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Review

Demystifying acupuncture

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Acupuncture refers to the insertion of fine needles into the body at specific points for a therapeutic effect. The term comes from the Latin words 'acus' (needle) and 'punctura' (to puncture). The technique has been practiced in the Far East for at least 3000 yrs but it is only in the last 30 yrs that interest has developed in the West underpinned by increasing scientific research. One of the main uses of acupuncture has been to treat musculoskeletal pain and this article will review the evidence base and outline the main theories of mechanisms of action.

Key words: Acupuncture, Complementary medicine, Systemic review, Pain, Management, Physiology.

Methods of acupuncture

The two main approaches to acupuncture practiced in the West are the *Traditional*—based on traditional Chinese theories of 'energy-balancing'—and the *Western Medical*—based on western concepts of anatomy and physiology. Traditional Chinese acupuncture defines good health as a balance between two opposing polarities (*yin* and *yang*). In health, *chi* (life force, also spelt 'qi') is said to flow freely through a system of channels (*meridians*), whilst in disease this flow is disrupted causing an imbalance between *yin* and *yang*. Needles inserted into specific points along *meridians* are said to redress imbalances in the flow of *chi* and hence treat disease [1]. This traditional Chinese explanation has no scientific basis.

In contrast, Western Medical acupuncture places emphasis on the concept of trigger points. In the 1930s, Kellgren found that injecting irritants into tender 'spots' in muscles could cause specific patterns of non-dermatomal referral of pain and tenderness (usually distally), which could be abolished by the injection of local anaesthetic into the 'spot' [2]. Simons *et al*. [3] coined the term 'trigger points' for these 'spots' and developed the idea that activated trigger points were responsible for regional *myofascial pain syndromes* [3]. They emphasized 'four cardinal features [of the syndrome]: a palpable nodular or band-like hardness in the muscle, a highly localized spot of extreme tenderness in the band, reproduction of the patient's distant pain complaint by digital pressure on that spot [referred pain], and relief of the pain by massage or injection of the tender spot'. The histology of a trigger point does not reveal any gross anatomical abnormalities [4] but there is evidence for a localized increase in neural activity; thus insertion of a needle electrode into a trigger point records spontaneous electrical discharge on EMG [5]. Trigger points can become activated by acute trauma, repetitive microtrauma and postural disorders [4]. Even after the inciting noxious stimulus is removed trigger points can remain active within taut muscle bands or muscle nodules ('knots') [4]. Trigger points can also be activated by emotional stress that can lead to muscles being held in a state of persistent tension [6] with associated increases in cortisol level and symphathetic tone [7]; in this context, acupuncture may be especially beneficial since needling increases the parasympathetic tone as demonstrated by a reduction in both salivary cortisol and in heart rate on tilt table testing [8].

The early work of the importance of trigger points in the aetiology of musculoskeletal pain received scant attention in mainstream medicine and indeed even now pain primarily of muscular origin is barely discussed in medical textbooks. This common source of pain, if overlooked, can lead to diagnostic confusion. As an illustration, many physicians will have encountered patients with radicular-sounding symptoms, who have normal neurology and subsequently a non-diagnostic MRI scan or EMG. Such cases commonly reflect a myofascial pain syndrome; in the upper limbs trigger points in the supraspinatus, infraspinatus, levator scapulae or scalene muscles can radiate pain and *paraesthesia* into the arm or fingers [9], whilst in the lower limbs trigger points in the erector spinae, gluteals or piriformis can radiate symptoms into the legs and mimic sciatica [10, 11]. There is >70% spatial correlation between trigger points and traditional acupuncture points [12, 13] suggesting that acupuncture may work, at least in part, by the same pathophysiological mechanisms as trigger point deactivation. Trigger points should be distinguished from the tender points found in fibromyalgia, which do not cause radiation of symptoms and respond poorly to treatment [14]. Unlike tender points, trigger points can be deactivated by numerous methods including physiotherapy, local anaesthetic injection or by acupuncture [15].

