

# The role of acupuncture in pain management

Joseph F. Audette, MA, MD<sup>a,b,\*</sup>,  
Angela H. Ryan, MD<sup>a,b</sup>

<sup>a</sup>*Department of Physical Medicine and Rehabilitation, Harvard Medical School,  
Boston, MA, USA*

<sup>b</sup>*Spaulding Rehabilitation Hospital, 125 Nashua Street, Boston, MA 02114, USA*

Acupuncture has been used as a therapeutic modality for more than 3000 years, but it is only since the 1970s that a greater understanding of the underlying mechanisms of acupuncture analgesia (AA) has developed. This growth in understanding of AA has paralleled the scientific advances made in uncovering the physiology of pain perception. Similar to many ancient healing traditions, acupuncture has accumulated a wealth of anecdotal experiences documenting its clinical effectiveness for a variety of problems. Although acupuncture has survived the test of time, medicine today demands more, and ultimately acupuncture must withstand the scrutiny of science if it is to become a mainstay in the treatment of pain. Given the explosion of interest within the scientific and clinical medical community in acupuncture, it is fortunate that a substantial body of evidence to support the efficacy of acupuncture exists, in contrast to many other complementary and alternative medicine (CAM) therapies. This article outlines understanding to date of the underlying physiologic mechanisms of AA, then reviews current use of acupuncture in pain management for some common musculoskeletal conditions seen in clinical practice.

## Philosophy of acupuncture

Employed as one of many therapeutic interventions in Traditional Chinese Medicine, acupuncture traditionally was believed to work by maintaining and balancing the flow of *Qi* in the human body. *Qi* is a concept that is difficult to translate into English, but it commonly is equated with “vital energy” and has been subsumed under the various Western traditions

---

\* Corresponding author.

E-mail address: [jaudette@partners.org](mailto:jaudette@partners.org) (J.F. Audette).

of vitalism. The concept of Qi is much more complex and broad reaching, however, and interconnects living and inanimate objects in nature and the universe. Qi is essentially an energetic concept that is postulated by Chinese philosophy as a tangible force that allows energy transfer, movement, growth, and development to occur. To maintain physical and mental health, the flow of Qi must stay fluid and in balance macroscopically, as individuals relate to their environment, and microscopically, as organ functions interact. A blockage in the flow of Qi can cause an imbalance and eventually manifest as disease.

According to Traditional Chinese Medicine, individuals can influence this balance of Qi internally, by analyzing the flow of Qi along defined pathways on the surface of the body in a set of channels called *meridians* (Fig. 1). The meridians all are connected to each other and to all the internal organs in complex patterns. Treatment involves first correctly identifying the internal and external imbalances, then, by inserting needles into appropriate points along the meridians, helping to realign Qi flow in the body to restore internal homeostasis [1,2].

**Pain and analgesia**

From a modern scientific perspective, the Chinese notion of Qi and meridians has not been documented with current technologies. The basic premise of acupuncture, in simplified terms, is that stimulation at one site on the body has an effect on another, more distant site. Perhaps at a more profound level, a second premise of acupuncture theory is that internal pathology can be diagnosed and treated with surface evaluation and

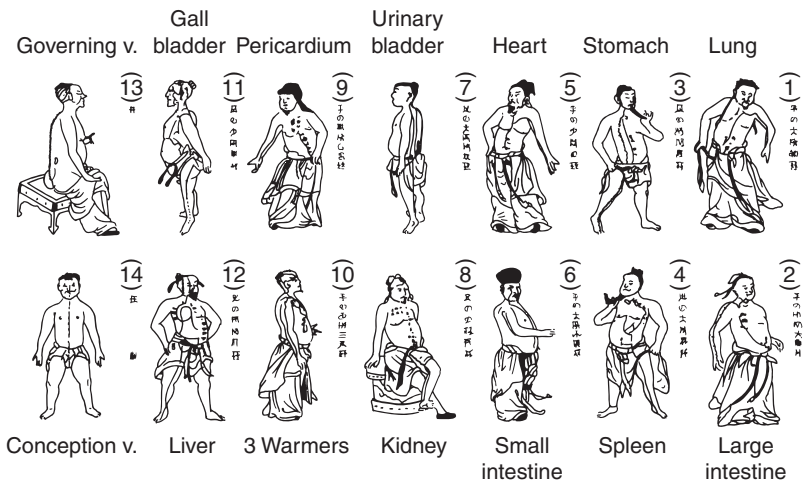


Fig. 1. Acupuncture meridians.

stimulation by taking advantage of somatovisceral and viscerosomatic reflexes. The substantiation of these hypotheses has been made more plausible with the growth in understanding of the neuroanatomy of pain processing (discussed subsequently). First, the physiology of pain as it is currently understood is outlined. Second, the evidence of how acupuncture alters the transmission and perception of pain is presented. Finally, the clinical evidence for the role of acupuncture in treating various pain syndromes is reviewed.

## **Pain physiology**

The physiology of pain perception and modulation is a sophisticated, multilayered system that is activated with injury under normal circumstances. This activation leads to a complex series of events that includes signal processing along neural pathways, immunologic and hormonal releases, and psychobehavioral responses. The current thinking underlying pain perception and inhibition accepts a dynamic, malleable, and complex set of interacting neurons, with gene regulation and expression producing a variety of neuropeptides and cytokines at the peripheral nervous system and central nervous system (CNS) level. The recognition of the plasticity of the nervous system has revolutionized the understanding of pain, especially chronic pain. After reviewing the neural pathways involved with pain modulation, the authors explain how acupuncture is believed to influence each of these domains.

### *Peripheral nervous system*

The neuroanatomy of nociception can be organized into three distinct but connected domains: the peripheral sensory apparatus, the spinal cord, and the brain. Starting in the periphery, small-fiber sensory axons that respond to various types of noxious input are called *nociceptors*. There are two main nerve types that carry pain and temperature information—the small, unmyelinated C fibers and the larger, thinly myelinated A $\delta$  fibers. In the skin, the C fibers, which conduct more slowly than the A $\delta$  fibers and are considered high-threshold nociceptors, carry more diffuse and dull pain information and require higher levels of stimulation and tissue damage to activate. The A $\delta$  fibers carry the sensation of sharp pain and are considered low-threshold nociceptors, providing more discriminative information. Similar sensory afferents are found in muscle; however, in muscle, both fiber types convey a dull aching sensation when activated, in contrast to skin nociceptors (Fig. 2). In addition to nociceptors responding to mechanical pain and temperature input, the release of chemical substances in tissues, such as histamine, protons, bradykinin, vasoactive polypeptide, and a whole array of others, can lead to nociceptor activation.

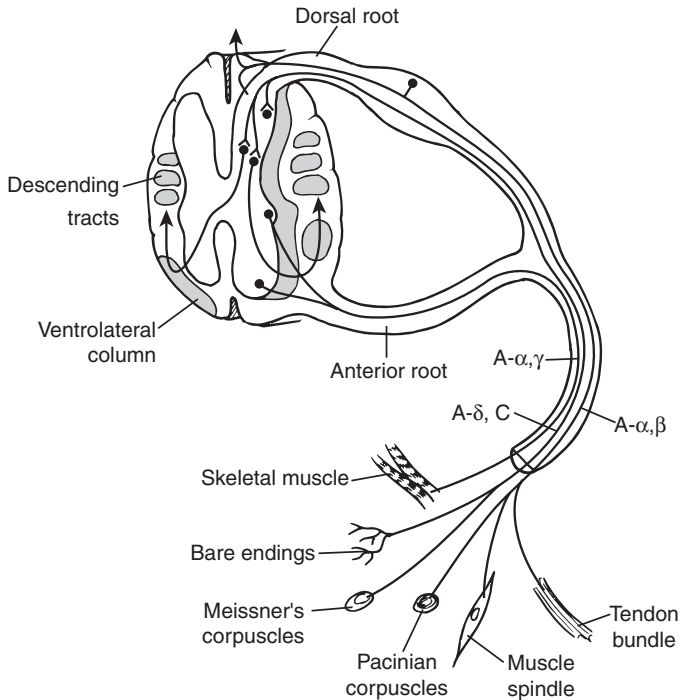


Fig. 2. Afferent sensory fibers enter the spinal cord via the dorsal root ganglion. Small, thinly myelinated and unmyelinated fibers (A $\delta$  and C) enter the dorsal horn and distribute in the lamina as indicated.

