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Chapter 11

The Role of Acupuncture in Pain Management

Lucy Chen

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1. Introduction

Acupuncture is one of the most significant components of the healthcare system in China for more than 3,000 years. Over the last a few decades, acupuncture has garnered increasing popularity and scrutiny in Western nations. It was reported that office visits for alternative therapy were two times as many as the visits to primary care physicians in a nationwide survey in 1998. The total out-of-pocket expenditures relating to alternative therapies in 1997 were comparable to that for all US physician services, which was conservatively estimated at $27 billion [1]. This number has further increased to $33.9 billion in next 10 years [123]. Consistent with the ever-growing demand for acupuncture, an important component of complementary/alternative medicine, FDA classified acupuncture needles as medical equipment, subject to the same strict standards for medical needles, syringes and surgical scalpels in 1996 [2]. The National Institutes of Health (NIH) organized a Consensus Development Conference on Acupuncture in 1997, which recognized that acupuncture has been extensively practiced by medical physicians, dentists, non-MD acupuncturists, and other practitioners. One of the reasons for patients seeking acupuncture treatment is the incidence of adverse effects is substantially lower than that of many drugs and commonly accepted medical procedures [3].

2. Traditional Chinese acupuncture theory

In the ancient theory of Chinese medicine, the human health is maintained through a delicate balance of two opposing but inseparable elements: *Yin* and *Yang*. Yin represents 'cold, slow, and passive elements', whereas Yang represents 'hot, exciting, and active elements'. Accordingly, the human internal "organs" are also divided into the Yin and Yang system. Health can be achieved by maintaining the human body in a 'balanced state of Yin and Yang'. Furthermore, this theory stipulates that *Qi* (pronounced as 'chee') is the life force or vital energy that

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influences health. *Qi* is thought to flow through specific pathways in a human body, so called meridians. Acupuncture involves the insertion of fine sterilized needles through the skin at specific points so-called Acupoints which mostly located in the meridians. Human body consists of 12 main meridians and 8 secondary meridians. There are also acupoints located beyond the meridians. Since the balance of the opposing forces of Yin and Yang is considered to be the basis for a healthy flow of *qi*, any imbalance would cause the disruption or blockage the flow of *qi* and lead to a state of disease or pain. Acupuncture treats a state of disease or pain through strengthening the weak *qi*; releasing the excessive *qi* or removing the blockage from the flow of qi in order to restore the normal balance of the Yin and Yang system.

3. Research in the mechanism of acupuncture

Although acupuncture has been used for thousands of years, its mechanism remains unclear. A large number of studies in humans and animals have demonstrated that acupuncture results in various biological effects on peripheral or central nerve system, neurohumoral factors neurotransmitters, and other chemical mediators.

Peripheral nervous system – Studies have showed that an intact peripheral nerve system appears to be necessary for the analgesic effects of acupuncture, because the analgesic effects can be abolished if the acupuncture site is affected by postherpetic neuralgia or intervened with local anesthetics [124,125].

Central nervous system -- Earlier studies showed that Electric Acupuncture (EA) at different frequencies could have different effects on the synthesis and release of neuropeptides, particularly synthesis of different opioid peptides in the central nervous system [11]. Moreover, an μ-opioid receptor antagonist or antiserum against endorphin blocked acupuncture analgesia induced by EA at 2 Hz but not at 100 Hz [12,13]. In addition, cholecystokinin-like immunoreactivity was increased within the medial thalamic area after EA [13], and EA enhanced or restored the activity of natural killer cells suppressed by the hypothalamic lesion [14].

