

# A literature review of basic studies on the mechanisms of acupuncture therapy in ischemic stroke rehabilitation

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### ABSTRACT

The World Health Organization (WHO) suggests acupuncture as an alternate and complementary method for treating strokes and for enhancing stroke care. Results from clinical trials and meta-analyses have shown that acupuncture is effective in restoring balancing function after a stroke, decreasing spasticity, boosting muscle strength, and enhancing general well-being.

It is yet unknown what causes acupuncture to be effective in stroke therapy. This study's objectives were to perform a review of the literature, synthesise the current theories behind ischemic stroke rehabilitation using acupuncture and Electroacupuncture (EA) therapy, and describe the most often used acupoints linked to these outcomes. The research in this review suggests that acupuncture/EA

has positive effects on ischemic stroke rehabilitation through five main distinct mechanisms: 1) Support for neurogenesis and cell proliferation in CNS. 2) Controlling cerebral blood flow in the ischemic area, 3) Preventing apoptosis there, 4) Controlling neurochemicals, and 5) Improving memory and Long-Term Potentiation (LTP) after a stroke.

**Key Words:** *Acupuncture; Cerebral ischemia; Basic research; Stroke; Rehabilitation*

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### INTRODUCTION

According to a recent text, a stroke is "rapidly developing clinical signs of focal (or global) disturbance of cerebral function, lasting more than 24 h or leading to death, with no apparent cause other than that of vascular origin" [1]. It is defined as an acute focal injury of the Central Nervous System (CNS) caused by a vascular cause such as cerebral infarction, intracerebral haemorrhage, or subarachnoid haemorrhage. After ischemic heart disease, stroke was the second-leading cause of death globally in 2013, accounting for 11.8% of all fatalities worldwide. Between 1990 and 2010, the global burden of ischemic and hemorrhagic stroke increased dramatically [2].

#### Pathophysiology: Ischemic stroke

A number of different events can cause or be induced by one another in the ischemia cascade, which is a heterogeneous phenomena [3,4]. Vascular impairment is the main cause of 85%–90% of acute strokes. because of its poor respiratory reserve, the brain has a high risk of ischemia injury, as well as reliance on aerobic metabolism. Damage duration, severity, and location all affect how much damage is done

and the site of the ischemia [5]. Computed tomography and macroscopic alterations in the brain's tissue.

The progression of a stroke can be divided into three stages using macroscopic changes in the brain tissue and alterations seen on Computed Tomography (CT) or Magnetic Resonance Imaging (MRI) scans.

In the acute stage, the depletion of oxygen and glucose will result in the following effects: 1) ion gradient disruption, which results in cytotoxic edema and the release of excitatory neurotransmitters (such as glutamate from the astrocytes); and 2) a change from aerobic to anaerobic metabolism, which results in metabolic acidosis. Acute necrosis or cell death is the result of these initial events [6].

In the subacute stage of stroke, the upregulated genes and stress signals lead to apoptosis signals and activation of the inflammatory cascade and during the chronic stage of stroke Neurogenesis, angiogenesis, and synaptogenesis are the dominant mechanisms during the chronic stage of the disease.

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### Treatment of Ischemic Stroke through western medicine

The main treatment objective after focal cerebral ischemia is to avoid or reverse brain damage and to improve cerebral perfusion in the surrounding ischemic penumbra by widening blood vessels. The use of thrombolytic and anticoagulant medication can aid in the restoration of nervous system function [7]. Recombinant Tissue Plasminogen Activator (rtPA) administration within three hours of the beginning of a stroke increases clinical outcomes; Intravenous (IV) rtPA failure to open big vessel occlusions alone are candidates for endovascular revascularization with the injection or by using an endovascular mechanical thrombectomy or a thrombolytic agent [8]. Thrombolytics therapy includes taking aspirin with an antiplatelet within 48 hours after the stroke starts to lower the likelihood of a recurrence.