### *Spinal cord*

As with all afferent information, the sensory nerves from the skin enter the dorsal side of the spinal cord. The cell bodies of these sensory nerves are in the dorsal root ganglion. When in the spinal cord, the fibers synapse in laminae I through IV of the dorsal horn gray matter, with laminae I and II receiving the bulk of the nociceptive input from the skin. Before entering the dorsal horn, the primary sensory afferents branch and commonly ascend and descend multiple segmental levels before ending in a synapse with interneurons and second-order neurons. Most of the second-order neurons cross the midline and travel to the brain on the contralateral side from the site of nociception. Interneurons play a role in pain inhibition. The main pathways involved are the spinothalamic and the spinoreticular tracts. Together, these tracts make up the anterolateral system of the CNS [3].

### *Brain*

In the brain, multiple areas have been implicated as having some role in pain perception and regulation. Spinal cord pathways synapse directly in the

brainstem reticular formation, the amygdala, the hypothalamus, and the thalamus. At a higher level, the somatosensory cortex and higher cognitive brain regions also are activated, although not directly [4]. These higher levels contribute to the affective and emotional aspects of pain sensation. Research has shown that stimulation of many nociceptors in the periphery are not transmitted uniformly to the somatosensory cortex, but are transmitted to other areas of the brain, such as the frontal cortex, subcortical areas involved in the limbic system, and the hypothalamus [5].

### *Muscle pain physiology*

The nociceptive information carried from muscles takes a slightly different route than that carried from the skin. Outlining the different pathways is important not only in understanding the experience of pain, but also in understanding the possible neural mechanisms of acupuncture. Acupuncture stimulation typically involves needle penetration to the muscle and deeper connective tissue structures than the skin level. Similar to nociceptive information from the skin, low-threshold and high-threshold small fibers, named *group III* and *IV fibers*, travel to the dorsal horn of the spinal tract and correspond to cutaneous A $\delta$  and C fibers, respectively. These fibers synapse in the same lamina as cutaneous information, but have a higher representation in laminae IV and V. In laminae IV and V, wide dynamic range (WDR) second-order neurons reside. In contrast to second-order neurons in laminae I and II, which have an on-off response to sensory input, WDR neurons have a graded response to sensory input. To illustrate, normal stretch of a muscle stimulates low-frequency output of the WDR neurons, which should not be perceived as painful, whereas high-frequency input into the dorsal horn, such as after pathologic stretch and injury of a muscle, causes high-frequency output and pain. Under pathologic conditions, wind-up can occur in the second-order WDR neurons found in laminae IV and V, and low-frequency input can lead to high-frequency output. This heightened firing pattern of neurons in the CNS is believed to be one of the factors involved with chronic pain [6]. Another unique feature of WDR second-order neurons is that there is convergence of sensory information from the afferents of skin, muscle, viscera, tendons, and joints [7]. This convergence of sensory information opens the door to understanding how sensory stimulation of muscles with acupuncture can influence other visceral and somatic structures.

### *Chronic pain*

Neuroplasticity of the peripheral nervous system and CNS lies behind much of the current research and theory of chronic pain. Changes in intracellular signal transduction, gene expression, receptor and ion channel density, and depolarization thresholds contribute to a peripheral sensitization

and central wind-up phenomenon in the pain pathway. Sensitization in the periphery can occur directly at the small-fiber, nociceptor terminals by repeated high-frequency stimulation or by the prolonged presence of signaling molecules that signify “damage” or “inflammation.” These signaling molecules include substance P, serotonin, bradykinin, epinephrine, adenosine, and nerve growth factor, among others [8].

The changes in the dorsal horn of the spinal cord in response to persistent nociceptive input invoke the wind-up phenomenon, as mentioned earlier. Adopting the theory of long-term potentiation in the hippocampus as the neuroplastic changes responsible for the learning and retention of new information to form memories, a similar theory is hypothesized in the spinal cord for the “learning” of chronic pain. Long-term potentiation represents a long-lasting change in neuronal synapses as a result of high-frequency input. In the context of pain, nociceptive input from a prolonged noxious stimulus may lead to neuroplastic changes in the spinal cord, which result in a “learned” perception of pain, even when the noxious input is no longer present. As discussed later, acupuncture may have a role in reversing some of these neuroplastic changes.

### *Pain inhibition*

At the peripheral and spinal cord level, the role of pain inhibition originally was described via the gate control theory. Although the gate control theory of pain as introduced by Melzack and Wall [9] in 1965 does not fully explain pain inhibition, some of the segmental analgesic effects of AA do invoke this system. It is a useful and applicable theory, especially when it comes to understanding some of the theories of AA [10]. According to the gate control theory, large, myelinated A $\beta$  sensory afferents synapse on inhibitory interneurons in the dorsal horn, which when activated can inhibit the activation of second-order neurons that receive input from the smaller nociceptor fibers (Fig. 3).

Since the time of Melzack and Wall, theories of pain perception and inhibition have focused more on a biochemical level involving gene regulation, receptor expression, and depolarization thresholds. On the peripheral level, central pathologic changes and peripheral injury can lead to sensitization of the nociceptor terminal. Small-fiber, unmyelinated afferents have been found to have retrograde, neurosecretory properties similar to sympathetic fibers. Under pathologic conditions, substance P, a neuropeptide that normally acts centrally, can be secreted peripherally at the nociceptor terminal. This peripheral secretion of substance P can lead to a cascade of events, including the degranulation of local mast cells, which can cause a sensitizing chemical soup with molecules such as serotonin, bradykinin, epinephrine, adenosine, and nerve growth factor (Fig. 4). This process of peripheral sensitization has the consequence of lowering the threshold by which the peripheral nociceptor fires in response to stimulation

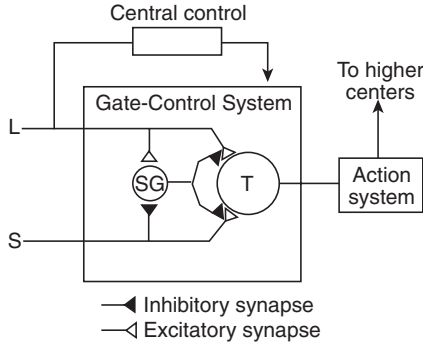


Fig. 3. Gate control theory. (Modified from Mense S, Simons DG. Central pain and centrally modified pain. In: Muscle pain: understanding its nature, diagnosis and treatment. Philadelphia: Lippincott Williams & Wilkins; 2001. p. 176; with permission.)

and can lead to the clinical phenomenon of hyperalgesia. In addition, it has been found in animal models that acupuncture points have elevated levels of substance P, suggesting a mechanism as to why needle stimulation at these points may be activating sensitized peripheral nociceptors [11].

