

# Acupuncture Concepts and Physiology- Application on Stroke and Knee Osteoarthritis

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## ABSTRACT

**Background:** Acupuncture, based on theory of meridians and acupoints, is a key component of traditional Chinese medicine that has been practiced for more than three thousand years. Stroke and knee pain are two diseases and conditions for which acupuncture has been proved effective in World Health Organization (WHO) official report published in 2003.

**Methods:** Taking stroke and knee osteoarthritis (KOA) as two examples, systematic review and Cochrane review in Pub Med were searched with keywords as “acupuncture & stroke” and “acupuncture & knee osteoarthritis” from Jan. 1st, 2016 to present. Four reviews related to stroke and 5 reviews about knee osteoarthritis were included. Other literatures associated with mechanism or clinical practices were also cited.

**Results:** Acupuncture showed its therapeutic effects on both stroke and knee osteoarthritis, including but not limited to improvement of motor function, cognitive function, swallowing function and depression for post stroke patients; pain relief and enhancement of functional mobility for KOA cases. Acupuncture's mechanism involved multilevel and complicated. No serious adverse event is reported for acupuncture in these two conditions.

**Conclusion:** Acupuncture could be one of the alternative therapies in care of stroke and knee osteoarthritis, but may be better applied in integrated practice. More rigor studies with high quality of methodology are warranted to provide further higher-level evidence.

**Keywords:** Acupuncture; Stroke, Knee osteoarthritis; Efficacy; Mechanism; Adverse effect

## INTRODUCTION

Acupuncture has been a widely used therapy in mainstream interventions after stroke in China, especially on ischemic stroke and has been shown to be effective in promoting recovery after stroke. The therapeutic effects of acupuncture for cerebral ischemia have been studied both in the clinic and in laboratory. But acupuncture's efficacy is still being questioned and sometimes ascribed its outcome to placebo effects. Its mechanism is also not fully understood though many clinical and experimental studies have explored. This chapter would elucidate acupuncture's effect by citing the recent studies or reviews on two examples of neurology and musculoskeletal diseases, stroke and knee osteoarthritis, which are also 2 of totally 28 diseases, symptoms or conditions for which acupuncture has been proved to be an effective treatment in WHO official report that published in 2003. This report was based on data from 255 controlled clinical trials before the end of 1998 or beginning of 1999 [1]. In addition to the evidence about efficacy of acupuncture in these two conditions, the mechanism of acupuncture's effect and its adverse effect is also described.

## MATERIALS AND METHODS

Systematic review and Cochrane review in Pub Med were looked up with keywords as "acupuncture & stroke" and "acupuncture & knee osteoarthritis" from Jan. 1st, 2016 to present. Protocols, single clinical trial, irrelevant article, or literature about symptoms repeated in Cochrane reviews were excluded. Among 37 literatures by "acupuncture & stroke" (filtered by clinical trials, systematic review, time range), 4 reviews were cited. Among 21 reviews by "acupuncture & knee osteoarthritis" (filtered by clinical trials, systematic review, time range), 5 reviews were cited. Other literatures about mechanism, comparable or relevant studies were also included for relatively complete elucidation.

# RESULTS

## Application of Acupuncture on Stroke

Though the worldwide prevalence of stroke varies and inconsistent, the data from the United States in 2011 could present its impact. Stroke is the leading cause of chronic disability, the second leading cause of dementia, and the fourth leading cause of death [2]. In the clinical guidelines for stroke management published in 2017, acupuncture was recommended for stroke with depression or depressive symptoms [3]. And some evidence supports acupuncture and behavioral interventions (dietary modification, swallowing exercises and environmental changes including positioning) may reduce dysphagia [4].

### Efficacy

An updated systematic review on acupuncture's efficacy and safety for cerebral infarction cited the data that sixty-six percent of Chinese doctors apply acupuncture for stroke and sixty-three percent believe its efficacy. This review included total of 25 trials with 2224 patients. The results showed that the acupuncture groups had better effect than control groups in the Clinical Efficacy Rates, motor function by Fugl-Meyer Assessment, activities of daily life by Barthel Index Score and neural function by Neurological Deficit Score [5].