### Treating ischemic stroke through acupuncture

One of the oldest and most well-researched methods of Chinese medicine is acupuncture, which involves inserting a tiny needle into the skin or deeper tissues at certain spots on the body (called acupoints). Manual, electrical, or thermal manipulation of this needling is possible. Acupoints may be excitable muscle/skin-nerve complexes with a high density of nerve endings, according to recent studies [9]. Afferent fibres are activated by manual acupuncture or Electroacupuncture (EA) at certain acupoints, which then convey signals to the spinal cord. The primary biological mediators of the therapeutic effects of this age-old practise in the CNS are endogenous opioids. A recent number of certain groups of chemicals, including neurotransmitters (catecholamine, acetylcholine, serotonin, glutamate, and Gamma-Aminobutyric Acid [GABA], neuropeptides, cytokines, and growth factors) have been suggested as potential mediators for the effects of acupuncture. The neuronal specificity of acupoints has been investigated using Diffusion Tension Imaging (DTI) and Functional MRI (fMRI) [10]. This mini-review examines the findings from a survey of the literature on the mechanisms involved in acupuncture's effectiveness in ischemic stroke recovery, lowering post-stroke infarct volume, and neurological impairment. The preclinical data in this review support the advantages of ischemic stroke five key techniques are used to achieve rehabilitation [11]:

- (1) Encouraging the spread of cells that remain in the CNS.
- (2) Control of cerebral blood flow through angiogenesis and vasoactive mediators.
- (3) Direct inhibition of the intrinsic and extrinsic pathways or associated mechanisms to prevent apoptosis.
- (4) Potentiation and modulation of ischemia cascade neurochemical pathways.
- (5) Regulation of ischemic cascade neurochemicals and regaining hippocampal learning and memory processes [12].

### DISCUSSION

In this review, acupuncture demonstrated a positive impact on the rehabilitation of ischemic stroke in animal trials through five key processes (Scheme 1):

- (1) Stimulation of cell growth.
- (2) Control of cerebral blood flow, confined to neurogenic regions and some ischemic tissues.
- (3) Anti-apoptosis through direct involvement in angiogenesis and

vasoactive mediator regulation; the associated pathways of the intrinsic and extrinsic routes.

- (4) Control of the implicated neurochemicals as neurotransmitters, antioxidants, and inflammatory-related molecules at critical stages of the ischemia cascade [13]. Additionally by chemicals, neurotrophic factors, metabolic substrates; and finally, the memory and learning functions of the hippocampus [14].

The first review examined the effects of acupuncture treatment on neurogenesis following a preclinical study that was published up until August 2015 in a systematic review and meta-analysis. Ischemic stroke in experimentation [15]. The study's findings show that acupuncture may help with neurological symptoms, ischemic stroke impairments, and cerebral edema reduction and that the processes have a good correlation with the promotion of natural neurogenesis (Figure 1). The second article is a Cochrane review of the effectiveness of conclusions on the efficacy and safety of acupuncture therapy in subacute or chronic ischemic or hemorrhagic stroke that acupuncture may help with some specific neurological deficits as well as general insufficiency, with no clear significant side effects, despite the fact that the majority of the included trials were of low quality, size [16].

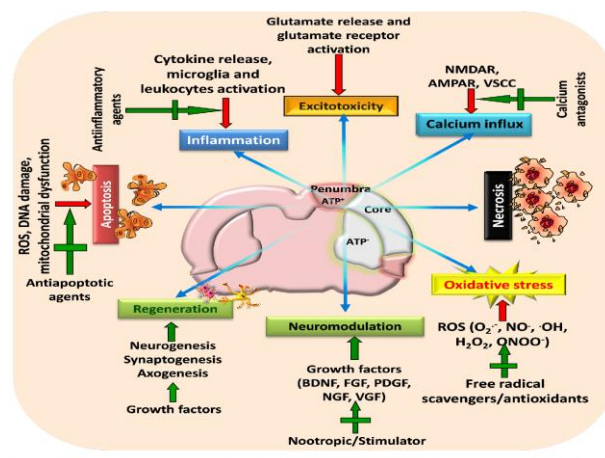


Figure 1) Acupuncture mechanisms in stroke rehabilitation

The five main pathways that contribute to the therapeutic benefits of acupuncture/EA therapy in the treatment of ischemic stroke are depicted [17]. According to the data from the literature review, these five mechanisms are supported:

- (1) Enhancing neurogenesis and cell proliferation in the central nervous system (demonstrating neurogenesis in the subventricular zone of the LV and the Dentate Gyrus (DG) areas in the hippocampus, as well as cell proliferation in ischemic tissue).
- (2) Regulating cerebral blood flow in the ischemic area (demonstrating angiogenesis in the LV and DG, as well as vasoactive modulation in ischemic tissue).
- (3) Inhibiting apoptosis (through modulation of specific and non-specific apoptotic pathways).
- (4) Regulating the release of neurochemicals such as (a) neurotransmitters and receptors, (b) antioxidant enzymes, (c) inflammatory mediators, (d) neurotrophic factors, and (e) anaerobic metabolism.
- (5) Improving memory and LTP deficits following stroke by enhancing LTP in the DG and CA1 regions of the hippocampus [18].

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