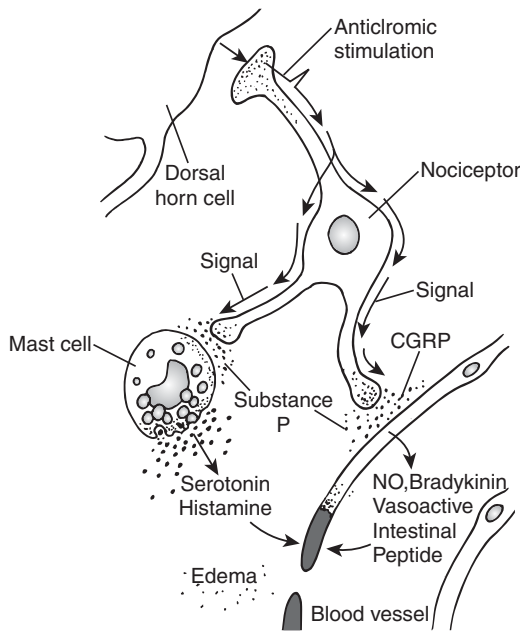


Fig. 4. Diagram illustrates the neurosecretory actions of peripheral nociceptors and the role the release of substance P plays in causing mast cell degranulation and peripheral sensitization. CGRP, calcitonin gene-related peptide; NO, nitric oxide.

At the level of the spinal cord, the interneurons, which receive nociceptive and non-nociceptive afferent information, act on WDR and other second-order neurons to alter pain perception. Presynaptic inhibition, which acts to hyperpolarize presynaptic pathways and reduce their activation of pain tracts, is often mediated by  $\gamma$ -aminobutyric acid. Interneurons also act postsynaptically by inhibiting signal transmission to second-order neurons. Postsynaptic inhibition is mediated primarily by opioids and glycine. It is also at the postsynaptic level that supraspinal signals from the descending pathways exert their influence. These signals are mediated by, among other things, norepinephrine, serotonin, and acetylcholine [12].

Inhibition of pain at the level of the brain has come to be understood well through the role of endogenous opioids and the descending pain inhibitory system. Endogenous opioids, such as endorphins, dynorphins, and enkephalins, are peptides that act in the CNS to modulate pain. There are a few well-identified areas of the brain and spinal cord that are known to be sites of opioid action: the hypothalamus, limbic system, basal ganglia and periaqueductal gray area, nucleus raphe magnus, reticular activating system, and spinal cord in the dorsal horn. The descending inhibitory system travels from the hypothalamus and periaqueductal gray, through the medulla (where the nucleus raphe magnus and reticular activating system are) to the dorsal horn of the spinal cord, where inhibition of the afferent nociceptive information occurs (Fig. 5). As discussed later, acupuncture research has shown that it has a role in activating this descending inhibitory system.

## **Mechanism of acupuncture analgesia**

### *Acupuncture and the peripheral nervous system*

It has been possible to explain some of the Traditional Chinese Medicine experiences of acupuncture, such as the sensation of *De Qi* and the meridian system, by more modern understanding of anatomy and physiology. Traditionally, Chinese acupuncture needle manipulation at specified points is verified to be accurate when the recipient experiences a *De Qi* sensation, which is described as a deep aching sensation. It now is believed that this sensation is a sign of the activation of group III and IV fibers in skeletal muscle. An analogy has been drawn in tying the physiologic benefits of sustained physical exercise and the stimulation of the same muscle afferents that are activated with acupuncture stimulation [13]. As mentioned earlier, the distribution of these muscle sensory afferents to the dorsal horn of the spinal cord may play an important role in the observed physiologic effect of acupuncture stimulation, especially if these afferents are sensitized, as evidenced by elevated substance P found in animal models of acupuncture points.

Additionally the correlation between acupuncture points and myofascial trigger points has been mapped [14]. Keeping in mind the differences in



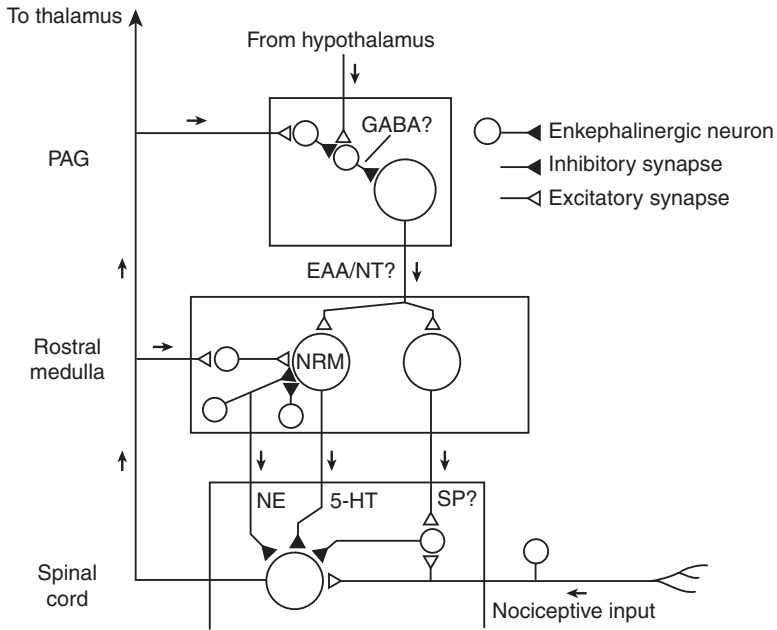


Fig. 5. The descending pain modulation system. The periaqueductal gray area (PAG) is in the mesencephalon and is a major control area for the descending system. The rostral medulla level is where the nucleus raphe magnus (NRM) and the reticular activating system (RAS) are located and is where multiple descending antinociceptives tracks originate. Cells in these centers are activated by excitatory amino acids (EAA), such as glutamate and aspartate and possibly neurotensin (NT). From here, the descending tracks enter the dorsal horn of the spinal cord, and inhibition is mediated mainly by norepinephrine (NE) and serotonin (5-hydroxytryptamine [5-HT]). (Modified from Mense S, Simons DG. Central pain and centrally modified pain. In: Muscle pain: understanding its nature, diagnosis and treatment. Philadelphia: Lippincott Williams & Wilkins; 2001. p. 177; with permission.)

muscle and skin pain pathways previously outlined, stimulation of muscle tissue (as in trigger point injections and acupuncture) not only may have a pain-inhibitory effect, but also may influence visceral structures and remote somatic structures because of sensory convergence on the same WDR second-order neurons.

### *Acupuncture and descending pain inhibition*

The most well-delineated effect that acupuncture has on pain inhibition is the way it influences the descending inhibitory pain system. In the late 1970s and early 1980s, many studies investigated the relationship between acupuncture and pain inhibition. The studies measured either opioid activity in the brain in relationship to AA or a reduction in AA with the administration of opioid antagonists, such as naloxone or naltrexone, and compared the analgesic effects of acupuncture with those of morphine.

Acupuncture has been shown to influence pain perception by modulating the activity of key subcortical and brainstem sites along the descending pain modulating system pathway [15].

Given the variety of neurotransmitters discussed so far involved in the peripheral sensitizing soup and the wind-up phenomenon, it is not surprising that there are potentially many nonopioid mechanisms of analgesia that may be involved. As just one example, low-intensity and high-frequency electrical stimulation has a faster onset of action but does not have as prolonged an effect as high-intensity and low-frequency stimulation. The former is thought to be serotonergic mediated and the latter opioid mediated [16].

