

ACUPUNCTURE FOR DEMENTIA

About dementia

An estimated 637,000 people in the UK have dementia syndrome and the annual cost of their care is £17 billion (Alzheimer's Society 2007). Alzheimer's disease is the commonest type of dementia (affecting around 60% of those with dementia), followed by vascular dementia (20–25%) and dementia with Lewy bodies (10–15%) (Overshott 2005; DTB 2003).

About 80% of people with dementia will have behavioural changes or psychological symptoms at some time (Overshott 2005), which can reduce quality of life for both patients and carers, and often result in transfer to residential care and higher costs (Finkel 2000; O'Donnell 1992; Lawlor 2002; Donaldson 1997). The symptoms can include anxiety, depressed mood, psychotic symptoms, and behavioural symptoms such as aggression, agitation, wandering, sexual disinhibition, and screaming and swearing (Finkel 1997). Psychotic symptoms such as delusions and hallucinations occur in 30–50% of all patients with dementia (Jeste 2000), and in about 80% of patients with dementia with Lewy bodies (McKeith 2006).

There are 2 main types of medication used to treat Alzheimer's disease – cholinesterase inhibitors and NMDA receptor antagonists. Cholinesterase inhibitors include donepezil hydrochloride (Aricept), rivastigmine (Exelon) and galantamine (Reminyl). The NMDA receptor antagonist is memantine (Ebixa). Drugs may also be used to treat symptoms of dementia, for example, antipsychotic drugs, antidepressants, anti-anxiety drugs and hypnotics (Burns 2009). However, the generally recommended practice for such symptoms of dementia is to try non-drug methods first (e.g. behavioural and psychological interventions, occupational activities, environmental approaches), unless the patient is severely distressed or there is an immediate risk of harm to themselves or others (DTB 2003; NICE 2006). NICE guidelines recommend that people with dementia with mild-to-moderate non-cognitive symptoms should not be prescribed antipsychotic drugs, and that those with severe non-cognitive symptoms (i.e. psychosis and/or agitated behaviour causing significant distress) should only be offered treatment with an antipsychotic drug if specific conditions have been met (NICE 2006).

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How acupuncture can help

This factsheet focuses on the evidence for acupuncture in dementia. One systematic review found that the evidence available for acupuncture does not demonstrate effectiveness in Alzheimer's disease (Lee 2009), although only three randomised controlled trials (RCTs) were located for this. By contrast, a review for dementia in general found 22 RCTs, which demonstrated a significant positive advantage for acupuncture over control groups (Gu 2008). Since most of the trials were for vascular dementia, it's notable that a Cochrane review one year earlier had found no suitable RCTs at all for this condition (Peng 2007)

There have been several randomised controlled trials published since these systematic reviews, all with promising results. All are for vascular dementia (not Alzheimers) and all are from China. All of them compared acupuncture to medication; two also used a combined acupuncture plus medication group. In five trials, acupuncture was significantly better than medication (Zhang 2011, Chen 2011, Wang 2010, Zhang 2008, Liu 2008b) and in three it was similar in effect (Zhao 2009, Chen 2009, Liu 2008a). Various different acupuncture treatment modalities were used: manual needling (Zhang 2011, Liu 2008a), electroacupuncture (Zhao 2009, Zhang 2008, Liu 2008b), moxibustion (Chen 2011, Wang 2010) and ear taping/pressing (Chen 2009). Most studies used recognised outcomes measures relevant to dementia and some also investigated possible biochemical mechanisms (see below).

Despite this, there is certainly a need for larger, better quality trials, preferably from a wider range of countries.

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 in dementia by:

- regulating neuropeptide substances (somatostatin and arginine vasopressin) relevant to learning and memory (Chen 2011; Wang 2010);
- reducing the levels of 8-OHdG (Shi 2012) and decreasing lipid peroxidation in the brain (Zhu 2010; Yang 2007), suggesting that acupuncture helps to prevent oxidative damage;

- activating certain cognitive-related regions in the brain(Wang 2012);
- decreasing the overproduction of nitric oxide and strengthening the ability to eliminate free radicals (He 2012);
- decreasing cholinergic neuron damage and reducing the abnormal activation and hyperplasia of astrocytes (Miao 2009);
- decreasing the number of activated glial cells so as to protect the neurons (Zhu 2009);
- lowering acetylcholinesterase activity (Yang 2007);
- suppressing vascular dementia-induced increase of interleukin-1beta and tumor necrosis factor-alpha levels in the hippocampus (Li 2007);
- improving glucose metabolism in the bilateral frontal lobes, bilateral thalamus, temporal lobe and lentiform nucleus (Chen 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).