The development in neuroimaging techniques such as functional magnetic resonance imaging (fMRI) and positron emission topographic (PET) scan has made it possible to further understand the acupuncture effects on human brain neuronal activity. Pain activates neuronal activity in periaqueductal gray (PAG), thalamus, hypothalamus, somatosensory cortex, and prefrontal cortex regions in the human brain [15], which appears to be attenuated by the sensation of 'de-qi' after acupuncture [16,17]. EA, particularly at a low frequency, produced more widespread fMRI signal changes in the anterior insula area (signal increases) as well as in the limbic and para-limbic structures (signal increases) than manual acupuncture. These findings are further supported by the data that different acupuncture points evoked a signal increase or decrease in specific areas within the central nerve system, suggesting that there might be a correlation between the effects of acupuncture and neuronal changes in the brain [18]. Other studies have also showed that neuronal responses to EA stimulation can be visualized in the rat primary somatosensory cortex using an optical imaging system [19]. This process may help understand the neural mechanisms of acupuncture treatment and Meridian

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phenomena [20]. Of interest to note is that using so-called 'Bi-digital O-ring Test Imaging Technique', researchers found that each meridian is connected to a representative area in the cerebral cortex, suggesting that the meridian system defined in the theories of Chinese medicine might overlap with distinct supraspinal regions [21].

Humoral factors and Neurotransmitters -- Scientists have found that acupuncture significantly increases the endogenous endorphin production and this effect can be blocked by the opioid receptor antagonist naloxone [4]. Humoral factors may mediate acupuncture analgesia by releasing substances into the cerebrospinal fluid after acupuncture. This notion was supported by a cross-perfusion experiment in which acupuncture-induced analgesic effects were replicated in the recipient rabbit which were not receiving acupuncture but received the cerebrospinal fluid from the donor rabbit with acupuncture treatment [5]. EA also has been shown to alter the condition of polycystic ovaries induced by steroids through the modulation of ovarian nerve growth factors [6].

In a study comparing with the sham group, EA increases the anandamide (an endogenous canabinoid) level in inflammatory skin tissues, and local pretreatment with a specific cannabinoid (CB2) receptor antagonist (AM630), significantly attenuated the antinociceptive effect of EA [7]. A presynaptic CB1 receptor likely contributes to the mechanism of the effects of EA modulating the sympathoexcitatory reflex responses in periaqueductal gray region of the brain by decreasing the release of gamma-aminobutyric acid (GABA, an inhibitory neurotransmitter), but not glutamate (an excitatory neurotransmitter) [8]. Animal study also showed that the N-Methyl-D-aspartic acid (NMDA) receptor subunit (NR2B or N-methyl D-aspartate receptor subtype 2B) was involved in the analgesic effects of EA in pain in the thyroid region by down regulating the NR2B phosphorylation level [9]. In a clinical randomized study, the local nitric oxide content in those subjects in acupuncture group was significantly higher than those in the non-acupuncture group, indicating that acupuncture stimulation can up-regulate nitric oxide content [10].

A large body of evidence indicates that acupuncture significantly affects the production and release of neurotransmitters including epinephrine, norepinephrine, dopamine, and 5-hydroxytryptamine [19]. Specifically, stress-induced increases in norepinephrine, dopamine, and corticosterone were inhibited after EA, a process that could be blocked by naloxone, suggesting that the EA effects on the release of neurotransmitters are likely to be mediated through endogenous opioids [22]. Similar results were observed in other animal studies of acupuncture analgesia [23-27]. The functional significance of acupuncture-induced changes in neurotransmitters was clearly indicated in a number of studies. For instance, EA at different frequencies (2, 10, or 100 Hz) elicited the analgesic effects and such effects could be at least partially blocked by a serotonin receptor antagonist [28]. Many brainstem regions could be selectively activated by EA at both 4 Hz and 100 Hz, whereas other regions could only be activated by EA at 4 Hz [29]. Importantly, the selective supraspinal activation by EA at difference frequencies may be related to the neurotransmitter release resulting from EA at a particular frequency. For instance, the analgesic effect from EA at 4 Hz was mediated through endogenous opioids [29], while the analgesic effect from EA at 2 Hz may involve substance P as its mediator [30].

Besides its effect on acupuncture analgesia, the EA-induced modulation of neurotransmitter release may also mediate other therapeutic effects of acupuncture. There is evidence that EA at 100Hz could protect axotomized dopaminergic neurons from degeneration by suppressing the axotomy-induced inflammatory response [31], raising the possibility that acupuncture may be used to treat certain neurological disorders such as Parkinson's disease [32]. Another example is that the excitatory effects on gastrointestinal mobility following EA or moxibustion in rats could be abolished by serotonin inhibitors [33], suggesting that serotonin may be a critical mediator of acupuncture regardless of its effects on gastric emptying or analgesia. Similarly, the reduced production of nitric oxide within the gracile nucleus after acupuncture has been considered to mediate the effect of acupuncture on reversing bradycardia [34].