Although the demonstration that endogenous opioids and other neurotransmitters can be released consistently in animal and human experimental models has been an important step in verifying that AA has a physiologic basis, there continues to be debate about whether this effect is sufficient to explain the observed clinical benefits. One of the problems is that such humoral effects are nonspecific and short-lived and cannot explain why certain treatment methods for particular conditions would have a sustained or permanent disease-modifying result. The chemical releases observed with electroacupuncture (EA) and manual acupuncture (AP) may just be an epiphenomenon, indicating that there has been an influence on the CNS without fully comprehending what the actual homeostatic influence has been.

One theory that may help to explain better the long-term effect of EA and AP is that by stimulating peripheral sensory afferents of the skin and muscle, sustained changes occur in the CNS via central neuromodulation. A fundamental concept that has emerged is that sustained nociceptive input can have profound effects on the CNS causing pathologic neuroplastic changes. Continuing along this line of argument, in contrast to transcutaneous electrical nerve stimulation (TENS), AP and EA do rely on a more “painful stimulation” of the peripheral nervous system. In effect, through controlled stimulation of peripheral nociceptors, acupuncture may be causing a reverse neuroplasticity in the CNS.

A clue to the neuroplastic changes that may be occurring in the CNS with EP and AP can be found in the literature looking at *c-Fos* expression. The expression of the gene *c-Fos* in the CNS occurs in cells believed to be activated after noxious peripheral stimulation. The Fos protein is the nuclear product of the immediate-early gene *c-Fos* and couples transient intracellular signals to long-term changes in gene expression and is believed to herald neuroplastic changes in the CNS [17]. A body of literature has looked at *c-Fos* expression in the spinal cord and brain in relation to acupuncture. Acupuncture has been shown to suppress c-Fos expression in the spinal cord and the brain after noxious peripheral stimulation, suggesting a possible neuromodulatory mechanism that is independent of endogenous opioid release [18].

### *Acupuncture and the brain*

The advent of functional MRI has provided an intriguing method to look into the effect that acupuncture has on brain activation. These studies give some of the strongest evidence for acupuncture point specificity and help to argue against critics who argue that AA is due to nonspecific, inhibitory control mechanisms induced by the noxious needle stimulation. This evidence for point specificity was shown elegantly by Cho et al [19]. An acupuncture point on the lateral aspect of the small toe, Bladder 67 (B67), which in some acupuncture systems is believed to be an influential point for vision, was stimulated and observed to cause increased functional MRI activity in the occipital lobes in 12 subjects. Stimulation of the eyes directly with light caused a similar activation, whereas stimulation of a sham acupuncture point 2 to 5 cm away from B67 failed to cause occipital lobe activation [19]. In another study, comparison has been made between tactile sensation (tapping the skin with a wire at 2 Hz) versus AP using a classic Chinese manual stimulation technique in which the needle is twisted at 2 Hz in LI4 (a point in the first dorsal interosseous muscle of the hand). Stimulation of an acupuncture point in this manner produces a De Qi sensation, which is a full, aching feeling at the point of the needle and is believed by some to be important in obtaining the clinical effect with AP. The results of unilateral AP showed bilateral neural modulation of cortical and subcortical structures. The primary action was to decrease signal intensity in the limbic region and other subcortical areas. Tactile stimulation did not produce these changes in functional MRI. This finding suggests a differential response of the organism to AP depending on whether there is activation of the muscle sensory afferents versus the superficial afferents in the skin [20].

### *Acupuncture and placebo mechanisms*

Similar to many CAM interventions, the effects of acupuncture sometimes are attributed to the placebo effect. Some authors theorize that placebo is an endorphin-mediated effect, making acupuncture a particularly powerful form of placebo [21]. The ritual of CAM interventions may lend themselves to causing an enhanced placebo effect, which can have powerful therapeutic implications [22]. Acupuncture has the advantage of activating reproducible biologic mechanisms, while bringing to the therapeutic encounter some of the attributes of a psychological interaction, such as longer patient-healer time together and the power of touch and suggestion. Nevertheless, in an attempt to validate the scientific efficacy of acupuncture, the trend is to eliminate from the traditional therapeutic model the elements that may have a profound effect on the efficacy of the intervention. Great emphasis has been placed on identifying appropriate “sham” acupuncture controls and taking into account things such as patient expectation of success before treatment. Time will tell whether acupuncture and many

other CAM interventions will survive the scientific constraints imposed on them.

### **Acupuncture in the clinical setting**

In the early 1990s, by an act of Congress, the National Institutes of Health (NIH) formed an Office of Alternative Medicine, which subsequently became the National Center for Complementary and Alternative Medicine in 1998. The main objective of the center was to fund basic and clinical research in various CAM therapies with the ultimate goal of providing clinicians evidence to guide care. The first NIH-sponsored event for acupuncture was the 1994 “Workshop on Acupuncture,” which resulted in the Food and Drug Administration changing the status of acupuncture needles from experimental to a nonexperimental but regulated medical device status. In 1997, the NIH held its first consensus conference in acupuncture and published a guideline to clinicians summarizing the evidence to date on the use and effectiveness of acupuncture in a variety of medical conditions [23]. In the realm of pain conditions, the panel concluded that the literature showed acupuncture is effective in treating postoperative dental pain. The panel also concluded that acupuncture may be useful in treating headache, menstrual cramps, tennis elbow, fibromyalgia, myofascial pain, osteoarthritis, low back pain, and carpal tunnel syndrome. This statement was based on an exhaustive review of the literature, much of which can be characterized by poorly powered studies of marginal experimental design. As a result of the paucity of quality studies reviewed, the NIH consensus statement often relied on only a single study for any given pain syndrome, and as a result, a strong endorsement could not be made.

### **Acupuncture in clinical research**

One of the issues that should be addressed in reviewing the acupuncture literature is the methodologic problems faced by CAM researchers in their attempts to apply reductionist, scientific paradigms to clinical methods whose efficacy may depend on the interplay of a variety of nonreducible factors. The practice of acupuncture is practitioner dependent, making it hard to compare studies given the variety of techniques and treatment paradigms used in different clinical settings (Fig. 6). Often care also includes dietary recommendations, soft tissue and manipulative techniques, and at times recommendations for herbal combinations. In contrast, a standard research design, in an attempt to eliminate bias and maintain reproducibility, may reduce this robust acupuncture treatment paradigm to a fixed set of points, potentially robbing the treatment of its efficacy.

Another common problem for nonpharmacologic clinical studies due to underfunding is the issue of small sample size, leaving the study un-

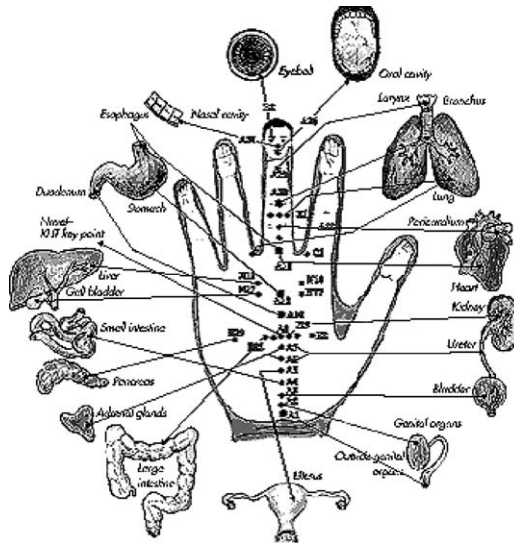


Fig. 6. Korean hand acupuncture montage illustrates the variety of clinical methods used in the United States and around the world. This is a microsystem commonly used by Korean acupuncturists. Often these points would not be needled, but rather heated by burning a combustible herb, mugwort. This technique of heating points by burning mugwort is called *moxibustion*.

derpowered to draw valid conclusions. This is a particular problem when the study design includes use of a powerful placebo stimulus, such as sham needle stimulation of points on the body considered to be off meridian. Sham needling, which involves the insertion of an acupuncture needle into the tissue of a subject on a point off meridian and manipulating the needle as one would at an actual point, often has a strong, nonspecific, physiologic effect. As a result, large numbers of subjects would be required to distinguish the main effect of true point stimulation compared with this type of aggressive placebo needling and avoid a type 2 error or rejection of the null hypothesis. Other placebo needling methods are noninvasive, but there is much debate in the scientific community about the validity of such devices (Fig. 7). It is impossible to blind the practitioner and difficult to blind the subjects in controlled trials, often necessitating the recruitment of acupuncture-naive subjects. This being said, the number of clinical studies evaluating the efficacy of acupuncture for treating various pain syndromes has continued to increase, with studies of better quality being published in the past few years, which are reviewed here.

