>Zhongguo Zhen Jiu</i> 2011; 31: 155-7.</p>	<p>A randomised controlled trial that compared the difference between transcutaneous electrical acupoint stimulation (TEAS) assisted general anaesthesia and simple general anaesthesia on stress response during laparoscopic cholecystectomy in 40 older patients. The haemodynamic indices (i.e. mean arterial pressure, heart rate) had decreased in the general anaesthesia only group at 5 minutes compared to before anaesthesia and compared to the TEAS plus general anaesthesia group ($p < 0.05$). After surgery, the haemodynamic indices and plasma endothelin and cortisol in the TEAS group had not changed from baseline (all $p > 0.05$), but they had all increased significantly in group general anaesthesia group. There were also significant differences between the two treatment groups in favour of TEAS at each time point ($p < 0.05$, $p < 0.01$). The researchers concluded that acupuncture-assisted anaesthesia helps to keep haemodynamics stable and reduce the stress response during laparoscopic cholecystectomy in older patients.</p>
<p>Huang W et al. An investigation into the effectiveness of traditional Chinese acupuncture (TCA) for chronic stress in adults: a randomised controlled pilot study. <i>Complement Ther Clin Pract</i> 2011; 17: 16-21.</p>	<p>An exploratory pragmatic randomised controlled trial that investigated the effectiveness of traditional Chinese acupuncture (TCA) using an individually targeted treatment protocol delivered by a traditionally trained Chinese acupuncturist. The trial examined the treatment of chronic stress as perceived by the 18 participants who all self-reported high stress levels. They were allocated to weekly TCA for 5 weeks; weekly attention only (practitioner present and participant supine) for 5 weeks or were in a waiting list control group. The Perceived Stress Scale 14 (PSS-14) and the Measure Yourself Medical Outcome Profile (MYMOP) were completed before and after treatment. After 5 weeks, the acupuncture group reported significant changes in MYMOP profile score and both MYMOP reported symptoms ($p < 0.05$); the attention only group had significant changes in MYMOP profile score and one symptom ($p < 0.05$); the waiting list group showed no changes. The PSS-14 scores decreased in all 3 groups, but the difference between pre- and post-treatment within and between the groups did not reach significance. In addition, there were self-reports of improvements with acupuncture for other health problems. The researchers concluded that the lack of clarity concerning the definition of stress makes it complex to investigate, but that their study results suggest Traditional Chinese acupuncture might be successful in treating the symptoms of chronic stress.</p>
<p>Kwong EY, Yiu EM. A preliminary study of the effect of acupuncture on emotional stress in female dysphonic speakers. <i>J Voice</i>. 2010; 24: 719-23.</p>	<p>A randomised placebo-controlled trial that investigated the effects of acupuncture (genuine vs. sham) on emotional stress in 18 people with phonotraumatic injuries. Cortisol levels were measured in samples of the participants' saliva. Samples were collected from</p>

each subject at 10 minutes pre-needling, immediately pre-needling, mid-needling, immediately post-needling, and 10 minutes post-needling time points. The findings suggested that the subjects' salivary cortisol concentrations did not reduce after acupuncture, and thus, acupuncture may not be able to reduce the emotional stress level in female dysphonic speakers.

Fassoulaki A et al. Pressure applied on the extra 1 acupuncture point reduces bispectral index values and stress in volunteers. *Anesth Analg*. 2003; 96: 885-90.

A crossover study that investigated the effect of pressure application on the acupuncture "extra 1" point in 25 healthy volunteers. Acupressure applied for 10 minutes on the extra 1 point significantly reduced bispectral index values and the verbal stress score when compared with acupressure applied on a control point.

Middlekauff HR et al. Acupuncture inhibits sympathetic activation during mental stress in advanced heart failure patients. *J Card Fail* 2002; 8: 399-406.