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	
Lee MS et al. Acupuncture for Alzheimer's disease: a systematic review. <i>Int J Clin Pract.</i> 2009; 63(6): 874-9.	A systematic review that assessed the clinical evidence for or against acupuncture as a treatment for Alzheimer's disease. Three randomised controlled trials were included, 2 of which assessed the effectiveness of acupuncture on cognitive function compared with drug therapy. Their results suggested no significant effect in favour of acupuncture (weight mean difference [WMDs] -0.55; $p=0.15$). Two of the trials tested acupuncture for activities of daily living; 1 found favourable effects of drug therapy compared with acupuncture while the other did not. The meta-analysis of these data showed significant effects of drug therapy compared with acupuncture ($n=72$, WMD, -1.29; $p<0.001$). The reviewers concluded that, even though the number of studies is small, the existing evidence does not demonstrate the effectiveness of acupuncture for Alzheimer's disease.
Guo XX et al. Meta-analysis on acupuncture for treatment of dementia. [Article in Chinese] <i>Zhongguo Zhen Jiu.</i> 2008; 28(2): 140-4.	A meta-analysis that assessed the therapeutic effects of acupuncture on dementia. It included 22 randomised controlled trials, pooling data from 19 of them. The total odds ratio in favour of acupuncture was 3.72. The results showed that the curative effect of acupuncture was better than that of the control ($p<0.00001$). The reviewers concluded that acupuncture therapy is effective in dementia, but that more and better quality studies are needed to confirm this.
Peng WN et al. Acupuncture for vascular dementia. <i>Cochrane Database Syst Rev.</i> 2007 Apr 18;(2):CD004987.	A Cochrane systematic review that found more than 105 studies of acupuncture for treating vascular dementia. However, while benefit was reported in up to 70-91% of the treatment groups in the studies, none of them was of sufficient quality to be useable in the Cochrane review. According to the reviewers, in the absence of any suitable randomised placebo-controlled trials in this area, they were unable to perform a meta-analysis. They concluded that the effectiveness of acupuncture for vascular dementia is uncertain;

there are no RCTs and high quality trials are few.

Randomised controlled trials

Zhang R et al. A clinical research on treating vascular dementia with nourishing kidney and brain acupuncture. *International Journal of Clinical Acupuncture* 2011; 20(2): 65-8.

A randomised controlled trial that looked at the clinical efficacy of treating vascular dementia with acupuncture. Sixty patients were allocated to acupuncture or medication (almitrine). The overall clinical effective rate was 83.3% for acupuncture, which is significantly better than the control group. ($p < 0.05$) The researchers concluded that acupuncture has a significant effect in patients with vascular dementia, decreasing the patient's dementia and the degree of neurological impairment, and improving the quality of their lives significantly.

Chen H et al. Impacts of moxibustion on vascular dementia and neuropeptide substance content in cerebral spinal fluid. [Article in Chinese]. *Zhongguo Zhen Jiu*. 2011; 31(1): 19-22.

A randomised controlled trial that looked at the effects of moxibustion therapy compared with medication (piracetam) on the improvements of clinical symptom scale score and neuropeptides related to learning and memory in 87 patients vascular dementia. The total effective rate was greater with moxibustion (81.4%) than piracetam (63.6%; $p < 0.01$). The scores in Hasegawa's Dementia Scale (HDS), Mini Mental Status Examination (MMSE) and Activity of Daily Living Scale (ADLS) after treatment were all improved compared with those before treatment in both groups ($p < 0.05$, $p < 0.01$). The improvements in MMSE and ADLS scores were better with moxibustion that with piracetam (both $p < 0.05$). After treatment, somatostatin and arginine vasopressin content in cerebral spinal fluid increased remarkably as compared with those before treatment in both groups (all $p < 0.01$), and more so with moxibustion ($p < 0.05$, $P < 0.01$). The researchers concluded that moxibustion therapy is superior to piracetam in symptom scores or in the regulation of neuropeptide substances relevant to learning and memory.

Wang P et al. Effects of moxibustion at head-points on levels of somatostatin and arginine vasopressin from cerebrospinal fluid in patients with vascular dementia: a randomized controlled trial. [Article in Chinese]. *Zhong Xi Yi Jie He Xue Bao*. 2010; 8(7): 636-40.

A randomised controlled trial that compared the clinical efficacy of moxibustion with medication (piracetam) in 65 patients with vascular dementia, and that assessed its effects on memory-related neuropeptides. Total response rate was significantly higher in the moxibustion group than in the piracetam group ($p < 0.01$). There were significant differences in the HDS, MMSE and ADLS scores before and after treatment in both groups ($p < 0.05$, $p < 0.01$), and more so with moxibustion ($p < 0.05$, $p < 0.01$). The levels of the learning and memory-related neuropeptides from cerebrospinal fluid, somatostatin and arginine vasopressin after treatment were higher than those before treatment in both groups ($p < 0.01$), and more so with moxibustion ($p < 0.01$). The researchers concluded that moxibustion is effective in improving the clinical symptom scores and regulating the levels of neuropeptides associated with learning and memory in patients with vascular dementia.

