Point specificity of acupuncture in the light of recent clinical and imaging studies

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Abstract

One fundamental question that is still not resolved is whether acupuncture needles must be inserted in specific points to have their greatest effects. In the majority of large RCTs recently conducted in Germany, acupuncture was significantly more effective than doing nothing but not than sham acupuncture. Only for one study of chronic knee pain was acupuncture superior to sham. Brain imaging with functional magnetic resonance (fMRI) and positron emission tomography (PET) may be helpful but is still in its early stages. Several studies have shown differences between the way the deep central areas of the brain respond to genuine acupuncture compared with sham. Acupuncture can clearly produce complex changes that are relevant to pain transmission and perception, though it is still uncertain how specific these are. Similar changes have been seen after the application of placebo cream and after hypnosis. A previous paper discussed the likely central role of the limbic system in acupuncture, evidenced by euphoria and out of body experiences. There may be a good deal of common ground between acupuncture, placebo treatments, hypnosis, and even manipulative treatments. This understanding could offer a way out of the sterile debate about whether acupuncture is merely a placebo: acupuncture could be one effective way of stimulating responses within these deep areas of the brain, though not the only way.

Keywords

Acupuncture, placebo response, brain imaging, limbic system.

Introduction

There is continuing uncertainty about the specificity of acupuncture needling sites. Adherents of the traditional system insist that individual points have identifiable and reproducible clinical effects, while some practitioners of modern (Western) medical acupuncture find that it makes little difference exactly where the needles are inserted. There are also variations in the depth of insertion, presence or absence of stimulation, the importance attached to obtaining de qi, and other matters.

Such variability suggests to some that acupuncture works largely or entirely as a complex placebo. Alternatively, it could be the case that the insertion of needles has a therapeutic effect in itself, more or less irrespective of the choice of sites or the depth of needling. The well known difficulty of devising adequate control procedures for acupuncture makes questions of this kind difficult to resolve.

The traditional point that has received most support from controlled trials is probably PC6 for nausea, but even this is not conclusive, and in any case PC6 is only one point out of several hundred in the traditional literature. Questions about point specificity in acupuncture thus remain open.

Although these issues have been recognised for a long time, they have come to the fore recently as a result of some well designed trials in Germany. The acupuncture practitioners who took part were trained in traditional acupuncture and presumably were persuaded of its validity, which makes the results all the more interesting. All four trials found that needling appeared to relieve symptoms effectively compared with doing nothing, but three found that it made no significant difference how or where the needles were inserted.

The availability of sophisticated brain imaging methods such as functional magnetic resonance (fMRI) and positron emission tomography (PET)
has prompted their use to study acupuncture. This has led to claims that acupuncture has demonstrable effects on the brain which provide evidence for the specificity of particular classic points. Although these studies are interesting, they are still in their infancy and it would be premature to build too much on them.

In what follows I discuss evidence from clinical and brain imaging studies and consider what it tells us about possible similarities between acupuncture and other treatment modalities, including placebo.

**Evidence from recent RCTs**

**Migraine**

This was a three-armed RCT involving 302 patients, 88% of whom were women. The trial compared the results for ‘real’ (i.e., classic) acupuncture, ‘sham’ acupuncture (superficial needling at non-acupuncture points), and waiting list (no treatment). The patients received 12 treatments over eight weeks. Diaries were used to assess the frequency of headaches. The main outcome measurement was headache differences four weeks before and 8-12 weeks after randomisation.

Response rates were 51% for patients having ‘real’ acupuncture, 53% for ‘sham’ acupuncture, and 15% for those in the waiting list group. The authors conclude that true acupuncture was no better than sham but both were better than no treatment. This could indicate a placebo response or an effect derived from needling anywhere in the soma (i.e., not specific to acupuncture points).

**Tension headache**

This trial was similar in design to the preceding one. Two hundred and seventy patients (74% women) in 28 centres in Germany participated; they had episodic or chronic tension-type headaches. As before, ‘real’ acupuncture was compared with ‘sham’ acupuncture. The number of days with headache decreased by 7.2 (SD 6.5) days in the real acupuncture group compared with 6.6 (SD 6.0) days in the sham acupuncture group and 1.3 (SD 3.7) days in the waiting list group. The proportion of responders (at least 50% reduction in days with headache) was 46% in the acupuncture group, 35% in the sham acupuncture group, and 4% in the waiting list group. The authors conclude that the acupuncture intervention investigated in this trial was more effective than no treatment, but not significantly more effective than sham acupuncture for the treatment of tension-type headache.