Western Medical acupuncture involves the insertion of dry needles into trigger points to treat myofascial pain syndromes. As a result of the aforementioned significant spatial correlation this system frequently uses local and distal points used in Traditional acupuncture. However, whilst the latter aims for the improvement of '*chi*', thus balancing energy (energy-balancing acupuncture), this is not a concept recognized in the Western Medical acupuncture.

Efficacy of acupuncture

For many years clinical research in acupuncture has been of poor methodological quality. Studies have suffered from investigator bias, poor design, inadequate randomization and blinding, and small patient numbers. Specific problems for acupuncture trials have included the diversity of types of acupuncture, individualized treatments, the use of traditional diagnostic criteria and finding a credible control ('*sham*') [16]. Control groups have included alternative treatments [transcutaneous electrical nerve stimulation (TENS), physiotherapy, medications] and sham acupuncture, where either needles are inserted into non-acupuncture points or non-penetrating sham needles are used. The first sham needle was developed in 1998 (the 'Streitberger' needle). The blunted tip telescopes back into the handle when tapped and the needle appears to be inserted but does not actually penetrate the

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skin [17]. Although this was heralded as a major advance high-quality clinical studies still remain limited.

A further issue is whether the randomized controlled trial (RCT) design is appropriate for acupuncture studies. Paterson and Dieppe [18] believe that acupuncture is not just about needling but that non-specific elements such as traditional Chinese diagnostic processes and explanations that would generally be categorized as placebo in RCTs may be an integral component of actual treatment [18]. The authors conclude that using placebo-controlled trial designs for acupuncture may lead to false-negative results.

The majority of randomized clinical studies in musculoskeletal pain have found acupuncture to be superior to no treatment whilst those that have compared acupuncture with sham tend to show statistically significant benefits in short-term analyses (<3 months). The evidence for musculoskeletal acupuncture is summarized subsequently. Most of the clinical studies within the cited reviews have been meridian based with use of traditional acupuncture points located locally and distally along the meridians.

Neck pain

A Cochrane review in 2006 [19] examined 10 RCTs of patients with chronic (>90 days) mechanical neck pain treated with acupuncture. There were a total of 661 patients and 4 of the 10 studies were considered high quality. Effect size was reported as standardized mean differences (SMD) and interpreted as small (−0.20), medium (−0.50) and large (−0.80) [20]. There was evidence for moderate pain relief immediately after treatment and in the subsequent 3 months compared with sham acupuncture [pooled SMD −0.37, 95% confidence interval (CI) −0.61, −0.12]. One high-quality study involving patients with chronic neck pain and radicular symptoms [21] reported, on average, better pain relief with acupuncture in the short-term than those who were on a waiting list with a mean 40% reduction of pain scores.

Shoulder pain

A Cochrane review in 2005 [22] included eight RCTs in a meta-analysis of patients with non-inflammatory shoulder pain of >3 weeks' duration. Most patients had either adhesive capsulitis or rotator cuff disease. Acupuncture was compared with either placebo (three studies) or other interventions (five trials) including steroid injection and physiotherapy. There was little evidence to either confirm or reject acupuncture as a useful therapy due to small sample sizes (median sample size 44) and methodological diversity.

Elbow pain

In 2002 Cochrane reviewed the efficacy of acupuncture for lateral epicondylitis [23]. The numbers were small and methodology varied and no definite conclusions could be reached. Since the Cochrane study there have been four further RCTs and these have been included in a more recent review of six RCTs by Trinh *et al.* [24]. These studies were of high quality with four trials randomized against sham acupuncture and two against ultrasound therapy. All six studies showed positive results for acupuncture with the reviewers concluding that 'there is strong evidence suggesting that acupuncture is effective in short-term pain relief for lateral epicondyle pain'. However, there were limitations that included small samples in studies, varying treatment protocols and non-uniformity of outcome measures with 'short-term pain relief' definitions ranging from immediate to 3 months. More trials are needed but current evidence suggests that acupuncture can be a useful treatment in this condition.