Zhao L et al. Electroacupuncture on the head points for improving gnosis in patients with vascular dementia. *J Tradit Chin Med*. 2009; 29(1): 29-34.

A randomised controlled trial that investigated the clinical effects of electroacupuncture (EA) on head points for improving gnosis in 90 patients with vascular dementia. Patients were randomly divided into a drug group (nimodipine), an EA group and an EA plus drug group. Gnosis improved after treatment in all the 3 groups with no

significant difference between them. The researcher concluded that EA, drug treatment and a combination of both can all improve gnosis, reduce psychological stress, strengthen attention and shorten the time to recognition.

Chen Q et al. Controlled study of auricular point taping and pressing therapy for treatment of vascular dementia. [Article in Chinese] Zhongguo Zhen Jiu. 2009; 29(2): 95-7.

A randomised controlled trial that compared auricular point taping and pressing with medication (nimodipine) in 180 patients with vascular dementia. The scores of MMSE and ADL had improved in both groups after treatment (both $p < 0.01$), with no difference between them (both $p > 0.05$). In the auricular point taping and pressing group, 2 patients withdrew from the study because an allergic reaction to adhesive plasters caused severe itching. In the nimodipine group, one patient had mild dizziness and another had diarrhoea. The researchers concluded that auricular point taping and pressing, and nimodipine have a similar beneficial therapeutic effect on vascular dementia.

Zhang H et al. Clinically multi-central randomized controlled study on scalp electroacupuncture for treatment of vascular dementia. Zhongguo Zhen Jiu. 2008; 28(11): 783-7.

A randomised controlled trial that compared electroacupuncture (EA) with medication (nimodipine), and with EA plus nimodipine in 270 patients with vascular dementia. The total effective rate for cognition improvement was 86.6% in the EA plus nimodipine group, 82.0% in the EA alone group and 43.2% in the nimodipine alone group. Their total effective rates for improvement of ability of daily life were 59.8%, 65.4% and 32.1% respectively. Scores for mini-mental state scale, ability of daily life-rating scale and P300 examination indicated that there were significant differences in the EA plus nimodipine group and the EA alone group compared with the nimodipine alone group ($p < 0.01$). The researchers concluded that EA and EA plus nimodipine both have a better therapeutic effect in improvement of recognition function and the ability of life activity than nimodipine alone.

Liu YC et al. Therapeutic effects of scalp-acupuncture in patients with vascular dementia induced by cerebral infarction: a randomized controlled trial. [Article in Chinese] Zhongguo Zhong Xi Yi Jie He Za Zhi. 2008a; 28(8): 689-93.

A randomised controlled trial that compared acupuncture with medication in 108 patients with vascular dementia. The scores of MMSE, Blesse Dementia Scale (BDS), HDS and ADL significantly improved in both groups before and after ($p < 0.05$), with no difference between the groups. There was also no difference in the total effectiveness between the two groups ($p > 0.05$). The researchers concluded that acupuncture therapy could improve the clinical intelligence of patient with vascular dementia.

Liu ZB et al. Clinical investigation on electroacupuncture treatment of vascular dementia with "Xiusanzhen". Zhen Ci Yan Jiu. 2008b; 33(2): 131-4.

A randomised controlled trial that compared electroacupuncture (EA) with medication (almitrine) in 60 patients with vascular dementia. After the treatment, the total effective rates of acupuncture and medication groups were 80.0% and 73.3% respectively ($p < 0.05$). After treatment, the HDS and MMSE scores had increased and the Functional Activities Questionnaire (FAQ) scores had decreased in both groups ($p < 0.01$), with the difference in scores being better with EA ($p < 0.05$). The researchers concluded that acupuncture is an effective treatment for vascular dementia.

Other clinical studies

Shi GX et al. Influence of acupuncture

A human study that tested the effects of acupuncture in vascular

on cognitive function and markers of oxidative DNA damage in patients with vascular dementia. *J Tradit Chin Med* 2012; 32(2): 199-202.

dementia by assessing the cognitive function and a marker of oxidative DNA damage in 16 patients before and after treatment. The Folstein mini-mental state examination-revised and the dementia quality of life questionnaire scores were higher after acupuncture than before ($p<0.05$), while there were no obvious differences in the activities of daily living or scale for the differentiation of syndromes of vascular dementia scores ($p>0.05$). In addition, the urine concentration of 8-hydroxy-2'-deoxyguanosine (8-OHdG) – a marker of oxidative damage – was quantified with enzyme-linked immunosorbent assay. Levels significantly decreased after acupuncture ($p<0.05$). The researchers concluded that acupuncture reduces the levels of 8-OHdG and improves cognitive function and quality of life in patients with vascular, suggesting that acupuncture is beneficial at least in part by preventing oxidative damage.