**Knee pain**

This has been addressed in two recent RCTs from Germany. In the first, 294 patients were studied. After eight weeks’ treatment, pain and joint function improved significantly more in those who received real acupuncture than in those who received either minimal or no acupuncture. The mean baseline-adjusted WOMAC index at week eight was 26.9 (SE 1.4) in the acupuncture group, 35.8 (1.9) in the minimal acupuncture group, and 49.6 (2.0) in the waiting list group. After 52 weeks the difference between the acupuncture and minimal acupuncture groups was no longer significant (P=0.08).

The findings in this trial disagree with those in the other trials discussed here as regards the difference between real and minimal acupuncture. This might be explained by the hypothesis of Lund and Lundeburg, who suggest that superficial acupuncture may be effective in disorders with a large affective component but less so in those, such as knee osteoarthritis, which have a bigger sensory component.

However, a second (and larger) knee osteoarthritis study did not show this difference. 1007 patients with at least six months’ pain took part. They received physiotherapy plus non-steroidal anti-inflammatory drugs, plus one of the following: 10 sessions of ‘real’ acupuncture, 10 sessions of ‘sham’ acupuncture, or 10 physician consultations. There was no blinding between acupuncture and conventional treatment. Response rates were 53.1% for real acupuncture, 51.0% for sham acupuncture, and 29.1% for conservative treatment. The authors’ conclusions were similar to those in the preceding two headache studies.

In summary, then, three out of four well designed studies found that while it is easy to show that insertion of needles has a therapeutic effect (although non-specific influences such as increased physician attention are difficult to discount), there is no demonstrable difference between real and sham acupuncture. Note that the ‘sham’ acupuncture was both superficial and at non-classic points, which introduces two independent kinds of variable; it is not clear how much, if at all, either may have contributed to the outcome.
Education, Practice and Debate

Recent brain imaging studies
Several studies have found that acupuncture appears to have effects on numerous brain areas, and these effects are often claimed to be specific, occurring only at 'real' and not 'control' acupuncture sites. For example, Hui et al report that needle stimulation at LI4 caused reduction of signal intensity in the nucleus accumbens, amygdala, hippocampus, parahippocampus, hypothalamus, ventral tegmental area, anterior cingulate gyrus, caudate, putamen, temporal lobe and insula in all of 11 subjects who experienced acupuncture sensation, together with increased signal intensity in the somatosensory cortex. Two subjects who experienced pain instead of acupuncture sensation showed increased instead of decreased signal intensity in the anterior cingulate. Superficial tactile stimulation at LI4 elicited signal increases in the somatosensory cortex as expected but no signal increases in the deep structures. The authors hypothesise that modulation of subcortical structures may be an important mechanism in the production of acupuncture effects.

Similarly, Wu et al found that stimulation at LI4 and ST36 resulted in increases in signal intensity in the hypothalamus and nucleus accumbens and decreases in the rostral part of the anterior cingulate cortex, amygdala formation, and hippocampal complex; control stimulations did not produce these effects. The authors conclude that acupuncture at these sites 'activates structures of descending antinoceptive pathway and deactivates multiple limbic areas subserving pain association.'

These studies are interesting but the effects they describe are probably not specific to acupuncture, because quite similar changes are reported to occur when patients are treated with a placebo cream. Wager et al found that placebo analgesia was related to decreased brain activity in thalamus, insula, and anterior cingulate cortex and to increased activity in prefrontal cortex during anticipation of pain. The similarity to the findings in the acupuncture studies is evident.

In a further investigation of the question, Wager reviewed possible mechanisms for placebo pain reduction and reported preliminary work which supports the hypothesis that 'placebo treatments work by facilitating shifts [of attention] away from the site of pain', although he cautions that further research is needed to test this more directly.

There are similarities here with what happens in acupuncture. Clinical experience suggests that patients receiving acupuncture have to expect to be treated, the insertion of needles for diagnostic reasons seldom seems to relieve pain. This suggests that patients must view the setting as a therapeutic one (although belief in the efficacy of treatment does not seem to be so important). One possible basis for acupuncture effects might thus be changes in the direction of patients’ attention.

The findings in hypnosis are also quite similar to those in acupuncture. For example, Rainville et al, using PET scanning, found that hypnosis altered the unpleasantness of noxious stimuli without changing their perceived intensity and these effects were linked with limbic system activity. Hypnotic suggestion to relieve pain reduced blood flow in the anterior cingulate but not in the somatosensory cortex. Hence, hypnosis can alter this activity in much the same way as acupuncture does. Very similar results are reported by Faymonville et al.