A study to assess whether acupuncture is sympatho-inhibitory in patients with 15 patients with heart failure, in whom muscle sympathetic nerve activity is increased. Heart failure patients with the greatest sympathetic activation have the poorest prognosis. The patients underwent acute mental stress testing before and during "real" acupuncture, non-acupoint acupuncture or no-needle acupuncture control. Muscle sympathetic nerve activity (MSNA) was recorded. Resting MSNA was not different before and after acupuncture. During mental stress, sympathetic nerve activity increased significantly; this increase was eliminated following real acupuncture ($p=0.03$), but not after non-acupoint or no-needle acupuncture controls. The changes in blood pressure and heart rate during mental stress were not attenuated by real or control acupuncture. The researchers concluded that acute acupuncture might attenuate sympatho-excitation during mental stress in patients with advanced heart failure.

Uncontrolled studies

Pavao TS et al. Acupuncture is effective to attenuate stress and stimulate lymphocyte proliferation in the elderly. *Neurosci Lett* 2010; 484: 47-50.

A study that investigated the effects of acupuncture on stress-related psychological symptoms and cellular immunity in young adults and older subjects. Psychological variables (depression, anxiety and stress) were investigated by means of self-assessment inventories. Peripheral blood mononuclear cells were isolated and cultured in vitro to measure mitogen-induced T-cell proliferation as well as cellular sensitivity to dexamethasone. All data were assessed before and after the intervention. Acupuncture was able to significantly reduce depression ($p<0.001$), anxiety ($p<0.001$) and stress ($p<0.001$) scores. The intervention also increased T-cell proliferation, with greater intensity in the older group ($p=0.004$). No changes in cellular sensitivity to dexamethasone were observed following acupuncture. The researchers concluded that acupuncture was effective in attenuating psychological distress, as well as increasing T- cell proliferation.

Balk J et al. The relationship between perceived stress, acupuncture, and pregnancy rates among IVF patients: a pilot study. *Complement Ther Clin Pract* 2010; 16: 154-7.

An observational prospective cohort study that looked at the effect of acupuncture on perceived stress levels in 57 infertile women on the day of embryo transfer (ET), and assessed whether perceived stress levels at embryo transfer correlated with pregnancy rates. In all, 64.7% of the women who received acupuncture became pregnant compared with only 42.5% of those who did not have

acupuncture. When stratified by donor recipient status, only non-donor recipients potentially had an improvement with acupuncture (35.5% without acupuncture vs. 55.6% with acupuncture). Those receiving acupuncture also had lower stress scores, both pre- and post-ET, compared to those who did not. Those who perceived that their stress levels decreased compared to baseline had higher pregnancy rates than those who did not, regardless of acupuncture status. The researchers concluded that acupuncture was associated with less stress both before and after embryo transfer, and that it possibly improved pregnancy rates.

Chan J, et al. An uncontrolled pilot study of HT7 for 'stress'. *Acupunct Med* 2002; 20: 74-7.

The acupuncture point Ht7 was needled in four weekly sessions using 17 volunteers recruited from staff in a hospice. 16 of them (94%) showed improved 'psychological stress' according to the Edinburgh Postnatal Depression Scale (EPDS). The greatest fall in the EPDS scores was observed within the first two treatments and at the end of the study the average reduction was 44%,

Possible mechanisms of acupuncture

Kim H et al. The effects of acupuncture (PC6) on chronic mild stress-induced memory loss. *Neurosci Lett.* 2011; 488: 225-8.

An animal study that examined the effects of the PC6 acupuncture point on chronic mild stress-induced memory loss in rats. Memory storage and acetylcholinesterase (AChE) activity in the hippocampus were measured using a passive avoidance test (PAT) and AChE immunohistochemistry, respectively. In the PAT, the chronic mild stress group showed a markedly lower latency time than the control group ($p < 0.01$ at 72 hours; $p < 0.05$ at 96 hours; $p < 0.001$ at 120 hours). However, acupuncture at PC6 significantly recovered the impairment of memory at 120 hours ($p < 0.001$). Exposure to chronic mild stress also significantly decreased AChE activity in the hippocampus, and acupuncture stimulation at PC6 produced an increase in AChE reactivity. These results show that the acupuncture point is effective in restoring chronic mild stress-related biochemical and behavioural impairments in rats.