4. Clinical research data on acupuncture

While acupuncture has become popular among patients and medical professionals, there is still debate regarding its application and overall efficacy. The challenges that we faced in clinical trials of the efficacy of acupuncture have their unique issues such as placebo controls, crossover design, and the individualization. It is encouraging to see that more controlled, randomize clinical studies of acupuncture have replaced the bulk of anecdotal case reports. The increasing numbers of clinical trials on acupuncture treatments have provided more information, particularly on the role of acupuncture in clinical pain management.

4.1. Low back pain

Chronic low back pain is a very common health problem associated with high medical expenses and disability. An estimated 70% of individuals in western countries have back pain sometime in their lifetime. Patients with back pain account for more than $90 billion in health care expenses every year [35]. Although there are many medical treatment options, long-term effects from these medical treatments remain limited. Recently, acupuncture has become one of the most frequently used alternative therapies in treating low back pain. In a randomized, placebo-controlled clinical trial with a 9 month follow up period, 131 patients with non-radiating low back pain for at least 6 months were divided into three groups for treatment of 12 weeks: control (only received physical therapy), acupuncture, or sham acupuncture (received 20 sessions of either acupuncture or sham acupuncture in addition to physical therapy. The results indicate that acupuncture was superior to physical therapy regarding pain intensity, pain-related disability, and psychological distress. When compared with sham acupuncture, acupuncture was also superior in the reduction of psychological stress [36].

In another study, the benefit from 8 weeks of acupuncture treatment on low back pain in 50 patients lasted up to 6 months in many aspects including returning to work, quality of sleep, and reduced use of analgesics [37]. The duration of acupuncture in a single session appeared to be an independent parameter to a treatment outcome. For example, a 30-min acupuncture session was more effective than a 15-min session, whereas a 45-min

session did not further improve the outcome [38]. Similar finding was also been found in electrical acupuncture stimulation using percutaneously placed needles in 30-min and 45-min durations produced similar improvements in the visual analog pain scale, physical activity, quality of sleep scores, and a reduction in the oral analgesic requirements, which is better than 0 (no treatment) or 15-min duration [39]. Of interest to note is that both acupuncture and transcutaneous electrical stimulation (TENS) showed significant effects on pain reduction, although acupuncture appeared to be more effective than TENS in the improvement of lumbar spine range of motion [40].

In a recently conducted large study involved 1162 patients with chronic low back pain, acupuncture therapy improved low back pain for at least 6 months. The effectiveness of acupuncture, either verum (47.6%) or sham (44.2%), was almost twice that of conventional therapy (27.4%) [41]. In another large-scale clinical trial, 3,093 patients with chronic low back pain were recruited randomly into two groups: acupuncture and conventional medical care. Back function (Hannover Functional Ability Questionnaire), pain, and quality of life were assessed at the baseline and 3 and 6 months of duration. In addition, the cost-effectiveness was also analyzed. The results showed that acupuncture plus routine care was associated with a marked clinical improvement in these patients and was relatively cost-effective [42]. Overall, the clinical practice guideline from American College of Physicians and the American Pain Society for chronic low back pain patients recommend physicians to consider acupuncture as an addition of nonpharmacologic therapy with proven benefits for low back pain [43, 44].

4.2. Chronic neck and shoulder pain

There are promising results on the treatment of chronic neck and shoulder pain using acupuncture. In one study, the acupuncture treatment reduced chronic pain in neck and shoulders for at least three years with a concomitant improvement in depression, anxiety, sleep quality, pain-related activity impairment, and quality of life [39, 45, 46]. Several other clinical trials of acupuncture on chronic neck pain with sample sizes from 115 to 177 patients also have positive results. These studies demonstrated that acupuncture was superior to controls in reducing neck pain and improving the overall range of motion [47-51]. Moreover, in patients with balance disorders caused by cervical torsion after whiplash injuries, acupuncture has been shown to be effective in treating their symptoms [52].