Low back pain

In 2005 Cochrane reviewed 35 RCTs on adults with mechanical low back pain [25]. A total of 1718 patients had chronic pain (>12 weeks duration). Acupuncture led to improvement of subjective pain scores by 32% compared with 6% with no treatment and 23% with sham acupuncture in outcome measures of pain up to the 3-month time point. The authors concluded that acupuncture has a positive effect for pain relief compared with no treatment or sham in the short-term. Acupuncture was not more effective than conventional therapies (physiotherapy, pain medication or back care education) but was a useful addition to these therapies for pain and functional outcomes in short-term measurements (3 months). In the same year, a meta-analysis that included 22 RCTs was published by Manheimer *et al.* [26]. The authors found that for short-term (<6 weeks) pain relief of chronic back pain acupuncture was significantly more effective than sham (SMD −0.54, 95% CI −0.35, −0.73). Trials included in these meta-analyses were heterogeneous with respect to population, acupuncture technique, control groups and outcome measures. Furthermore, the methodological quality of the studies was generally poor. In the largest clinical acupuncture studies to date—the German Acupuncture Trials (GERAC) trials—Traditional Chinese acupuncture was tested against sham acupuncture (needling into non-acupoints) and against standard treatments (drugs, physical therapy, exercise). In the GERAC back pain study [27], 1162 patients with chronic low back pain were randomized. The studies found the effectiveness of acupuncture to be almost twice that of standard therapy with 6-month response rates being 47.6, 44.2 and 27.4% for true acupuncture, sham and standard groups, respectively.

Knee pain

White *et al.* [28], in 2007, included 13 RCTs (2362 patients) in a review of acupuncture for patients with chronic knee pain. Most had a radiological diagnosis of OA and most patients underwent at least weekly needling for at least six treatments with either manual or electro-acupuncture, where an electric current is passed between the needles. Eight trials had sufficient homogeneity of population, technique and outcome measures to be combined into a meta-analysis. Acupuncture was found to be superior for both pain reduction and functional improvement in both the short-term (<25 weeks) and long-term (up to 52 weeks) compared with sham acupuncture. The effect on pain was moderate (pooled SMD −0.4, 95% CI −0.1, −0.6). Also in 2007, Manheimer *et al.* [29] published a meta-analysis of nine RCTs evaluating the effects of acupuncture for knee OA. This review reported statistically and clinically significant benefits of acupuncture compared with patients in usual care control groups that were maintained for up to 6 months. However, although there were also reported statistically significant benefits of acupuncture compared with sham groups, both for pain and function, the authors concluded that this statistical improvement did not translate into a clinically significant benefit either in the short- or the long-term (up to 6 months). The authors were unable to assess the credibility of the sham treatments used. The GERAC knee trial [30] enrolled 1007 patients with chronic pain due to knee OA and gave them all up to six physiotherapy sessions and analgesics before randomizing them to true acupuncture, sham or conventional treatment. As with the GERAC back pain trial acupuncture was twice as effective as standard treatment at 26 weeks with no statistical differences between the true and sham groups. The most recent RCT of knee acupuncture compared the addition of either true or sham acupuncture (six treatments over 3 weeks) to a course of six sessions of physiotherapy-led advice and exercise for patients with clinically diagnosed knee OA. The study found that acupuncture did not provide for any additional improvement in pain scores at 6 months when given as an adjunct to the physiotherapy programme [31]. It has been hypothesized that since both acupuncture and physiotherapy cause peripheral sensory stimulation they may work via similar pain inhibitory pathways [32], and hence intensive physiotherapy in this study may have maximized

the therapeutic effect and masked any potential benefit from acupuncture [33].

Fibromyalgia

Five RCTs (316 patients) were included in a recent review of acupuncture treatment for patients with fibromyalgia [34]. The trials were of reasonable quality but did not completely control for placebo effect. Acupuncture was provided at least weekly with the duration varying between 6 and 40 sessions. Due to methodological heterogeneity a meta-analysis could not be performed. Three studies, all of which used electroacupuncture, showed small, short-term beneficial effects on pain. The other two studies showed no significant effect. No firm conclusions could be drawn but the authors concluded that 'acupuncture cannot be recommended for fibromyalgia' based on current evidence.