*Spine-related disorders*

Of all the pain-related conditions, back pain is the most frequently studied with acupuncture as an intervention. Meta-analyses of randomized

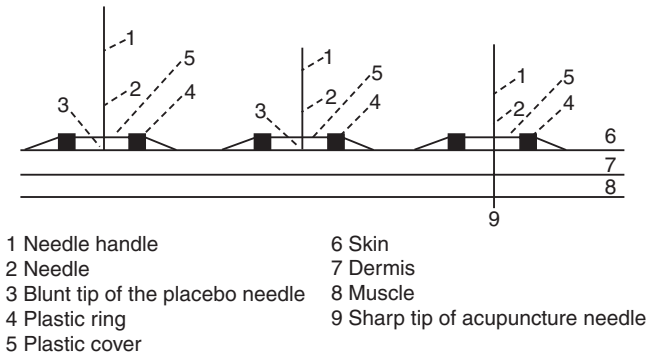


Fig. 7. The placebo needle. (From Kleinhenz J, Streitberger K, et al. Randomized clinical trial comparing the effects of acupuncture and a newly designed placebo needle in rotator cuff tendinitis. *Pain* 1999;83:235–41; with permission.)

controlled trials using acupuncture for back pain conclude that acupuncture has been shown to be superior to various control interventions, but not enough data are currently available to support its efficacy over sham acupuncture needling [24,25].

In a prospective, randomized controlled trial, 186 subjects with chronic low back pain were recruited, 124 of whom completed the full treatment and follow-up protocol. Subjects were randomized to three groups: acupuncture with conservative orthopedic treatment, sham acupuncture with conservative orthopedic treatment, and conservative orthopedic treatment alone. Subjects in the verum (or true acupuncture) and sham acupuncture groups received 12 treatments while undergoing spine rehabilitation for conservative orthopedic treatment. Significant improvement in visual analogue scale pain scores in the acupuncture group was found at the end of treatment and at a 3-month follow-up compared with the sham and conservative orthopedic treatment groups [26].

In 1999, the *Journal of the American Medical Association* published a well-designed randomized crossover study comparing percutaneous electrical nerve stimulation (PENS) versus TENS versus sham PENS versus exercise. The study included 60 patients with low back pain secondary to degenerative joint disease. Each patient had 3 weeks of each treatment three times a week with a 1-week break in between treatment types. The PENS treatment showed significant improvements in pain scores, function, and reduced use of analgesics compared with the control groups [27]. PENS is similar to acupuncture in that it involves the insertion and subsequent electrical stimulation of acupuncture-type needles into the deep tissue and muscles. Needle placement is not motivated by acupuncture theory, however; rather needles are placed to surround the dermatomal and myotomal distribution of the patient's pain condition (Fig. 8). Some methodologic problems with the study include concerns about the validity of using TENS

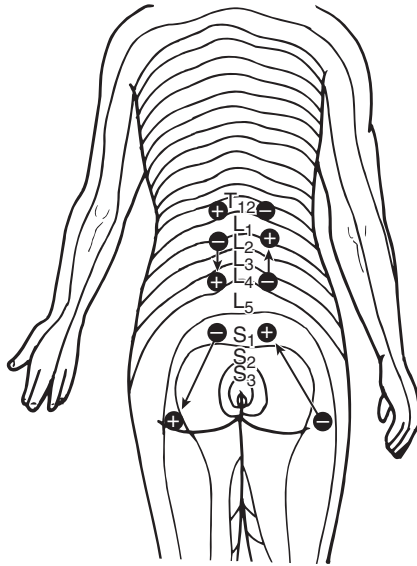


Fig. 8. Percutaneous electrical nerve stimulation montage for low back pain following a dermatomal distribution of pain. Plus and minus circles represent the application of positive and negative electrodes from an electro-acupuncture stimulator to the inserted needles. Needles are inserted through the cutaneous layer into deep muscle tissue.

as a placebo control for needle stimulation. In addition, the exercise protocol used was oversimplified, and long-term outcomes were not studied.

A randomized trial compared acupuncture with massage therapy and self-education for treatment of chronic low back pain. The sample size was large; the participants were evaluated 1 year after treatment, which was 10 weeks long; and multiple providers were used. The study concluded massage therapy to be superior to acupuncture and self-education at the end of the 10 weeks and at 1-year follow-up [28]. The positive effect of acupuncture was concentrated in the first 4 weeks of treatment. Many factors could account for the less favorable outcome of the acupuncture group, including point selection, limited treatment sessions, and, most importantly, the fact that the acupuncturists felt constrained by the study protocol in treating their patients in most cases. This last factor speaks to the issue that the acupuncturists who agreed to participate in the study were not permitted to go beyond needling in their treatment protocol, limiting them from using various massage and nutritional methods that they normally would incorporate into their care.

There are far fewer well-designed studies looking at acupuncture for neck pain. A review published by White and Ernst [29] found that most of the studies failed to satisfy methodologic quality standards. When they looked specifically at the eight methodologically most rigorous studies, they found

that five of them had results that did not support acupuncture for the treatment of neck pain. The most rigorous studies inevitably included a sham needling control group or other interventions with strong, nonspecific therapeutic effects. The review supported the conclusion that acupuncture is superior to a waiting-list control, but it is unclear if it is equivalent or superior to physical therapy.

In another randomized controlled trial, designed specifically to correct some of the weaker points of previous trials, including recruitment of a larger sample size, use of blinded outcome observers, and use of blinded patients for a placebo control using sham acupuncture points. Subjects ( $n = 177$ ) were randomized to acupuncture versus massage versus sham acupuncture. Each treatment group received five treatments over 3 weeks. The investigators concluded that acupuncture was more effective than massage, but not more effective than the sham acupuncture points in decreasing pain with motion. They also found that the patients who had greater than 5 years of pain and patients with myofascial pain did the best with acupuncture [30]. A reanalysis of the data using a linear regression model supported the fact that acupuncture was more effective in reducing pain than sham acupuncture [31]. The support for acupuncture as a treatment modality for chronic neck pain shows some promise given this well-designed study.

### *Arthritis*

One of the most thorough and more recent systematic reviews looked exclusively at acupuncture for the treatment of osteoarthritis of the knee. The strength of the review is that it rated seven different clinical trials on the basis of whether or not the acupuncture treatment they used conformed to guidelines and recommendations put forth by many acupuncture experts. These guidelines included (1) an average of 10 treatment sessions for a chronic condition, (2) stimulation of at least eight points per session, (3) elicitation of the De Qi sensation, and (4) use of a combination of high-frequency and low-frequency stimulation when EA is used to avoid accommodation to the electrical stimulation. The review also rated studies on the quality of their design and the type of control group they used. Four of the seven studies found acupuncture to have a positive effect on pain, and three of the studies were neutral. No studies reported acupuncture as having a negative effect on pain associated with knee osteoarthritis. Three high-quality studies compared real acupuncture with sham acupuncture, and two of them reported positive results. None of the trials conformed to all four of the guidelines deemed necessary by the acupuncture experts for adequate acupuncture treatment. The most important guideline is treatment duration for a chronic condition, such as osteoarthritis of the knee. The three studies that administered the minimum of 10 treatments all had positive results [32].