Another study compared the treatment effect of acupuncture combining with physical therapy to that of acupuncture or physical therapy alone for patients with neck pain due to neck tension syndrome. All groups showed significant improvement after 10 weeks of treatment, but the group receiving a combination of acupuncture and physical therapy was superior in pain reduction and function disability improvement than other groups with acupuncture or physical therapy alone. The improvements of all groups were maintained ($p < 0.05$) at the 6 months of follow-up. The data suggest that acupuncture treatment may assist and/or enhance the physiotherapy effect on musculoskeletal rehabilitation for tension neck syndrome [53].

Chronic myofascial neck pain has been frequently treated with trigger point injection either with local anesthetics or using dry needling technique. One prospective, randomized, double-blind, sham-controlled crossover study compared acupuncture, sham acupuncture and dry

needling of local myofascial trigger points in patients with chronic neck pain and limited cervical spine function. Acupuncture showed better results in reducing motion-related pain and improving range of motion [54]. For neck pain induced by cervical spondylosis, one study enrolled 106 subjects and randomly divided these subjects into real acupuncture group and control sham acupuncture group. The effective rate was 75.5% in the acupuncture group and 52.8% in the control group ($P<0.05$) [55]. To investigate the effectiveness of acupuncture in addition to routine care as compared to routine care alone in patients with chronic neck pain, a randomized controlled multi-center trial was conducted in Germany. A total of 14,161 patients with chronic neck pain (duration >6 months) were randomized to an acupuncture group (1,880 subjects; 15 acupuncture sessions over 3 months) or a control group receiving no acupuncture (1,886 subjects). In addition, 10,395 patients were included in a non-randomized acupuncture group. The results showed a significant improvement in neck pain and disability in the randomized acupuncture group ($P<0.001$). Of interest, patients in the non-randomized acupuncture group had more severe symptoms at baseline but showed more neck pain and disability improvement as compared to the randomized patients, suggesting a possible placebo effect. This large scale clinic trial demonstrates that integrating acupuncture with routine medical care in patients with chronic neck pain may result in both pain improvement and a reduction of disability [56].

In two meta-analysis studies with 10 to 14 clinical trials included, there was moderate evidence that acupuncture was more effective for pain relief than some types of sham controls or inactive, sham treatments, when measured immediately after the treatment and at short-term follow-up (pooled standardized mean differences, -0.37; 95% confidence interval, -0.61 to -0.12). There was limited evidence that acupuncture was more effective than massage at short-term follow-up. Overall, the short-term effectiveness and efficacy of acupuncture in the treatment of neck pain appear to be present [57, 58]. However, the cost-effectiveness of additional acupuncture treatment in patients with chronic neck pain as compared to patients receiving routine care alone remains to be determined. More interestingly, another study with a total of 3,451 patients (1,753 acupuncture-group, 1,698 control-group), acupuncture treatment was associated with higher costs over the first 3 months duration as compared to routine care. This cost increase was mainly due to the costs of acupuncture. Private medical expenses such as over the counter medication were not included. Beyond the 3 months study duration, acupuncture might be associated with further health economic effects. According to international cost-effectiveness threshold values, the conclusion of this study is that acupuncture is a cost-effective treatment strategy in patients with chronic neck Pain [59].

4.3. Headache

Even with the recent advancement in the diagnosis and treatment of different headache disorders, many patients with headaches are still suffering due to lack of effective treatment. Selective serotonin receptor agonists such as sumatriptan type medications have effectively treated millions migraine sufferers, there are still at least 30% of migraine patients who do not respond to such treatment. Alternatively, acupuncture has become a new modality of treatment for those patients suffering from tension headache, migraine,

and other types of headaches [125]. In a multi-center study, 302 patients suffering from migraine headache were randomized into three groups (acupuncture, minimal acupuncture and waiting list). The trial found a significant effect of those treated with acupuncture and minimal acupuncture as compared to those on the waiting list for treatment [60]. Many other headache studies either with tension headache or migraine headache, with a sample size from 50 to 2,022 patients, also showed similar results [61-70]. According to international cost-effectiveness threshold values, acupuncture is a cost-effective treatment in patients with primary headache [71]. Moreover, the pediatric patient population also benefits from this alternative therapy for headache treatment [72]. For many patients, acupuncture not only has a similar, if not better, efficacy as compared with sumatriptan in preventing full migraine attack, acupuncture has unique benefits over sumatriptan-related medications because of its negligible side effects [67].