Acupuncture mechanisms

Any proposed mechanism of acupuncture must address the clinical observations noted by practitioners (Table 1) [35]. Work has highlighted the effects of acupuncture on the immuno-inflammatory response and the hypothalamic–pituitary axis [36, 37] but this review will concentrate on the peripheral and central neural mechanisms that might explain the clinical observations. Neural mechanisms that have been proposed as an explanation for short-term analgesic effects of acupuncture include spinal gating and descending inhibitory pathways.

Spinal gating

Pain is mediated by two types of peripheral fibres: myelinated Aδ-fibres responsible for sharp, well-localized pain ('fast' pain) and smaller unmyelinated C-fibres responsible for prolonged and ill-defined pain ('slow' pain). Melzack and Wall's [38] gate theory proposes that the substantia gelatinosa (SG) layer of the superficial dorsal horn of the spinal cord can be 'opened' by these nociceptive fibres and 'closed' by larger fibres (Aβ) or by descending control.

Electroacupuncture stimulates the large Aβ-fibres [39] and is presumed to activate this gating mechanism. Manual acupuncture stimulates Aδ-fibres [40, 41] that synapse with inhibitory interneurons within the dorsal horn. This can inhibit central pain transmission through enkephalin-dependent mechanisms [42, 43].

For inhibition to occur at the spinal level the stimulus is applied to the same spinal segment as the pain source (segmental acupuncture) though not necessarily directly into the trigger point. Segmental acupuncture is opioid-dependent as evidenced by naloxone blocking or reversing any analgesic response [44]. Pain relief by local anaesthetic injection into trigger points is also reversed by naloxone suggesting that similar neural pathways are involved [45]. Spinal inhibition, however, only occurs during needle stimulation and thus it may explain immediate pain relief but cannot explain any delayed or prolonged analgesic effect from therapeutic acupuncture.

Descending inhibitory pathways

Over the last few decades much has been written on the importance of descending inhibitory pathways for acupuncture analgesia involving opioid-, serotonin- and noradrenergic-systems [46].

Peripheral stimulation by a noxious stimulus, such as pinprick, results in impulses ascending in the spinothalamic pathway to the thalamus. At the midbrain a collateral pathway projects to the periaqueductal grey area (PAG). Electrical stimulation of the PAG leads to analgesia that is reversed by naloxone [47]. Neurones from the PAG preoject to the nucleus raphe magnus of the medulla and from there serotonergic fibres descend to the stalked cells of the dorsal horn where release of enkephalin inhibits SG cells [41, 42] thereby blocking the centripetal transmission of pain from C-fibres. By peripheral stimulation acupuncture can activate this loop leading to descending inhibition. Thus in animal experiments, methysergide, a serotonin antagonist impairs the analgesic effects of acupuncture [48], whilst pargyline, which blocks serotonin degradation, potentiates the analgesia [46]. Simultaneous inhibition of opioid and serotonin leads to a dramatic reduction of acupuncture analgesia [49]. A number of other descending inhibitory systems may be involved including a noradrenergic pathway as demonstrated by Takeshige *et al*. [50] who showed antagonism of acupuncture analgesia with phentolamine administration. A further opioid-mediated pathway, diffuse noxious inhibitory control (DNIC) was described by Le Bars *et al*. [51]. DNIC is the phenomenon where the pain-transmitting spinal dorsal horn neurons are strongly inhibited when a nociceptive stimulus is applied to any part of the body, distinct from their excitatory receptive fields. DNIC works via opioid-mediated descending pathways from the subnucleus reticularis dorsalis of the caudal medulla; these fibres project down to all spinal levels to have an inhibitory effect following Aδ-fibre stimulation [52]. DNIC has been suggested as the mechanism of pain relief when acupuncture needles are inserted at sites distant from the pain source (extrasegmental acupuncture) [53].

