

REVIEW

Acupuncture for Parkinson's Disease: a review of clinical, animal, and functional Magnetic Resonance Imaging studies

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Abstract

Acupuncture has been commonly used as an adjuvant therapy or monotherapy in the treatment of Parkinson's disease in China and in other countries. Animal studies have consistently show that this treatment is both neuroprotective, protecting dopaminergic neurons from degeneration and also restorative, restoring tyrosine hydroxylase positive dopaminergic terminals in striatum, resulting in improvements in motor performance in animal models of Parkinsonism. Studies show that this protection is mediated through the same common mechanisms as other neuroprotective agents, including anti-oxidative stress, anti-inflammatory and anti-apoptotic pathways at molecular and cellular levels. Restoration of function seems to involve activation of certain compensatory brain regions as a mechanism at the network level to correct the imbalances to the nervous system resulting from loss of dopaminergic neurons in substantia nigra. Clinical studies in China and Korea, in particular, have shown a positive benefit of acupuncture in treating Parkinson's disease, especially in reducing the doses of dopaminergic medications and the associated side effects. However, large and well-controlled clinical

trials are still needed to further demonstrate the efficacy and effectiveness of acupuncture in the treatment of Parkinson's disease.

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Key words: Parkinson disease; Acupuncture; Neuroprotective agents; Tyrosine 3-monooxygenase; Review

The use of acupuncture for treating different illnesses originated in China about three thousand years ago, as an important part of Traditional Chinese Medicine. The treatment of Parkinson's tremor with acupuncture and herbal medicine has a long history under the category of "trembling" and "convulsive" disease. Acupuncture treatment not only treats the brain where the dopaminergic neurons have been lost, which is the hallmark of Parkinson's disease (PD), but also benefits the other organ systems of Traditional Chinese Medicine, and is therefore, also helpful for coping with non-motor related symptoms and overall quality of life in PD patients. This review summarizes the current understanding of how acupuncture works in treating PD, based on information obtained from preclinical and clinical trial studies, and functional network studies in humans.

INTRODUCTION TO ACUPUNCTURE AND ITS USE IN THE TREATMENT OF PD

Acupuncture is the primary therapy of Chinese medicine, as described in *Huang Di Nei Jing* in the first century BC.^{1,2} Acupuncture is very much respected in China, so much so that its use was approved even during the Chinese culture revolution.³ Classical acupuncture is based on 14 mapped main channels on the body with about 365 acu-points distributed on the channels

(meridian system); the flow of *Qi* (the vital life force or some kind of "energy") maintains the balance and harmony of *Yin* and *Yang*. Any blockage of these channels or abnormal movement of *Qi* will result in illness, and acupuncture by stimulating these acupoints along the meridian channels with needles helps to restore movement of the *Qi* and *Qi* homeostasis (De *Qi*), thus modulating the autonomic nervous system and relieving the symptoms of various illnesses.^{4,5} Acupuncture is especially known for its effectiveness in reducing pain such as dental and back pain due to triggering release of analgesic neuropeptides.^{1,6,7} Acupuncture is delivered by manual insertion of a needle or an additional maneuver through twisting of the needles periodically. In addition, the needles can serve as electrodes to deliver a current stimulation with certain frequency (electroacupuncture, EA).⁸ For example, in rodents studies, 100 Hz is considered the most effective frequency to achieve a beneficial effect by acupuncture.^{9,10}

The substrate for the meridian channels have been under intense investigation. For example, connective tissues or perivascular space with decreased electrical impedance and increased electrical conductivity have been suggested to constitute the meridian channels with acupoints along the pathway.^{4,11} In addition, the brain regions responsible for acupoint and triggered activity in central nervous system are identified as extending from the dorsomedial prefrontal cortex, medial mesencephalic reticular formation and brainstem network through the medial thalamus and the hypothalamus and lateral habenular nucleus, medulla oblongata and ventrolateral periaqueductal gray.^{3,5,8} Interestingly, the habenula is suggested to be an anatomical substrate for the control of depression in a PD model,¹² and relief from depression is one of neuropsychiatric benefits resulting from acupuncture treatment of PD. Functional MRI (fMRI) studies suggest additional involvement of posterior medial cortex and temporal cortex in the central effect of acupuncture, named the "limbic-paralimbic-neocortical network".¹³ For example, acupuncture modulates the fMRI BOLD signal in areas associated with pain (anterior cingulate cortex and periaqueductal gray), emotion (the amygdala), and memory (hippocampal formation and middle temporal gyrus).^{13,14} These areas are thought to be activated in acupuncture which disrupts the pathophysiological neuronal networks and therefore relieves the symptoms by replacing them with "therapeutic" network activation.¹⁵

PD is the second largest neurological disorder next to Alzheimer's disease. With L-dopa medication treatment, patients often develop involuntary motor movements called L-dopa-induced dyskinesia after 5-10 years of use.¹⁶⁻¹⁸ When conventional treatment with medication is not satisfactory, patients often resort to complementary alternative medicine such as acupuncture in hope of getting symptomatic improvement without having disruptive side effects of pharmacotherapy.¹⁹

In practice, complementary alternative medicine (CAM) with acupuncture as the key component is widely used world-wide in treating PD.¹⁹⁻²⁵ At least 61% of PD patients in East Asia (Singapore) and 50% of Latin-America (Argentina) and 1/3 in Sweden use at least one type of CAM treating PD symptoms, with acupuncture treating tremor in PD predominantly.²⁰⁻²² A study in America shows that 40% of PD patients use at least one type of CAM for treatment,²³ similar to the United Kingdom;²⁴ the number of CAM users has been increasing every year.^{19,25} In particular, with the coverage of acupuncture by health insurance, acupuncture users could be expected to further increase.^{1,22}

CLINICAL STUDIES OF ACUPUNCTURE IN TREATING PD

Just like the higher use of CAM in Asia, the evaluation of CAM tends to be more positive in Asia and foreign-language journals, for example, China, compared to well-known journals.^{22,26,27} Acupuncture has been used in Eastern Asia to treat PD under the category of "trembling" and "convulsive disease" long ago, in particular for the control of tremor and pain, along with herbal medicine.²⁸⁻³⁰ In China, clinical studies show that acupuncture can help improve both motor symptoms and non-motor symptoms such as insomnia, depression, constipation and overall life quality for PD patients, and additionally, the dose of medication and its side effect are reduced.³¹⁻³⁵ Consistently, Korean studies show that acupuncture improves unified PD rating score (UPDRS) and adjuvant therapy combined with medication helps to reduce the doses and side effects.³⁶⁻³⁸ Reviews of Chinese clinical trials, with meta-analysis on selected trials (meeting inclusion criteria) suggest that the effectiveness of scalp acupuncture (a type of acupuncture, in which needles are placed on the head) treatment for PD is promising and a larger well controlled trial is needed to confirm the efficacy of scalp acupuncture.³⁹

Acupuncture conducted in western countries has overall promising results, but they are not conclusive in particular for the motor rating score. For example, a practitioner's notes showed that acupuncture at different locations in the body for a PD patient with 25 treatments for 2-3 months helped to remove or reduced the pain / muscle rigidity, tremor and depression.⁴⁰ This treatment works well for the early treatment when PD is first manifested⁴⁰ and also for a patient who had PD for 12 years.⁴¹ Pilot studies with PD patients comparing before and after treatment in USA show that acupuncture is safe and well-tolerated,^{42,43} significantly improves sleep and rest in PD patients and the majority of patients reported subjective improvement in handwriting, depression, tremor and slowness.^{42,43} With a quite different acupuncture point placement, another clinical trial in USA showed that there is a trend of im-

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