Cochrane review in 2016 that included 31 trials with totally 2257 subjects in stroke with sub acute or chronic stages also showed acupuncture's beneficial effects on general neurological deficit, independency, and other specific neurological impairments such as motor function, cognitive function, depression, swallowing function and pain [6, 7]. Since stroke demands comprehensive rehabilitation, integrated pattern is commonly used in most of the rehabilitation departments or hospitals in China. This pattern always shows better outcome than routine rehabilitation from only biomedical perspective alone. For example, in a 2×2 factorial design randomized controlled trial involving 204 stroke patients with cognitive dysfunction. Acupuncture in combination with RehaCom cognitive training was compared with acupuncture only and the usual treatment by per-protocol analysis. After 12 weeks of treatment, acupuncture combined with RehaCom training has better therapeutic effects on cognitive function in post stroke patients than the use of either treatment alone, indicating the clinical significance of such combined therapy [8]. More studies on combination interventions including acupuncture and other rehabilitation therapies would better fit for clinical practice.

The topic that whether acupuncture is suitable for spasticity after stroke sometimes is controversial in clinical practice. A systematic review in 2016 showed significant effect by acupuncture, but the improvements are not related to clinical changes [9]. Another systematic review in 2017 showed significant improvement by electro acupuncture (EA) combined with routine care in spasticity in upper and lower extremities, indicating the potential effect on post stroke spasticity of acupuncture treatment [10]. Our earlier study showed EA in 100Hz of

combined with routine rehabilitation program was superior to EA in 2Hz for spasticity status of lower extremity in post stroke cases [11].

## **Mechanism**

A recent review included both the clinical and experimental studies about mechanisms of acupuncture therapy for ischemic stroke. The mechanism stated from clinical trials involved activation of relevant brain regions, promotion of cerebral blood flow and correlated molecules in stroke cases. Experimental studies found evidence about better blood circulation and metabolism, as well as the regulation on multiple molecules and signaling pathways in different levels that related to excitotoxicity, oxidative stress, inflammation, neurons death and survival, neurogenesis, angiogenesis and neuroplasticity as well [12].

## **Adverse events**

No serious side effects were reported [6]. Three trials reported minor adverse events, such as transient fainting, pain at insertion site, blood pressure change, dizziness and superficial hematoma [5].

## **Application on Knee Osteoarthritis**

A review cited that osteoarthritis is the eighth leading cause of disability worldwide, knee osteoarthritis is the most frequent condition with disability, and contributes to higher percentage of disability than any other medical condition in daily life activities, such as stair climbing, walking a mile and housekeeping. Ten trials with 1456 participants in this review provide evidence that acupuncture is an effective treatment for pain and physical dysfunction associated with KOA [13]. Chinese medicine expert consensus has reached that acupuncture was one of the non pharmacologic interventions for KOA [14].

Multidisciplinary treatment has been considered for osteoarthritis intervention in UK National Institutes of Clinical Excellence (NICE guideline 2008). Cochrane review published in 2010 about acupuncture for peripheral joint osteoarthritis included 16 trials with 3498 participants. Among them, 12 RCTs involved knee OA only. The results showed acupuncture improved osteoarthritis pain for short-term significantly by compared with sham control. But the better benefits are small and didn't show clinical relevance, which is probably attributed to placebo effects from incomplete blinding due to acupuncture's nature. But acupuncture for peripheral joint osteoarthritis showed significant and clinically relevant benefits compared with waiting list control, which may be involved expectation or placebo effects [15].