The involvement of the above mechanisms in acupuncture is supported by animal experiments. However, the inhibitory effects from these mechanisms are only short-lived [54]. Animal experimentation can thus explain the short-term effects of acupuncture analgesia generally seen in electroacupuncture but fail to explain the more long-term, delayed and prolonged analgesia cited with therapeutic acupuncture. Hence, most animal studies cannot be easily extrapolated to the usual clinical setting. A more probable hypothesis to explain any prolonged effects of acupuncture is neuroplasticity.

Neuroplasticity

How could therapeutic acupuncture change the functional output of the pain neuromatrix to cause longer-lasting effects? It is now accepted that the central nervous system is not, as originally believed, hard-wired with fixed neuronal circuits but instead can adapt its structure and function according to changes in inputs (*neuroplasticity*). Behaviour is influenced according to the underlying neural patterns that in turn are dependent upon neuron–neuron connections.

Neuronal reorganization can occur with or without structural change both centrally and peripherally. These mechanisms include pre- and post-synaptic alterations in membrane potential and changes in post-synaptic receptor density. These mechanisms do not alter the basic structure of the neuron—no new synapses or

Table 1. The clinical observations seen in therapeutic acupuncture

(1)	Few patients report immediate pain relief once the needles are inserted.
(2)	A more usual effect is for a response to be delayed for a few hours or days.
(3)	Patients who respond generally have greater and more prolonged pain relief with each subsequent treatment.
(4)	The maximum response is usually achieved after 3–6 treatment sessions.
(5)	Needle insertion can cause various sensations such as heaviness, tingling, warmth and relaxation.
(6)	Not all acupuncture points are trigger points and not all acupuncture points are tender.
(7)	Sometimes needling of a trigger point must be specific for an effect but at other times the effective treatment area is quite variable and large; at times needling distant from the area of pain can give response.

changes in axon or dendrite structure are needed. Alternatively structural synaptic changes *can* occur as a result of new axonal boutons (pre-synaptically) or dendritic spines (post-synaptically) and depend upon protein synthesis. Whole axonal or dendritic growth can occur to develop completely new synapses and result in 'rewiring'. Equally, synapses may be lost through the destruction of boutons or dendritic spines [55]. Finally, neurogenesis from stem cells plays an important role to place new neurons within existing circuits. Such changes can lead to long-lasting changes in synaptic efficiency, either long-term potentiation (LTP) or long-term depression (LTD) of synaptic strength.

Evidence that such mechanisms are important in the therapeutic effect of acupuncture is emerging. Napadow *et al*. [56] demonstrated that acupuncture's beneficial effects correlate with a reorganization centrally of the somatosensory cortex comparing baseline and 5-week functional MRI scans when digits 2, 3 and 5 are stimulated. No such changes were seen in a healthy control group.

Peripherally, low-frequency stimulation of Aδ-fibres *in vitro* has been shown to cause LTD of post-synaptic potentials within the substantia gelatinosa [57]. The NMDA (*N*-methyl-D-aspartic acid) receptor appears to be crucial in this process since application of an NMDA receptor antagonist abolishes spinal LTD [58]. The density of these receptors on the post-synaptic membrane can be altered by afferent stimulation and this effect occurs gradually over hours or days [59]. The understanding of the molecular mechanisms of neuroplasticity is incomplete but further studies may lead to a deeper understanding of how experiences such as acupuncture could cause long-term effects on pain behaviour.

Is acupuncture a placebo?

The perception of the sensory and affective components of pain involves the activation of the spinal cord, thalamus, primary and secondary somatosensory cortices (S1 and S2), insula, anterior cingulate and pre-frontal cortex. Depending upon experimental protocols, there may also be activation of the amygdala, hippocampus, posterior parietal lobe, basal ganglia and brainstem [60].

