

英国中医药学会
**The Association of Traditional Chinese Medicine and
Acupuncture UK**

TCM Research Updates

Issue No 10
1st April 2014



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Abundant expression and functional participation of TRPV1 at Zusanli acupoint (ST36) in mice: mechanosensitive TRPV1 as an “acupuncture-responding channel”

<http://www.biomedcentral.com/1472-6882/14/96/>

BMC Complementary and Alternative Medicine. Published: 11 March 2014.

By Shu-Yih Wu

Background

Acupuncture is a therapy that involves applying mechanical stimulation to acupoints using needles. Although acupuncture is believed to trigger neural regulation by opioids or adenosine, still little is known about how physical stimulation is turned into neurological signaling. The transient receptor potential vanilloid receptors 1 and 4 (TRPV1 and TRPV4) and the acid-sensing ion channel 3 (ASIC3) are regarded as mechanosensitive channels. This study aimed to clarify their role at the Zusanli acupoint (ST36) and propose possible sensing pathways linking channel activation to neurological signaling.

Methods

First, tissues from different anatomical layers of ST36 and the sham point were sampled, and channel expressions between the two points were compared using western blotting. Second, immunofluorescence was performed at ST36 to reveal distribution pattern of the channels. Third, agonist of the channels were injected into ST36 and tested in a mouse inflammatory pain model to seek if agonist injection could replicate acupuncture-like analgesic effect. Last, the components of proposed downstream sensing pathway were tested with western blotting to determine if they were expressed in tissues with positive mechanosensitive channel expression.

Results

The results from western blotting demonstrated an abundance of TRPV1, TRPV4, and ASIC3 in anatomical layers of ST36. Furthermore, immunofluorescence showed these channels were expressed in both neural and non-neural cells at ST36. However, only capsaicin, a TRPV1 agonist, replicated the analgesic effect of acupuncture when injected into ST36. Components of calcium wave propagation (CWP, the proposed downstream sensing pathway) were also expressed in tissues with abundant TRPV1 expression, the muscle and epimysium layers.

Conclusions

The results demonstrated mechanosensitive channel TRPV1 is highly expressed at ST36 and possibly participated in acupuncture related analgesia. Since CWP was reported by other to occur during acupuncture and its components were shown here to express in tissues with positive TRPV1 expression. These findings suggest TRPV1 might act as acupuncture-responding channel by sensing physical stimulation from acupuncture and conducting the signaling via CWP to nerve terminals. This study provided a better understanding between physical stimulation from acupuncture to neurological signaling.

Role of acupuncture in the management of diabetic painful neuropathy (DPN): a pilot RCT

<http://aim.bmj.com/content/early/2014/03/21/acupmed-2013-010495>.

Acupunct Med doi:10.1136/acupmed-2013-010495; Published Online First 21 March 2014.

By Adam P Garrow

Aims To examine the role of acupuncture in the treatment of diabetic painful neuropathy (DPN) using a single-blind, placebo-controlled RCT and to collect data that would be required in a future definitive study of the efficacy of acupuncture in DPN.

Methods 45 patients were allocated to receive a 10-week course either of real (53%) or sham (47%) acupuncture. Five standardised acupuncture points on the lower limb of each leg were used in the study: LR3, KI3, SP6, SP10 and ST36. Outcome measures included the Leeds Assessment of Neuropathic Symptoms and Signs (LANSS) scale, lower limb pain (Visual Analogue Scale, VAS); Sleep Problem Scale (SPS); Measure Yourself Medical Outcome Profile (MYMOP); 36-item Short Form 36 Health Survey and resting blood pressure (BP).

Results Over the 10-week treatment period, small improvements were seen in VAS -15 (-26 to -3.5), MYMOP -0.89 (-1.4 to -0.3), SPS -2.5 (-4.2 to -0.82) and resting diastolic BP -5.2 (-10.4 to -0.14) in the true acupuncture group. In contrast, there was little change in those receiving sham acupuncture. A moderate treatment effect in favour of active acupuncture was detected in MYMOP scores -0.66 (-0.96 to -0.35) but non-significant effect sizes in LANSS Pain Scale -0.37 (-2.2 to 1.4), resting diastolic BP -0.50 (-3.0 to 1.99) and the SPS -0.51 (-2.2 to 1.16).

Conclusions We have demonstrated the practicality and feasibility of acupuncture as an additional treatment for people with DPN. The treatment was well tolerated with no appreciable side effects. Larger randomised trials are needed to confirm the clinical and cost-effectiveness of acupuncture in the treatment of DPN.

Observation on the therapeutic effect of pricking needling at Sifeng (EX-UE 10) in combination with *Tuina* for antibiotic-associated diarrhea in infants

<http://www.sciencedirect.com/science/article/pii/S1003525714600052>

World Journal of Acupuncture – Moxibustion 2013; 23(4): 19-22. By Gang Feng

Objective

To observe the therapeutic efficacy of pricking needling at Sifeng (EX-UE10) in combination with *Tuina* in treating antibiotic-associated diarrhea (AAD) in infants.