Zhu H et al. Influence of acupuncture on isoprostane in patients with Alzheimer's disease. [Article in Chinese]. *Zhongguo Zhen Jiu*. 2010; 30(1): 18-21.

A study that explored the mechanism and clinical therapeutic effects of acupuncture in 20 patients with Alzheimer's disease. After treatment, the effective rate was 90.0%. The score of Alzheimer's Disease Assessment Scale-Cognitive Section was 35.70 before treatment and 31.45 after treatment ($p<0.001$). The concentrations of 8-IPF2alpha in cerebrospinal fluid, blood and urine were all significantly decreased after treatment (all $p<0.001$). The researchers concluded that acupuncture can improve the cognitive ability of patients with Alzheimer's disease and its possible mechanism may be relative to the decrease in lipid peroxidation in the brain.

Possible mechanisms of acupuncture

Wang Z et al. Effect of acupuncture in mild cognitive impairment and Alzheimer disease: a functional MRI study. *PLoS One*. 2012;7(8):e42730.

A study that aimed to clarify the mechanisms of acupuncture in treating mild cognitive impairment and Alzheimer disease by using functional MRI in 36 right-handed people (8 with mild cognitive impairment, 14 with Alzheimer's disease and 14 healthy older people). The researchers found that acupuncture at 2 acupoints – Tai chong (Liv3) and Hegu (LI4) – can activate certain cognitive-related regions in the brains of patients with mild cognitive impairment or with Alzheimer's disease.

He F. Influences of electro-acupuncture at related jing-well points in rats with vascular dementia. *J Tradit Chin Med*. 2012 Jun;32(2):238-42.

A study in rats that found electroacupuncture may improve memory impairment in rats with vascular dementia by decreasing the overproduction of nitric oxide and strengthening the ability of eliminating free radicals.

Goldman N et al. Adenosine A1 receptors mediate local anti-nociceptive effects of acupuncture. *Nat Neurosci* 2010; May 30.

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.

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 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.

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.

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.

Miao T et al. Effects of auricular acupuncture on the memory and the expression of ChAT and GFAP in model rats with Alzheimer's disease. [Article in Chinese] *Zhongguo Zhen Jiu*. 2009; 29(10): 827-32.

A study in rats that found auricular acupuncture can improve the learning and memory capability of rats with Alzheimer's disease, and that the mechanism might be related to decreasing cholinergic neuron damage and reducing the abnormal activation and hyperplasia of astrocytes.

Zhu SX, Sun GJ. Effects of electroacupuncture on learning and memory ability and glial cells of the hippocampus in the rat of Alzheimer disease. [Article in Chinese] *Zhongguo Zhen Jiu*. 2009; 29(2): 133-6.

A study in rats that found electroacupuncture treatment can decrease the number of activated glial cells so as to protect the neurons, improving the learning and memory ability in rats with Alzheimer's dementia.

Yang XB et al. Effect of warmth-promotion needling on cerebral SOD, MDA and AChE in vascular dementia

A study in rats that found needling with moxibustion helps to reduce lipid peroxidation injury and lowers acetylcholinesterase activity in rats with vascular dementia, which may contribute to its

rats. Zhen Ci Yan Jiu. 2007; 32(3): 170-3. effect in improving learning-memory ability.

Li W, Lai XS. Changes of interleukin-1beta and TNF-alpha contents in the hippocampus and the interventional effect of electroacupuncture in vascular dementia rats. Zhen Ci Yan Jiu. 2007; 32(1): 34-7. A study in rats with vascular dementia that found electroacupuncture can improve learning-memory abilities, and that this is closely associated with its effects in suppressing vascular dementia-induced increase of interleukin-1beta and tumor necrosis factor-alpha levels in the hippocampus.

Chen J et al. 18FDG PET cerebral function imaging in 10 vascular dementia patients receiving needling at Baihui(DU20), Shuigou(DU26) and Shenmen(HT7). Nan Fang Yi Ke Da Xue Xue Bao. 2006; 26(5): 610-2. A study in 10 patients with vascular dementia that found improved glucose metabolism in the bilateral frontal lobes, bilateral thalamus, temporal lobe and lentiform nucleus.