One of the critical questions posed of acupuncture is whether the therapeutic effects recorded are purely placebo and it is difficult to tease out differences in studies. In the GERAC studies for back and knee pain [26, 29] each involving more than 1000 patients, acupuncture was found to be almost twice as effective as standard therapy over 6 months. These studies clearly showed clinical effects of needling and on this basis acupuncture for chronic back pain and knee OA is now paid for in Germany by the national insurance scheme. However, there were no differences between Traditional Chinese and the sham acupuncture given to non-acupoints suggesting that the benefits may have been a placebo effect. Experimental studies have shown that placebo analgesia has a neurochemical basis with activation of opioid-dependent pathways involving both cortical and subcortical cerebral networks [61, 62], and animal models indicate that acupuncture activates similar pathways using opioidergic and monoaminergic neurotransmitters [44, 63]. Cho *et al*. [64] showed reduced functional MRI activation in the thalamus, anterior cingulate and pre-motor cortex to pain responses when patients had received acupuncture at either real or sham acupoints. These observations suggest that acupuncture may work as a complex placebo.

Others have argued that there is evidence that in addition to placebo analgesia, acupuncture does have a more specific effect. There are alternative explanations for the results seen in the GERAC trials. Skin-penetrating needles were used as sham in these studies and research has suggested that this is unlikely to be a physiologically inert control [65]. Indeed the authors acknowledge that their sham is 'probably a real minimal acupuncture' [66]. The GERAC trials have brought to debate the importance of selecting specific points for treatment. A number of practitioners have argued that it is the needle insertion itself that is therapeutic and that the site of insertion or degree of stimulation is less important [67]. If correct, sham needling to non-acupoints would not be a credible control in trials [68]. Others, however, have stressed the importance of point specificity, particularly in the treatment of nausea [69], but also in optimizing acupuncture's effects on musculoskeletal pain with demonstrations of elevation of the pressure pain thresholds following specific point treatment when compared with acupuncture at non-specific and non-manipulated sites [70]. The question remains unanswered but a general physiological effect of needling may be the reason why significant differences between sham and specific needling are not detected. Thus therapeutic acupuncture may be viewed as needling *per se* whether at 'acupuncture points' or at 'sham points' (defined as non-acupoints according to Traditional Chinese Medicine) since both appear to show significant clinical effects over standard treatments as demonstrated in the GERAC trials.

Further observations may suggest that acupuncture is more than a placebo. The effects of therapeutic acupuncture are not immediate and are frequently cumulative. In contrast, placebo effects are generally immediate and short-lived since they are dependent on patient expectation [71]. Furthermore, therapeutic acupuncture is associated with sensory activation (pins and needles, numbness) suggesting an active contribution to the somatotopic cortex, through which the pain neuromatrix is distributed. There is also evidence from neuroimaging studies using functional MRI or PET scanning of acupuncture-specific responses [72]. Thus, Pariente *et al*. [73] using PET found that true acupuncture, unlike sham, activated the ipsilateral insula. However, such functional studies have generally involved small patient numbers in an experimental scenario. Whether the findings can be generalized to the clinical setting is unclear and more work is needed. What is clear is that the pain neuromatrix is responsive to placebo and acupuncture with many overlapping areas [74].

Conclusion

Acupuncture research has been fraught with difficulties but evidence is emerging that, at least in short-term analyses, acupuncture can be a useful and relatively safe treatment for non-inflammatory musculoskeletal pain. In recent meta-analyses, acupuncture appears to have superiority over control arms. The most likely explanation for the mechanism of therapeutic acupuncture is the phenomenon of neuroplasticity. Acupuncture is likely to have a placebo effect but whether it has a more specific physiological effect remains unclear. Early work indicates that there are differences between the neural effects of expectation and acupuncture's therapeutic analgesia in functional studies in experimental settings. More work needs to be performed to explore these differences and this could lead to novel treatments to maximize the therapeutic benefits of acupuncture.

Rheumatology key messages

- Current evidence suggests that acupuncture is a useful treatment for non-inflammatory pain, although long-term data (>6 months) is lacking.
- Acupuncture has effects on the central nervous system, which may explain the clinical observations.

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