As a prophylactic measure of migraine without aura, acupuncture treatment for 2-4 months significantly reduced the number of migraine attacks comparing to oral therapy with flunarizine [73]. In a comprehensive review, 27 clinical trials were included to evaluate the efficacy of acupuncture in the treatment of primary headaches (migraine headache, tension headache, and mixed forms). The result revealed that the majority of trials (23 out of 27 trials) showed favorable outcomes in the treatment of headaches using acupuncture [74]. Another review included eleven trials with 2317 participants examined whether acupuncture is a) more effective than no prophylactic treatment/routine care only; b) more effective than 'sham' (placebo) acupuncture; and c) as effective as other interventions in reducing headache frequency in patients with episodic or chronic tension-type headache. The authors found that acupuncture treatment has statistically significant and clinically relevant short-term (up to 3 months) benefits over control in terms of the number of headache days and pain intensity. Small but statistically significant benefits of acupuncture over sham were also found. The authors conclude that acupuncture could be a valuable non-pharmacological tool in patients with frequent episodic or chronic tension-type headaches [75]. In another systemic review of 22 trials of 4,419 participants, there is consistent evidence that acupuncture provides additional benefit to treatment of acute migraine attacks as compared to routine care only [76]. However, more research is needed to investigate the treatment of specific tension-type headache subtypes [77].

5. Other pain conditions

Acupuncture has been used to treat many other pain conditions. Several studies have shown that patients who received acupuncture prior to operation had a lower pain level, reduced opioid requirement, a lower incidence of postoperative nausea and vomiting, and lower sympathoadrenal responses [78-81]. In another study of acupuncture treatment for labor pain, parturients who received acupuncture during labor significantly reduced the need of epidural analgesia with a better degree of relaxation but without a negative effect on delivery as compare with a control group [82-83]. Another active area of clinical acupuncture is the treatment of osteoarthritis of the knee. Acupuncture has been shown to provide some im-

provement in function and pain relief when compared with sham acupuncture or control groups using education [84]. In addition, the benefit of acupuncture treatment in fibromyalgia and rheumatoid arthritis is supported by several clinical trials, albeit in a small scale, suggesting that the large-scale clinical trials on these pain conditions may be warranted [85]. Similarly, chronic lateral epicondylitis (tennis elbow) may benefit from the acupuncture treatment in part due to the effect of acupuncture on the range of motion and reduction in pain on exertion [86]. In some cases, the effects of acupuncture on tennis elbow lasted up to one year after ten sessions of acupuncture [87].

6. Other uses of acupuncture

Besides its analgesic effects, acupuncture has been used for the treatment of many other conditions. For example, a number of clinical trials strongly support a therapeutic role of acupuncture (either needle acupuncture or applying acupressure to the relevant acupoints) in postoperative nausea and vomiting as compare with antiemetics such as droperidol and zolfran [88-94]. An increasing number of patients are turning to acupuncture either to supplement or replace their conventional treatments for many medical conditions including allergy, asthma, depression, anxiety, obesity, insomnia, cancer-related fatigue, premenstrual syndrome, menopause symptoms, assist conception and infertility, spinal cord injury, quitting smoking and detoxification from opioids or other drug addiction [95-117]. Table 1 lists a summary published in 2002 by the World Health Organization (WHO) for clinical pain conditions recommended for acupuncture [126].