One study, although it did not include a sham control group, did show an improvement in subjective pain and functional scores in a group of osteoarthritis patients who underwent acupuncture. One of the strengths of this study was the frequency of the intervention: The subjects completed biweekly acupuncture treatments for 8 weeks. The positive effect of acupuncture was sustained 12 weeks after treatment. However, The benefit, although it remained significant, decreased at this 12-week point, suggesting that maintenance therapy may be beneficial [33]. Future studies should compare the cost and health risks of sustained use of ongoing oral analgesics for osteoarthritis of the knee versus intermittent acupuncture treatments to maintain pain relief and function. To give an example of the possible cost savings, in one study of severe osteoarthritis of the knee in which the patients enrolled were on a waiting list for total knee replacement, Christensen et al [34] found a significant reduction in pain and use of analgesic medications compared with a control group. This benefit was sustained, and 7 of 29 patients enrolled declined the total knee replacement operation at the end of the wait, saving \$9000 per patient.

The literature on acupuncture for the treatment of rheumatoid arthritis is sparse. A Cochrane systematic review identified only two studies that met methodologic standards for inclusion. One study compared acupuncture with placebo and found no difference in pain after 5 weeks of treatment. The second study compared EA with placebo and found a significant decrease in knee pain after 24 hours, but not at 1 month, 2 months, or 3 months after treatment. The treatment protocols in both trials normally would not be deemed of sufficient length by acupuncture standards to have a sustained effect on such a chronic condition as rheumatoid arthritis of the knee. These studies of short treatment duration do not support the use of acupuncture in rheumatoid arthritis patients, but they lay the groundwork for future research [35].

### *Fibromyalgia*

Compared with spine-related disorders and arthritis, there is a paucity of studies looking at acupuncture for the treatment of fibromyalgia and other soft tissue pain conditions. A review found only three randomized controlled trials that fit their inclusion criteria [36]. Only one of the studies in the review was considered to be of high methodologic quality. In that study, 70 patients were randomized into sham and treatment groups. They each received six sessions of either verum or sham acupuncture over 3 weeks and subsequently were evaluated independently by a blinded physician. The treatment group had a 70% decrease in pain compared with the control group, which had only a 4% decrease. The treatment group also reported less morning stiffness and better global improvement ratings by the patient and the physician [37]. In another randomized controlled trial, verum and sham acupuncture groups were randomized with and without amitriptyline (25 mg) in 60 subjects with

fibromyalgia. Treatment was provided for 16 weeks with assessments at 4, 8, 12, and 16 weeks by a blinded investigator. The verum acupuncture group showed significant improvement in pain and mood compared with the sham group and amitriptyline-alone group [38]. These results may suggest that a chronic pain problem, such as fibromyalgia, that theoretically may result from abnormal central neuroplastic changes may respond better to acupuncture than would a pain condition such as rheumatoid arthritis of the knee, which involves severe structural damage to a joint.

### *Myofascial pain*

Myofascial pain syndrome frequently involves the supporting postural musculature of the spine and extremities and likely contributes to the pain seen in many of the spine studies already reviewed [39,40]. One widely accepted mechanism for the treatment of myofascial pain is hyperstimulation analgesia by stimulating the trigger points via dry needling, intense cold or heat, or chemical stimulation to the skin. The success of these techniques in the past has been ascribed to the gate control theory of pain [41]. Acupuncture needling potentially could be an additional method of hyperstimulation and might be expected to be a viable treatment for myofascial pain. Additionally, when examining the acupuncture literature from the Tang Dynasty (AD 581-682), one finds that Sun Si-Miao developed the theory of *Ah Shi* points. This theory states that whenever there is a local soreness or pressure, there is an active acupuncture point regardless of whether or not the point lies on a classic acupuncture meridian. Many acupuncturists routinely needle such points in therapy, effectively treating many trigger points by dry needling similarly to their allopathic colleagues (Table 1); this complicates the whole notion of sham acupuncture needling off meridian in controlled studies because the *Ah Shi* point needling is standard practice among acupuncturists when not constrained to a research protocol for the treatment of various pain problems.

Nabeta and Kawakita [42] compared acupuncture with sham acupuncture on tender points (*Ah Shi* points) in volunteers with complaints of chronic pain and stiffness in the neck and shoulder. They treated *Ah Shi* points once a week for 3 weeks. They found that there was a short-term improvement using verum acupuncture, but they did not show a long term superiority of verum over sham acupuncture. Irnich et al [43] published a randomized double-blinded, sham-controlled, crossover trial comparing dry needling and acupuncture at distant points for chronic neck pain. Each treatment was performed only once. Verum acupuncture was found to be superior to sham acupuncture in improving motion-related pain and improving range of motion, and acupuncture at distant points improved range of motion more than dry needling. Kung et al [44] evaluated a meridian-based treatment protocol for chronic myofascial pain in the cervical and upper back regions and found short-term, but not long-term,

Table 1  
Acupuncture and myofascial trigger point correlations

Acu-zone	Region of body	Acu-points	Muscles
<i>Tai Yang</i>	Dorsal zone:	B 2-B 7	Frontalis
	Frontal region	B 10	Sub occipital
	of forehead to	SI 9-14	Scapular
	occiput down	B 11-25, 41-45	Thoracic and lumbar paraspinals
	back to lateral	B 53, 54	Gluteus medius
<i>Shao Yang</i>	ankles	B 31, 34	Piriformis
	Lateral zone:	GB 3-6, 8	Temporalis
	Temporalis	GB 16	Sternocleidomastoid and scalenes
	region of head	GB 20, 21	Upper trapezius
	to lateral neck	TH 9	Finger extensors
	and down arm	GB 24-28	Abdominal obliques
	to wrist	GB 29	Tensor fasciae latae
	extensors.	GB 31	Iliotibial band
	Down flank to		
	lateral aspect		
<i>Yang Ming</i>	of leg		
	Ventral zone:	ST 5-7	Masseter
	Mouth to	ST 9, 10	Sternocleidomastoid
	anterior neck,	ST 14-18	Pectoral muscles
	anterior chest	ST 19-30	Rectus abdominis
	wall down	ST 31, 32	Quadriceps
	abdomen to		
medial aspect			
of leg and			
foot			

*Abbreviations:* B, urinary bladder; GB, gallbladder; SI, small intestine; ST, stomach; TH, triple heater.

pain relief. The study limited treatment to 3 weeks with two sessions each week. All of these trials found acupuncture to be effective in the short-term, with diminishing effects over time. All of these trials used extremely abbreviated treatment protocols, however, potentially influencing the long-term outcome.