Methods

According to random number table, 82 patients were randomized into a treatment group and a control group, 41 patients were included in each

group. The patients in the two groups were not subjected to fasting diet; fluid replacement, correction on electrolyte disturbance, withdrawal of antibiotics and other symptomatic treatments were all carried out for them. The patients in the treatment group were simultaneously treated by using pricking needling at EX-UE 10 in combination with *Tuina* manipulation, while the patients in the control group were orally administered with Medilac Vita. Five days were considered as a treatment course for both groups, and the therapeutic effect was evaluated after a treatment course.

Results

the number of patients with concurrent symptoms in the treatment group were significantly less than

that in the control group ($P<0.05$); the number of patients not showing leucopenia in the treatment group were significantly less than that in the control group ($P<0.05$); the total effective rate of 92.7% (38/41) in the treatment group was significantly higher than that of 73.2% (30/41) in the control group, and the difference in therapeutic effect between the two group was statistically significant ($P<0.05$).

Conclusion

The therapeutic effect of pricking needling at EX-UE 10 in combination with *Tuina* on the basis of conventional treatments is better than that of combination with Medilac Vita in treating AAD in infants, and it could rapidly improve systemic symptoms and indices of stool.

The Effects of Needling Fenglong (ST40) and Neiguan (PC6) on IL-17 of ApoE-Gene-Knockout Mice's Liver

<http://www.hindawi.com/journals/ecam/2014/691863/abs/>

Evidence-Based Complementary and Alternative Medicine Volume 2014 (2014), Article ID 691863, 5 pages

By Fu Yun Lee

Abstract

The aim of the present paper was to observe the effects of needling ST40 and PC6 on IL-17 of ApoE^{-/-} mice with fatty liver. Forty male ApoE^{-/-} mice were randomized into Needling-Acupoint Group, Simvastatin Intragastric Administration Group, Needling Nonacupoint Group, and Model Group. Each was fed with high fat diet for 8 weeks since 16 weeks of age; after 8 weeks of intervention, mice were sacrificed and tested for various examinations. Result showed that the body weight, TC, and

serum IL-17 in Needling-Acupoint Group decreased. Compared with Model Group, the immunohistochemical expressions of IL-17 in liver tissue were significantly decreased among the other three groups. In conclusion, acupuncture was able to lower the expression of IL-17 level both in serum and liver tissue in ApoE^{-/-} mice, which is helpful to reduce the inflammation and defers the progress from fatty liver to cirrhosis.

Cerebral blood flow-based evidence for mechanisms of low-versus high-frequency transcutaneous electric acupoint stimulation analgesia: A perfusion fMRI study in humans

<http://www.sciencedirect.com/science/article/pii/S0306452214002322>
Neuroscience. Available online 20 March 2014. By Y Jiang.

Brain activities in response to acupuncture have been investigated in multiple studies; however, the neuromechanisms of low- and high-frequency transcutaneous electric acupoint stimulation (TEAS) analgesia are unclear. This work aimed to investigate how brain activity and the analgesic effect changed across 30-min low- versus high-frequency TEAS. Forty-six subjects received a 30-min 2, 100-Hz TEAS or mock TEAS (MTEAS) treatment on both behavior test and functional magnetic resonance imaging (fMRI) scan days. On the behavior test day, the pain thresholds and pain-related negative emotional feeling ratings were tested five times – at 4.5 min before treatment, at 10, 20, and 30 min during treatment and 4.5 min after the treatment. On the fMRI scan day, to match the time-points in the behavioral testing session, the cerebral blood flow (CBF) signals were collected and incorporated with five independent runs before, during and after the treatment, each lasting

4.5 min. The analgesic effect was observed in both the TEAS groups; the analgesic effect was not found in the MTEAS group. The effect started at 20 min during the treatment and was maintained until the after-treatment states. In both TEAS groups, the regional CBF revealed a trend of early activation with later inhibition; also, a positive correlation between analgesia and the regional CBF change was observed in the anterior insula in the early stage, whereas a negative relationship was found in the parahippocampal gyrus in the later stage. The TEAS analgesia was specifically associated with the default mode network and other cortical regions in the 2-Hz TEAS group, ventral striatum and dorsal anterior cingulate cortex in the 100-Hz TEAS group, respectively. These findings suggest that the mechanisms of low- and high-frequency TEAS analgesia are distinct and partially overlapped, and they verify the treatment time as a notable factor for acupuncture studies.

Electroacupuncture and Moxibustion Hinder the Progression of Renal Disease by Modulating Systemic and Renal Renin-Angiotensin System (RAS)

http://www.fasebj.org/cgi/content/meeting_abstract/27/1_MeetingAbstracts/1110.25
The FASEB Journal. 2013;27:1110.25 By. Marcelo Andery Naves.

INTRODUCTION AND AIMS: Systemic and renal RAS are pivotal for the development and maintenance of renal disease. Traditional Chinese Medicine (TCM) is increasingly recognized as an effective therapy in several fields of medicine.

Among its therapeutic strategies are electroacupuncture (EA) and moxibustion (MO). We investigate the effects of EA and MO on RAS in an experimental model of hypertensive and progressive renal disease.

