



## Review article

## The effects of acupuncture on serotonin metabolism

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## ABSTRACT

**Introduction:** The release of the neurotransmitter, serotonin is associated with different diseases and symptoms and is thought to enhance mood. As acupuncture may effect serotonin metabolism. This paper aimed to review the evidence for changes in serotonin associated with the use of acupuncture.

**Methods:** PubMed, Scopus, RISS, and Web of Science were searched, together with manual searches for articles published between 1974–2015 using the key words “acupuncture” with “5-hydroxytryptamine (5-HT),” “tryptophan,” “5-hydroxytryptophan (5-HTP),” or “5-hydroxyindole acetaldehyde (5-HIAA).”

**Results:** Of the 61 studies identified, 37 (n = 27 animal and n = 10 human studies) were included in which investigators used serotonin or serotonin antagonists/agonists to examine the mechanisms of acupuncture for various symptoms. Investigators in 32 studies concluded that acupuncture improved symptoms, and of the 24 studies measuring serotonin, it was concluded that acupuncture changed the serotonergic mechanism. Acupuncture improves pain, which might be associated with increased levels of serum or plasma serotonin or tissue serotonin in the colon or the trigeminal nucleus caudalis, and decreased levels of platelet serotonin. Receptors 5-HT<sub>1</sub>, 5-HT<sub>2</sub>, and 5HT<sub>3</sub> and subtypes 5-HT<sub>1A</sub> and 5-HT<sub>2A</sub> are related to the mechanisms of acupuncture on pain. Acupuncture improves anxiety/depression, but the evidence for change in the serotonergic mechanism is conflicting. Acupuncture improves diarrhoea, which might be associated with reduced 5-HT expression in the colon and appeared to improve obesity, which might be associated with increased levels of tissue serotonin at the raphe nuclei.

**Conclusion:** Acupuncture appears to improve symptoms and conditions such as pain, obesity, and depression. Those symptoms might be associated with changes in 5-HT.

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**1. Introduction**

For more than 5000 years, acupuncture has been used to treat disease. While acupuncture uses needles to stimulate acupuncture points, electro-acupuncture (EA) uses needles with electric stimulation. A variety of explanations have been provided regarding how acupuncture may work.

In Oriental Medicine, the meridian theory suggests that a life force called qi flows through the body along certain channels (meridians). If the movement of qi is blocked, illness can occur and acupuncture stimulation at precise locations along those channels is thought to unblock the flow of qi, relieving pain and restoring health [1]. In Western models, the gate control theory and neurophysiological theories might explain how acupuncture works. According to the gate control theory, acupuncture closes the gate to pain and reduces pain perception in the brain through stimulation of large nerve fibres [2]. Neurophysiological theories suggest that acupuncture activates receptors and the secretion of neurotransmitters such as endorphins, serotonin, and norepinephrine [3]. For example, EA with low frequency activates the release of beta-endorphin, enkephalin, and endomorphin, which in turn stimulates the mu- and delta-opioid receptors, whereas EA with high frequency activates dynorphin, which stimulates the kappa-opioid receptor [4].

For 40 years, Western methods have measured neurotransmitters and hormones, including endorphins, dopamine, serotonin, epinephrine, norepinephrine, and cortisol, to investigate the physiological changes associated with acupuncture [4,5]. Although numerous clinical trials to examine the mechanisms of acupuncture have been published, reviews of how acupuncture effects changes in specific neurotransmitters are few. Serotonin is an important neurotransmitter related to symptoms such as pain, gastrointestinal functions, sleep, and emotions [6,7]. More than 1.5 billion people worldwide suffer from chronic pain [8]. Estimates also suggest that 9–23% of people worldwide suffer from irritable bowel syndrome and that it is the most common problem of gastrointestinal problems [9]. In addition, 10–15% of people worldwide suffer from insomnia [10] and depression is the 4th leading cause of disability worldwide [11]. Evidence suggests that acupuncture improves pain, diarrhoea, insomnia, and depression and that might be related to abnormal levels of serotonin [12–15]. Serotonin can be measured in urine, platelets, serum, tissues, and plasma. It is synthesized from its precursor amino acid tryptophan and metabolized into 5-hydroxyindole acetaldehyde (5-HIAA) [16] (Fig. 1). This exploratory review summarizes the effects of acupuncture on various symptoms and mechanisms related to serotonin metabolism.

**2. Methods**

*2.1. Search strategy and selection criteria*

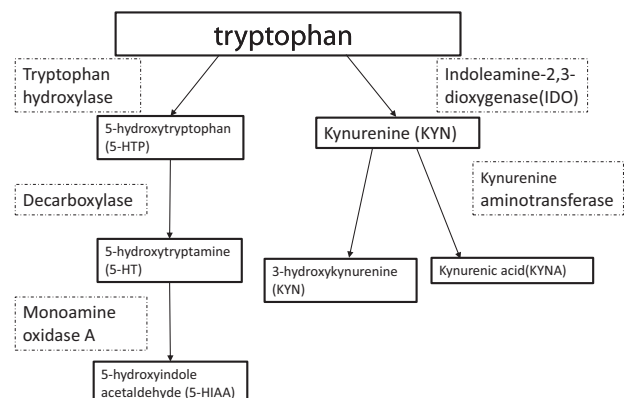
Using online literature search engines and manual searches of articles and their references were selected for review. PubMed, Scopus, Web of Science, and RISS were searched for articles

published from 1974 to 2015 using key words, “acupuncture” with “5-hydroxytryptamine (5-HT/5HT),” “tryptophan,” “5-hydroxytryptophan (5-HTP),” or “5-hydroxyindole acetaldehyde (5-HIAA).” The search was limited with the key phrases “clinical trial, human, English” or “experimental, animal, English.” Clinical trials and experimental studies were included if they examined the mechanisms of acupuncture on serotonin metabolism and if they were published in English. Exclusions were if the full text was unavailable; if they did not provide serotonin levels; if they did not investigate serotonin metabolism; if they used auricular or hand acupuncture with different acupuncture-point names than body acupuncture; if they used moxibustion, bee venom, far-infrared rays, or lasers; if they did not use acupuncture needles; or if they did not use an experimental design.

The effect size was calculated using Hedges’ g for each trial using differences in the means of serotonin levels and symptoms in the acupuncture and control groups [17]. Hedges’ g is the correction for Cohen’s d [18], and provides a superior estimate of the standardized mean difference with small samples [19]. Descriptive data synthesis was employed together with the Cochrane group’s tool to assess the risk of bias when evaluating clinical studies [20]. This tool consists of six domains: sequence generation; allocation concealment; blinding of participants, personnel, and outcomes; incomplete outcome data; selective outcome reporting; and other sources of bias. Experimental studies were evaluated for the presence of each domain and awarded one point for each domain present. Revised standards for reporting interventions in clinical trials of acupuncture (STRICTA) was used to evaluate quality of reporting [21]. STRICTA consists of the acupuncture rationale, details of needling, treatment regimen, other components of treatment, practitioner background, and control or comparator interventions.

**3. Results**

A total of 47 articles were identified in PubMed, 15 articles in Scopus, 33 articles in Web of Science, 34 articles in RISS, and one article was identified by a manual search in articles’ references.



**Fig. 1.** Tryptophan metabolism.

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