### *Tendinitis*

Tendinitis is a common problem among athletes and in the workplace, with repetitive injuries to the upper extremities. Lateral elbow pain, or lateral epicondylitis, has been treated by acupuncture in China for many years. A Cochrane systematic review compiled in November 2001 reviewed the literature and determined that only four randomized controlled trials met their methodologic search standards. Of the four, two showed a positive effect [45]. In one study, acupuncture improved pain scores after one session, an effect that lasted for approximately 20 hours. A total of 48 patients entered the study and received one session of needling of a point on the leg, Gallbladder 34 (a point influential for tendinomuscular problems), versus

sham needling of an unrelated point. In the treated group, the pain scores decreased 55.8% compared with the sham control, which had a 15% reduction in pain level [46]. Another study, done after the Cochrane review was published, looked at acupuncture versus sham needling at adjacent nonacupuncture points for lateral epicondylitis. The study design randomized 45 patients into the sham and verum acupuncture groups, and each subject received 10 sessions of acupuncture over 5 weeks. The acupuncture group did significantly better than the sham group in all measures at 2 weeks. At 2 months, arm function was better in the acupuncture group, but measures of pain intensity or strength were not significantly different from the sham group [47].

A randomized controlled trial using acupuncture for rotator cuff tendinitis offered some positive results. After eight acupuncture sessions provided in a 4-week period, subjects showed significant improvement in pain and function compared with the placebo control group [48]. An important methodologic aspect to this study was that the placebo control was a specially designed needle that replicated visually and tactilely the insertion of a real acupuncture needle (Fig. 7).

### *Neurologic disorders*

Although acupuncture in the studies available to date has not proved as effective for progressive neurologic disorders, such as human immunodeficiency virus neuropathy, studies have supported its efficacy in the treatment of carpal tunnel syndrome. A randomized controlled trial with a crossover design of 11 patients compared laser acupuncture and microamperage TENS stimulation versus sham laser acupuncture. Each group had 9 to 12 treatments over a 3- to 4-week period, then they were crossed over. There was a significant decrease in pain and improvement in the sensory latency as measured by nerve conduction studies 1 week after treatment [49]. Although there were only 11 subjects, the results are promising and provide a good foundation for future studies looking at acupuncture in carpal tunnel syndrome. Although the use of laser acupuncture is still controversial because of the lack of needle penetration to effect the treatment, this approach has the benefit of being more easily blinded. Because one cannot feel a cold laser, and the light spectrum applied is in the infrared wavelength, the subject and the practitioner can be blinded, making the results from the Naeser study even more impressive [50]. Another study found that cold laser stimulation of UB 67 in the foot (the same point used by Cho et al [19] with needles) activated the visual cortex when imaged by functional MRI, substantiating the physiologic effect of laser acupuncture [51].

### *Other pain disorders found in a rehabilitation setting*

A review of the literature for using acupuncture to treat other pain disorders, such as pain associated with spinal cord injury, stroke, and

phantom limb, reveals a sparse number of isolated and often poorly designed studies. Although acupuncture is used for these disorders and may be beneficial, currently there are few studies to draw any sort of clinically applicable conclusions.

## **Summary**

Recent years have shown an increase in the quality of trials examining the clinical efficacy of acupuncture for back and neck pain, arthritis, carpal tunnel syndrome, fibromyalgia, and upper extremity tendinitis. Randomization, appropriate sample size, and blinding using more sophisticated sham procedures raise the quality of the studies from a scientific, methodologic point of view. In addition, realistic treatment frequency and duration of some of the more recent studies have resulted in more favorable outcomes. Much work still has to be done, however, to find ways to preserve the clinical authenticity of acupuncture treatment methods when brought into the light of a research protocol. Attempts have been made to find a method of maintaining the standardization and reproducibility of a research protocol, while allowing the kind of flexible treatment that normally would be applied in a clinical setting [52,53].

Other questions that should be answered with future studies include understanding how treatment length influences outcome, if maintenance treatments are needed for chronic conditions, and cost and risk comparisons with standard pharmacologic treatment. In addition, future studies need more overt statements of the rationale for the treatment method used (eg, were Chinese or Japanese diagnostic methods used for point selection, what needling technique was used, was the De Qi sensation elicited) [54]. If an EA protocol is used, details of the frequency and intensity parameters are needed. Providing this kind of detail assists with reproducibility and helps clinicians gain a better understanding about whether certain treatment paradigms are superior to others for specific clinical conditions. Finally, physicians who have an interest in pursuing acupuncture research should educate themselves about the methodologic issues inherent with acupuncture research and about authentic acupuncture treatment protocols so that the literature is not populated with more poorly designed studies.

With the emerging interest in integrative medicine, there is a growing interest in collaboration and a greater number of physicians interested in obtaining training in acupuncture to help bridge this gap between CAM and conventional clinicians. The American Academy of Medical Acupuncturists (AAMA) has been formed to help as an educational and research forum for physician acupuncturists. Currently, physicians are able to satisfy the educational and clinical requirements demanded by most states by completing the training offered by the Office of Continuing Medical Education at the University of California Los Angeles. Harvard Medical School,

through the Department of Physical Medicine and Rehabilitation and the Department of Anesthesiology and Critical Care at Beth Israel Deaconess Medical Center, also now offers a 300-hour continuing medical education course in medical acupuncture that satisfies the AAMA requirements and most hospital and state requirements to practice acupuncture. The Harvard course also gives graduates a detailed understanding of the methodologic issues involved with scientific research in this field. In time, with more highly trained physicians, the future of acupuncture research should be secure, allowing clinicians to understand better the role of acupuncture in the treatment of pain disorders.

## References

- [1] Hsu DT. Acupuncture: a review. *Reg Anesth* 1996;21:361–70.
- [2] Mayer DJ. Acupuncture: an evidence-based review of the clinical literature. *Annu Rev Med* 2000;51:49–63.
- [3] Besson JM. The neurobiology of pain. *Lancet* 1999;353:1610–5.
- [4] Price DD. Psychological and neural mechanisms of the affective dimension of pain. *Science* 2000;288:1769–72.
- [5] Cailliet R. *Pain: Mechanisms and Management*. Philadelphia: FA Davis; 1993. p. 1–51.
- [6] Woolf CJ, Salter MW. Neuronal plasticity: increasing the gain in pain. *Science* 2000;288:1765–9.
- [7] Mense S, Simons DG. *Muscle pain: Understanding its nature, diagnosis and treatment*. Philadelphia: Lippincott Williams & Wilkins; 2001. p. 158–204.
- [8] Bolay H, Moskowitz MA. Mechanisms of pain modulation in chronic syndromes. *Neurology* 2002;59(5 Suppl 2):S2–7.
- [9] Melzack R, Wall PD. Pain mechanisms: A new theory. *Science* 1965;150:971–9.
- [10] Lewith GT, Kenyon JN. Physiological and psychological explanations for the mechanism of acupuncture as a treatment for chronic pain. *Soc Sci Med* 1984;19:1367–78.
- [11] Chan WW, Weissensteiner H, Rausch WD, Chen KY, Wu LS, Lin JH. Comparison of substance P concentration in acupuncture points in different tissues in dogs. *Am J Chin Med* 1998;26:13–8.
- [12] McHugh JM, McHugh WB. Pain: neuroanatomy, chemical mediators, and clinical implications. *AACN Clin Issues* 2000;11:168–78.
- [13] Andersson S, Lundberg T. Acupuncture—from empiricism to science: functional background to acupuncture effects in pain and disease. *Med Hypoth* 1995;45:271–81.
- [14] Melzack R. Myofascial trigger points: relation to acupuncture and mechanisms of pain. *Arch Phys Med Rehabil* 1981;62:114–7.
- [15] Mayer DJ. Biological mechanisms of acupuncture. *Prog Brain Res* 2000;122:457–77.
- [16] Debreceni L. Chemical releases associated with acupuncture and electric stimulation. *Crit Rev Phys Rehab Med* 1993;5:247–75.
- [17] Morgan JI, Curran T. Stimulus-transcription coupling in the nervous system: involvement of the inducible proto-oncogenes fos and jun. *Annu Rev Neurosci* 1991;14:421–51.
- [18] Pan B, Castro-Lopes JM, Coimbra A. C-fos expression in the hypothalamo-pituitary system induced by electroacupuncture or noxious stimulation. *Neuroreport* 1994;5:1649–52.
- [19] Cho ZH, Chung SC, Jones JP, et al. New findings of the correlation between acupoints and corresponding brain cortices using functional MRI. *Proc Natl Acad Sci U S A* 1998;95:2670–3.