## **Efficacy**

Pain relief for short term is the most recognized effect of acupuncture for KOA, but with short and long-term improvement of physical function [16]. A meta-analysis in 2017 that included 11 RCTs with 695 subjects about EA's effect on KOA showed that EA was more effective than

pharmacological therapy and manual acupuncture in pain relief and improvement of physical function. The review also implied that the EA should be applied for at least 4 weeks [17]. Many similar reviews with more participants provided evidence support for acupuncture as an alternative therapy for patients with osteoarthritis. For instance, a systematic review in 2016 that included thirty-one randomized controlled studies of 3,187 participants indicated that EA treatment could relieve the pain and other symptoms of knee osteoarthritis, improved the patients' quality of life [18]. The systematic review in 2014 about acupuncture used in osteoarthritis included 12 trials with 1763 subjects, and concluded that acupuncture significantly reduced pain intensity, improved functional mobility and life quality [19]. A systematic review with network meta-analysis in 2013 included 114 trials with 9709 participants. The results indicated that acupuncture could be one of the more effective physical treatments for relieving pain in short-term due to knee osteoarthritis. But better quality of research is warrants to confirm the effectiveness [20].

Acupuncture has better cost-effectiveness than transcutaneous electrical nerve Stimulation (TENS) in non-pharmacological interventions for KOA [21].

## **Mechanism**

Acupuncture intervention is associated with specific and nonspecific effects, specific needling components include location, insertion depth, stimulation, needle size and number, specific non-needling components are psychological and physiological components such as history, diagnosis, palpation, moxibustion. And non-specific components are time, attention, credibility and expectation [22]. Sham acupuncture is related to moderately large nonspecific effects, making relatively small specific effects difficult to be detected [23].

Some results in clinical trials show the equivalent effect between verum and sham acupuncture, especially when controlled by non-inert therapy or measured by subjective outcomes such as self-report scales [24]. However, individual patient data meta-analysis that included 8 high quality trials showed that true acupuncture's effect is superior to both sham and no acupuncture control in chronic pain conditions such as back and neck pain, osteoarthritis, chronic headache and shoulder pain. The results indicated the acupuncture is more than a placebo, and the factors for both specific effect and non-specific effects are important for effective acupuncture [25].

The mechanism study by functional magnetic resonance imaging (fMRI), other objective outcomes or results from experimental study also showed the different effects in verum acupuncture compared with sham acupuncture. Chronic pain condition such as osteoarthritis is relevant to neuropathic mechanism, which presented as central sensitization, more activity in the periaqueductal grey matter, etc. The study by fMRI revealed that the acupuncture's effect on knee OA pain involving prevention of cortical thinning and decrease of functional connectivity in major pain related areas through descending pain modulatory pathway. Acupuncture modulates cortical thickness and functional connectivity in knee osteoarthritis patients [26].

Another fMRI research on resting state functional connectivity in KOA patients showed compared with sham acupuncture, verum acupuncture enhanced functional connectivity (FC) with rostral anterior cingulate cortex/medial prefrontal cortex, which is a key area in the descending pain modulatory system. And the right frontoparietal network (rFPN) connectivity with the left insula is significantly correlated with symptomatic improvement and also enhanced with verum acupuncture [27].

These results indicated the different mechanism between verum and sham acupuncture. The mechanism of analgesia effect of acupuncture is complicated with central nervous system including the cerebral cortex, cerebral ganglia, brain stem and spinal cord, and related to neurotransmitters and neurohormones such as opioids and  $\gamma$ -aminobutyric acid, signaling pathways and immune response [28].

In our study of gait analysis during stair climbing before and after EA in KOA patients, though Western Ontario and McMaster Universities Arthritis Index (WOMAC) scores showed significant improvement in both EA group and minimal acupuncture (MA) control, stair-climbing efficiency measured by step velocity and cadence was improved only in EA group. Maximal ankle plantar flexor moments during both ascending and descending stairs, and second peak external knee adduction moment (PEKAM) during ascending stairs increased after EA treatment. First PEKAM and second PEKAM during descending stairs decreased after MA treatment. No significant difference showed between EA and MA groups, suggested the intergroup change might be too small. However, the result also confirmed that the minimal acupuncture is not inert intervention, and indicated the various mechanism of different effect between EA and MA on gait variables [29].

## Adverse events

A systematic review summarized the adverse events as localized swelling, pain, sleepiness, fainting, nausea and bruise at needling sites. And the odds ratio associated with acupuncture was 1.44 compared with controls [19], indicating acupuncture is a safe therapy of low risk with qualified practitioners.

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