Update on Mechanisms Underlying Peripheral and Central Neural Actions in Acupuncture Autonomic Cardiovascular Regulation

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Acupuncture is part of traditional Chinese medicine used for ~6,000 years for a number of clinical conditions. Both manual and electroacupuncture (MA, EA) stimulate group III and IV somatic afferent nerves to modulate sympathetic and parasympathetic outflow and hence cardiovascular function. MA but not EA stimulates afferent endings through a TRPV1 receptor mechanism. Hypothalamic, midbrain and medullary regions process EA evoked activity through the actions of endorphins, enkephalins, endocannabinoids, γ-aminobutyric acid (GABA), acetylcholine and glutamate, among others, to lower elevated and raise depressed blood pressure (BP). Low frequency EA applied at acupoints overlying the median (pericardial meridian, P5 and P6) and deep peroneal (stomach meridian ST36 and ST37) nerves is most effective. EA in cold-induced and DOCA salt models of hypertension lowers BP through an enkephalinergic mechanism in the rostral ventrolateral medulla. Using insights gained from experimental investigations, compared to sham stimulation of ineffective acupoints, EA applied for 30 min once weekly over eight weeks at P5-P6 and ST36-ST37 reduces systolic and diastolic BPs in ~ 70% of a group of patients with mild to moderate hypertension. The onset of action requires 4-6 weeks, but is prolonged, lasting for a month after terminating EA. Despite insight into many of acupuncture's mechanisms more work is required to determine if: 1) non-responders can be converted to responders, 2) EA chronically lowers BP in hypertensive patients, 3) auricular acupuncture lowers elevated BP and 4) there are additional physical-chemical mechanisms occurring at sites of peripheral stimulation that underlie acupuncture's local and systemic actions.

Effect of acupuncture on cardiac and renal sympathetic nerve activities

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Acupuncture is known to affect hemodynamics through modulation of sympathetic nerve activity (SNA). The sympathoinhibitory action of acupuncture is attractive as a treatment modality of cardiovascular diseases such as heart failure in which sympathetic hyperactivity is considered a major aggravating factor. To apply acupuncture to the treatment of cardiovascular diseases including heart failure, we have investigated an impact of acupuncture on hemodynamics and SNA. When cardiac SNA (CSNA) and renal SNA (RSNA) were simultaneously measured during electroacupuncture applied to hind limbs in anesthetized cats, arterial pressure (AP) and RSNA were usually decreased. In contrast, both heart rate (HR) and CSNA increased in response to electroacupuncture in some individuals. Although the hypotensive effect induced by the hind-limb electroacupuncture may be beneficial to hypertensive patients with bradycardia, it is desirable that electroacupuncture can reduce CSNA and HR for potential cardioprotection. As a result of searching for a stimulation site to decrease CSNA, it was found that acupuncture to a particular point of the auricle always decreased CSNA, AP and HR in anesthetized rats. In addition, we examined the responses of AP and HR to the auricular acupuncture in healthy volunteers. The auricular acupuncture significantly decreased HR but did not significantly decrease AP in humans. Thus, acupuncture may cause regional differences in efferent SNA, and the selection of a proper acupuncture point may lead to the development of a novel treatment modality for various cardiovascular diseases.

Spinal mechanism of analgesic effects of acupuncture in the rat models of persistent pain

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Background: Previously, we reported that the involvement of spinal α2 adrenergic pathway in the electroacupuncture (EA) induced analgesia in the rat model of ankle sprain pain. In the present study, we investigated the effects of combined treatment of EA and selective serotonin/norepinephrine-reuptake inhibitor (SNRI) on the neuropathic pain.
Aim: In the present study, we sought to determine whether a treatment with EA produces analgesia and whether EA in combination with a subeffective dosage of milnacipran (an SNRI) exhibits an additive effect in L5 spinal nerve ligation (SNL) induced neuropathic rats.
Methods: Mechanical allodynia and thermal hyperalgesia were assessed by measuring paw withdrawal thresholds and latencies in response to mechanical and thermal stimuli, respectively, 1 day before and 5 days after neuropathic surgery. In addition, on day 5 post-SNL, time courses of behaviors were assessed after intrathecal (i.t.) milnacipran (1, 5, and 20 μg) administration. EA (10 Hz/1 mA) was administered at the ST36 and GB34 acupoints for 30 minutes on day 5 and the time courses of behaviors were assessed. Similarly, when treated in combination (milnacipran [5 μg, i.t.] and EA [10 Hz/1 mA]), time courses of behaviors were assessed at the same time points.
Results: Combined treatment with EA and milnacipran (5 μL) produced more potent antiallodynic and antihyperalgesic effects than those obtained from EA or milnacipran alone at 1, 2, and 4 hours after treatment, indicating an additive effect. In addition, the analgesic effect of EA plus milnacipran was almost completely abolished by the catecholamine neurotoxin 6-hydroxydopamine hydrobromide (25 μg), which depletes spinal norepinephrine, and by yohimbine (an α2-adrenoceptor antagonist, 30 μg, i.t.). Somewhat surprisingly, the analgesic effect of milnacipran plus EA lasted for 6 hours.
Conclusions: Our findings suggest that coapplication of EA and milnacipran enhanced analgesic effect by activating spinal noradrenergic systems coupled with spinal α2-adrenoceptors and prolongs the duration of analgesia.

Mechanism of acupuncture effect on chemotherapy-induced peripheral neuropathy

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Paclitaxel (PTX) is a mitotic inhibitor used in cancer chemotherapy, however, it causes chemotherapy-induced peripheral neuropathy (CIPN). The acupuncture stimulation (ACU) has been used to treat dysesthesia and paresthesia.
Therefore, we tested the influence of electro-ACU with PTX-CIPN model rats.

The SD rats were randomly divided into 4 groups: PTX group, ACU of PTX pre-treatment (ACU-prePTX; ACU started on day 0), ACU of PTX post-treatment (ACU-postPTX; ACU started on day 14), and control group. All rats were injected intraperitoneally on 4 alternate days (days 1, 3, 5, and 7) with vehicle (saline) or 2.0 mg/kg PTX. Electro-ACU, which caused slight muscle twitch, was applied to ZuSanli acupoint (ST36) in the limbs every other day (right side, 1Hz, 20 min., 3-5V). Behavioral assays were carried out by mechanical allodynia von Frey hair test in the feet. The lumbosacral spinal cord was collected for microscopy examination.

PTX and ACU-postPTX group produced significant mechanical allodynia in the feet, but ACU-prePTX group did not show any decrease in the mechanical threshold. In the PTX and ACU-postPTX, activity of astrocyte was recognized.

Our study indicates that applying ACU before PTX administration relieves PTX-CIPN by suppressing the astrocytes in the dorsal horn of spinal cord. Pathogenic basis of the CIPN have relation to peripheral microvascular damage. Our preliminary research indicated that acupuncture stimulation improves vascular endothelium NOS function and blood flow. These findings suggest that improvement of peripheral circulation function by acupuncture stimulation may constitute a novel treatment for this neuropathy.