- [20] Hui KK, Liu J, Makris N, et al. Acupuncture modulates the limbic system and subcortical gray structures of the human brain: evidence from fMRI studies in normal subjects. *Hum Brain Mapp* 2000;9:13–25.
- [21] Petrovic P, Kalso E, Petersson KM, Ingvar M. Placebo and opioid analgesia—imaging a shared neuronal network. *Science* 2002;295:1737–40.
- [22] Kaptchuk TJ. The placebo effect in alternative medicine: can the performance of a healing ritual have clinical significance? *Ann Intern Med* 2002;136:817–25.
- [23] NIH Consensus Conference. Acupuncture. *JAMA* 1998;280:1518–24.
- [24] Ernst E, White AR. Acupuncture for back pain: a meta-analysis of randomized controlled trials. *Arch Intern Med* 1998;158:2235–41.
- [25] van Tulder MW, Cherkin DC, Berman B, Lao L, Koes BW. Acupuncture for low back pain. *The Cochrane Database of Systematic Reviews*, Issue 3; 2002.
- [26] Molsberger AF, Mau J, Pawelec DB, Winkler J. Does acupuncture improve the orthopedic management of chronic low back pain—a randomized, blinded, controlled trial with 3 months follow up. *Pain* 2002;99:579–87.
- [27] Ghoname EA, Craig WF, White PF, et al. Percutaneous electrical nerve stimulation for low back pain: a randomized crossover study. *JAMA* 1999;281:818–23.
- [28] Cherkin DC, Eisenberg D, Sherman KJ, et al. Randomized trial comparing traditional Chinese medical acupuncture, therapeutic massage, and self-care education for chronic low back pain. *Arch Intern Med* 2001;161:1081–8.
- [29] White AR, Ernst E. A systematic review of randomized controlled trials of acupuncture for neck pain. *Rheumatology (Oxford)* 1999;38:143–7.
- [30] Irrnich D, Behrens N, Molzen H, et al. Randomised trial of acupuncture compared with conventional massage and “sham” laser acupuncture for treatment of chronic neck pain. *BMJ* 2001;322:1574–8.
- [31] Vickers A. Acupuncture for treatment for chronic neck pain: reanalysis of data suggests that effect is not a placebo effect. *BMJ* 2001;323:1306–7.
- [32] Ezzo J, Hadhazy V, Birch S, et al. Acupuncture for osteoarthritis of the knee: a systematic review. *Arthritis Rheum* 2001;44:819–25.
- [33] Berman BM, Singh BB, Lao L, et al. A randomized trial of acupuncture as an adjunctive therapy in osteoarthritis of the knee. *Rheumatology (Oxford)* 1999;38:346–54.
- [34] Christensen BV, Luhl IU, Vilbek H, Bulow HH, Dreijer NC, Rasmussen HF. Acupuncture treatment of severe knee osteoarthritis: A long-term study. *Acta Anaesthesiol Scand* 1992;36:519–25.
- [35] Casimiro L, Brosseau L, Milne S, Robinson S, Wells V, Tugwell P. Acupuncture and electroacupuncture for the treatment of RA. *The Cochrane Database of Systematic Reviews*, Issue 3; 2002.
- [36] Berman BM, Ezzo J, Hadhazy V, Swyers JP. Is acupuncture effective in the treatment of fibromyalgia? *J Fam Pract* 1999;48:213–8.
- [37] Deluze C, Bosia L, Zirbs A, Chantraine A, Vischer TL. Electroacupuncture in fibromyalgia: results of a controlled trial. *BMJ* 1992;305:1249–52.
- [38] Feldman D, da Costa EDM. Treatment of fibromyalgia with acupuncture: A randomized, placebo-controlled trial of 16 weeks duration. *Arthritis Rheum* 2001;44:S68.
- [39] Hong CZ, Simons DG. Pathophysiologic and electrophysiologic mechanisms of myofascial trigger points. *Arch Phys Med Rehabil* 1998;79:863–72.
- [40] Mense S, Simons DG. Muscle pain: Understanding its nature, diagnosis and treatment. Philadelphia: Lippincott Williams & Wilkins; 2001. p. 205–88.
- [41] Melzack R, Stillwell DM, Fox EJ. Trigger points and acupuncture points for pain: correlations and implications. *Pain* 1997;3:3–23.
- [42] Nabeta T, Kawakita K. Relief of chronic neck and shoulder pain by manual acupuncture to tender points—a sham-controlled randomized trial. *Complement Ther Med* 2003;10:217–22.

- [43] Irnich D, Behrens H, Gleditsch JM, et al. Immediate effects of dry needling and acupuncture at distant points in chronic neck pain: results of a randomized, double-blind, sham-controlled crossover trial. *Pain* 2002;99:83–9.
- [44] Kung YY, Chen FP, Chaung KL, Chou CT, Tsai YY, Hwang SJ. Evaluation of acupuncture effect to chronic myofascial pain syndrome in the cervical and upper back regions by the concept of meridians. *Acupunct Electrother Res* 2001;26:195–202.
- [45] Green S, Buchbinder R, Barnsley L, et al. Acupuncture for lateral elbow pain. *The Cochrane Database of Systematic Reviews*, Issue 3; 2002.
- [46] Molsberger A, Hille E. The analgesic effect of acupuncture in chronic tennis elbow pain. *Br J Rheumatol* 1994;33:1162–5.
- [47] Fink M, Wolkenstein E, Karst M, Gehrke A. Acupuncture in chronic epicondylitis: a randomized controlled trial. *Rheumatology (Oxford)*. 2002;41:205–9.
- [48] Kleinhenz J, Streitberger K, Windeler J, et al. Randomised clinical trial comparing the effects of acupuncture and a newly designed placebo needle in rotator cuff tendinitis. *Pain* 1999;83:235–41.
- [49] Shlay JC, Chaloner K, Max MB, et al. Acupuncture and amitriptyline for pain due to HIV-related peripheral neuropathy: a randomized controlled trial. *Terry Beinr Community Programs for Clinical Research on AIDS. JAMA* 1998;280:1590–5.
- [50] Naeser MA, Hahn KK, Lieberman BE, Branco KF. Carpal tunnel syndrome pain treated with low-level laser and microamperes transcutaneous electric nerve stimulation: a controlled study. *Arch Phys Med Rehabil* 2002;83:978–88.
- [51] Siedentopf CM, Golaszewski SM, Mottaghy FM, et al. Functional magnetic resonance imaging detects activation of the visual cortex during laser acupuncture of the foot in humans. *Neurosci Lett* 2002;327:53–6.
- [52] Schnyer RN, Allen JJ. Bridging the gap in complementary and alternative medicine research: manualization as a means of promoting standardization and flexibility of treatment in clinical trials of acupuncture. *J Altern Complement Med* 2002;8:623–34.
- [53] Hopwood V, Lewith G. Acupuncture trials and methodological considerations. *Clin Acup Oriental Med* 2003;3:192–9.
- [54] MacPherson H, White A, Cummings M, et al. Standards for reporting interventions in controlled trials of acupuncture: the STRICTA recommendations. *Clin Acup Oriental Med* 2002;3:6–9.