Park HJ et al. Electroacupuncture to ST36 ameliorates behavioral and biochemical responses to restraint stress in rats. *Neurol Res* 2010; 32 Suppl 1: 111-5.

A study that looked at the effect of electroacupuncture on the behavioural and biochemical responses to restraint stress in rats. The stress increased the response of the anxiety-related behaviour, serum levels of corticosterone and the number of tyrosine hydroxylase-immunoreactive cells. The acupuncture group showed a significant decrease of anxiety-related behavioural response, and also had decreased serum corticosterone levels and tyrosine hydroxylase-immunoreactive expression. The researchers concluded that the findings suggest that electroacupuncture might play a role in reducing the stress-related responses, which may be helpful for the treatment of stress-related disorders.

Hui KK et al. Acupuncture, the limbic system, and the anticorrelated networks of the brain. *Auton Neurosci* 2010; 157: 81-90.

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 mobilizes 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.

Hui K.K.-S. The salient characteristics of the central effects of acupuncture needling: limbic-paralimbic-neocortical network modulation. *Human Brain Mapping* 2009; 30: 1196-206.

A 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.

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.

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.

Kim H et al. The effects of acupuncture stimulation at PC6 (Neiguan) on chronic mild stress-induced biochemical and behavioral responses. *Neuroscience Letters*. 2009; 460: 56-60.

The effects of acupuncture on the behavioural responses induced by chronic mild stress (CMS) were evaluated in rats by using a maze and a sucrose intake test. C-fos expression in the brain was examined by immunohistochemistry. Acupuncture stimulation at point P6 (3 min) (but not at point SJ5) reversed stress-induced behavioural changes and significantly attenuated c-fos expression in the hypothalamus, suggesting that acupuncture has a therapeutic effect on chronic stress-related diseases such as depression and anxiety.

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

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

<p>Komori M et al. Microcirculatory responses to acupuncture stimulation and phototherapy. <i>Anesth Analg</i> 2009; 108: 635-40.</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 microcirculation.</p>
<p>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. <i>Int J Clin Acupunct</i> 2008; 17: 79-84.</p>	<p>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.</p>
<p>Arranz L et al. Effect of acupuncture treatment on the immune function impairment found in anxious women. <i>American Journal of Chinese Medicine</i>. 2007;35(1):35-51</p>	<p>A study in which 34 women with anxiety received 10 acupuncture treatments over a year, until complete remission. Twenty healthy, non-anxious women formed the controls. Impaired immune functions in anxious women (chemotaxis, phagocytosis, lymphoproliferation and NK activity) were significantly improved by acupuncture, coming to the values of the healthy controls. The effects peaked 72 hours after a session and lasted up to a month after the course finished.</p> <p>In an earlier paper, the authors had reported that acupuncture reversed the lowering of IL-2 levels and elevating of TNF-alpha and cortisol seen in anxious women. Therefore, these may be some of the parameters by which acupuncture could exert its therapeutic action on anxiety.</p>
<p>Kavoussi B, Ross BE. The neuroimmune basis of anti-inflammatory acupuncture. <i>Integr Cancer Ther</i> 2007; 6: 251-7.</p>	<p>Review article that suggests the anti-inflammatory actions of traditional and electro-acupuncture are mediated by efferent vagus nerve activation and inflammatory macrophage deactivation.</p>
<p>Zijlstra FJ et al. Anti-inflammatory actions of acupuncture. <i>Mediators Inflamm</i> 2003; 12: 59-69.</p>	<p>An 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.</p>

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