7. Possible complications of acupuncture

Acupuncture has significantly lower complication rate comparing to many other medical treatment. The 1997 NIH consensus panel on acupuncture stated that the documented occurrence of adverse events in practice of acupuncture has been extremely low. The most commonly reported complication is bruising or bleeding at the needle insertion site, followed by the incidence of a transient vaso-vagal response. Other rare complications include infection, dermatitis and broken needle fragments. In one prospective large-scale survey with 34,407 acupuncture treatments in the UK, no serious adverse events were reported that required hospital admission, prolonging hospital stays, permanently disabling, or death. A total of 43 minor adverse events were reported (0.13%), including severe nausea and actual fainting, unexpected, severe and prolonged aggravation of symptoms, prolonged and unacceptable pain and bruising and psychological and emotional reactions [118]. Another survey conducted in the UK with a total of 31,822 acupuncture treatments also found only 43 minor adverse events, a rate of 14 per 10,000 treatments (0.14%). Other minor adverse events can be avoided such as patients being left unattended, needles being left in patients, cellulites and moxa burns [119]. When compared with medications routinely prescribed in the primary care setting, acupuncture is a relatively safe treatment modality. However, since acupuncture is an invasive

medical intervention, serious complications such as pneumothorax, hemathorax, internal organ puncture, and pericardial effusion could happen if the treatment is not properly administered [120]. Some of these more serious complications generally occur in elderly and more fragile and debilitated patients with complex comorbidities or in the hands of less skilled practitioners. Thus, it is imperative that the acupuncture licensing and regulation mandate the use of standards of acupuncture training through adopting strict requirement for the knowledge of anatomy and sterile techniques.

8. Perspectives and future directions

Alone with the popularity of the acupuncture in recent years, an increasing number of physicians have integrated acupuncture into their practices. Many medical schools in the USA have already added topic courses of integrated medicine [121]. One recent survey of physicians regarding acupuncture use in their practice showed that an overwhelming majority of survey responders have a positive attitude and favorable experience with using acupuncture as an alternative modality for chronic pain management. However, the lack of insurance coverage and facility for acupuncture treatment are two primary barriers of acupuncture referrals. [122]. To face the ever-growing healthcare cost in the USA, more health insurance providers have begun to emphasize preventive and alternative measures. Third-party reimbursements for alternative therapies also have increased because of the demand from an increasing patient population. Accordingly, the National Center for Complementary and Alternative Medicine (NCCAM) has funded a good number of research projects related to acupuncture.

In the face of the positive development in the use of acupuncture as an alternative treatment modality, the current clinical research on acupuncture treatment is still challenged by a number of issues. First, although many studies on acupuncture treatment have been published, the scientific merits of these studies may be limited by the study design and non-standardized acupuncture practices. Second, it may be difficult to keep true blindness to patients in a clinical trial. Third, Non-specific needling (i.e. placing an acupuncture needle at an acupoint not intended for the treatment of the condition) or sham needling may elicit responses similar to responses to active acupuncture treatment, making it difficult to interpret the trial results. In this regard, it will be difficult to exclude a placebo effect in many clinical acupuncture trials. Fourth, in clinical setting, acupuncture treatment is often highly individualized for a given clinical condition, which varies from one practitioner to another. As such, it would be rather difficult to compare the treatment outcomes in different clinical trials if a given clinical condition were treated with various parameters including acupuncture points, needling techniques, electrical versus manual, duration of acupuncture in one session, and between-session intervals etc. Nonetheless, efforts should be made to standardize acupuncture clinical trials in order to improve the scientific merits of clinical trials. It can be anticipated that complementary medicine including acupuncture is likely to play a growing and positive role in pain management.

Diseases, symptoms or conditions for which acupuncture has been shown to be effective	Diseases, symptoms or conditions for which the therapeutic effect of acupuncture remains to be determined
Headache	Abdominal pain (acute gastroenteritis or acute cute gastrointestinal spasm)
Knee pain	Cancer pain
Low back pain	Earache
Neck pain	Eye pain due to sub-conjunctival injection
Dental pain	Fibromyalgia and fasciitis
Facial pain and craniomandibular dysfunction	Labor pain
Postoperative pain	Pain due to endoscopic examination
Rheumatoid arthritis	Pain due to thrombtic angiitis obliteran
Periarthritis of shoulder	Chronic prostatitis
Renal colic	Pruritus
Tennis elbow	Radicular and pseudoradicular syndrome
Sciatica	Reflex sympathetic dystrophy
Sprain	Acute spine pain
	Stiff neck
	Temporomandibular dysfunction

Table 1.

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