Even more remarkable is the finding that placebo analgesia can affect the spinal cord as well as the brain, once again emphasising the role of expectation in modulating central sensitisation. ‘Mechanical hyperalgesia’ was induced in subjects by heating the skin to 45 degrees centigrade for five minutes; the size of the affected area was reduced by a placebo. For an excellent discussion of brain imaging in relation to pain, see Jones et al.

In summary, there is evidence that acupuncture can produce complex brain changes in areas connected with pain transmission and pain perception, but there is uncertainty about how specific these effects are. Quite similar effects occur in response both to placebo and to hypnotic suggestion.

Discussion
I suggested several years ago that some acupuncture phenomena could be related to the limbic system. This hypothesis now seems to be receiving confirmation from the imaging studies alluded to above. The principal areas involved are the anterior cingulate, hippocampus, insula, amygdala, and nucleus accumbens, though many others may participate as well.

A possible explanation for the euphoria that is sometimes experienced during acupuncture, especially by strong reactors, is suggested by
experiments on normal volunteers using intravenous administration of procaine, which can modulate limbic system activity. Ketzer et al found this produced euphoria, related to reduced blood flow in the left amygdala. Visual and auditory hallucinations also occurred, and this is not the only intriguing report of strange phenomena caused by intravenous procaine. Servan-Schreiber et al., using PET, found that procaine-induced activation of anterior and paralimbic areas in normal volunteers ‘was associated with a range of emotional, somatic, and visceral experiences, often similar to those experienced during the aura of temporal lobe epilepsy’.

This is of interest in two ways. Firstly, patients receiving acupuncture occasionally have seizures and this might sometimes be due to limbic system effects rather than simply to cerebral anoxia. Secondly, some of the more bizarre responses to acupuncture that are occasionally encountered could arise from the limbic system, especially in patients with temporal lobe epilepsy (complex partial seizures). I know of one such case (personal communication). The patient, who had recently been diagnosed with temporal lobe epilepsy, had an out-of-body experience while acupuncture was actually being performed. Cases of this kind suggest that acupuncture can increase as well as decrease activity in the anterior limbic area, perhaps especially in the presence of brain pathology.

Blanke et al have reported a case in which an out-of-body experience occurred repeatedly in a patient with temporal lobe epilepsy when stimulation was applied to the right angular gyrus. They suggest that it was due to a failure to integrate complex somatosensory and vestibular information.

Limbic and paralimbic areas, especially the hippocampus, are involved in the processing of memory and appear to be essential for the formation of long term memory. Hui et al found marked reduction in hippocampal signals when subjects were receiving acupuncture, and changes of this kind might affect memory formation. I know of a case in which temporary memory loss during acupuncture reportedly occurred (personal communication). I have no further details about this but, if confirmed, it might suggest a hippocampal effect.

Some patients report that their pain, although still present, is less unpleasant after acupuncture than it was previously. The anterior cingulate appears to be involved in registering the unpleasantness of pain rather than perception of pain. Wu et al suggest that acupuncture works, at least in part, by reducing the unpleasantness of pain. This seems plausible, but in view of the similarity of the response to placebo and hypnosis the specificity of the effect remains doubtful.

The evidence available so far thus calls into question claims for the uniqueness of acupuncture effects in the central nervous system. A more plausible hypothesis is that there is a good deal of common ground between acupuncture and placebo treatments. Hypnosis, too, can have similar effects; and the common ground probably extends further than this: anecdotal evidence from some practitioners using manipulative treatments indicates that their patients report experiences which are very similar to those described by acupuncture patients. Hence many physical treatments may act on the same brain areas as acupuncture. The limbic system could thus be regarded as a final common path by which these treatments work.

If this idea is accepted it affords a possible way out of rather sterile debates about whether acupuncture is ‘merely a placebo’. Although the basis for the placebo response is not fully understood, brain imaging studies suggest that it may involve the same brain areas as does acupuncture. On this hypothesis, insertion of needles is an effective way of altering the reactivity of these central brain areas but not the only way. For similar reasons, location and method of needle insertion are likely to be less important than some suppose, and this may explain why it is difficult to demonstrate differences in effectiveness between ‘real’ and ‘sham’ acupuncture by means of RCTs.


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