METHODS: Male wistar rats were submitted to 5/6 nephrectomy (5/6 nx) and studied along eight weeks. There were three groups: 5/6 nx (NX), 5/6 nx and sham EA (NX-AS); 5/6 nx and EA-

MO session real acupuncture points (NX-AM). We evaluated 24h-proteinuria, plasma and renal Ang I, Ang II and Ang¹⁻⁷ and plasma renin activity.

RESULTS:

Groups	Ang I (ng/mL)	Ang II (ng/mL)	Ang 1-7 (ng/mL)	Renin Activity
NX	50 ± 13.5 ^ψ	58.7 ± 19.9 ^ψ	4 ± 2.1	22.9 ± 7.2
NX-AS	25 ± 6.6	22.5 ± 6.2	5 ± 1.3	40.1 ± 0.9
NX-AM	88 ± 21.6 [#]	32 ± 9.1 [#]	15.8 ± 7.2 [*]	29.8 ± 4.6 [*]

* (p=<0,05) vs NX and NX-AS;

(p=<0,05) vs NXAS;

^ψ (p=<0,05) vs NX-AS and NX-AM

CONCLUSIONS: EA-MO modulated RAS leading to higher production of systemic and renal Ang¹⁻⁷. Since A¹⁻⁷ is protective against endothelial dysfunction and has vasodilatory and antifibrotic effects, our findings suggest that it could be contribute to the improvement of the progression of renal disease in this model.

Effects of acupuncture at "Zusanli" (ST 36) on cerebral proinflammatory cytokine and plasma neuron specific enolase in septic rats

<http://europepmc.org/abstract/med/24617240/reload=0;jsessionid=CUGFAfkiUgaw3BEFN1yr.18>

Zhong Guo Zhen Jiu 2013; 33(12): 1105-1107. By Wang H.

OBJECTIVE: To explore protective effects of acupuncture at "Zusanli" (ST 36) on cerebral tissue in rats with sepsis.

METHODS: Cecal ligation and puncture (CLP) was applied to duplicate the rat model of sepsis. According to random number table, thirty SD rats were divided into a sepsis model group (group A), asepsis model plus electroacupuncture (EA) group (group B), and a sepsis model plus non-acupoint EA group (group C), ten rats in each one. EA with the same frequency and intensity at "Zusanli" (ST 36) and non-acupoint (0.5 cm laterally to "Zusanli") for 30 min was applied in the group B and group C, respectively. No treatment was given in the group A. 6 hours after CLP, blood was acquired from abdominal aorta to measure the levels of neuron specific enolase (NSE). Then the rats were sacrificed by abdominal aorta exsanguination to take their

cerebral tissue for measuring the levels of tumor necrosis factor-alpha (TNF-alpha) and interleukin-6 (IL-6).

RESULTS: Six hours after CLP, the level of NSE was (3.51 +/- 0.39) ng/mL in group B, which was significantly lower than (7.72 +/- 0.64) ng/mL in group A (P<0.05). The level of NSE was (8.02 +/- 0.72) ng/mL in the group C, which had no statistical significance with group A (P>0.05). The levels of TNF-alpha, IL-6 in cerebral tissue in group B were significantly lower than that of group A and C (all P>0.05).

CONCLUSION: EA at "Zusanli" (ST 36) has certain protective effect on septic rat's brain, which has some relationship with decreasing levels of cerebral tissue proinflammatory cytokine and plasma NSE. EA at non-acupoint has no the same action.

Two sets of acupoint combination of similar functions engage shared neural representation: A functional magnetic resonance imaging study

<http://link.springer.com/article/10.1007/s11655-014-1744-3>

Chinese Journal of Integrative Medicine. March 2014, Volume 20, Issue 3, pp 184-193. By Ling Zhao.

Objective

To investigate whether the neural representations underlying alternating two acupoint combinations (ACs) are the same or not.

Methods

In this functional magnetic resonance imaging study, two sets of analgesia ACs were utilized, including Waiguan (TE5) and Qiuxu (GB40) for Group A, and Neiguan (PC6) and Taichong (LR3) for Group B, which are the most commonly adopted in clinical treatment. Each group had 20 healthy subjects. An experimental design was proposed, which consisted of a pre-needling resting phase, a needling phase and a post-needling resting phase. This paradigm optimally mimics the clinical protocol as well as focuses on both the stimulation and the resting periods. The results were subjected to general linear model analysis, conjunction analysis and the functional connectivity analysis.

Results

The rostral anterior cingulate cortex was engaged in the initiative period of the acupuncture effect in both groups, and it was chosen as the seed region for the functional connectivity analysis for the following resting period. The results showed that several shared brain regions were involved in both groups, in particular the insula, amygdala and hypothalamus. Moreover, significant differences were located at the posterior cingulate cortex as revealed by a two sample *t*-test ($P < 0.05$, corrected). Other regions showed no significant differences. This finding was further supported by the spatial correlation analysis that the two groups were significantly correlated ($r = 0.51$, $P < 0.01$).

Conclusion

This preliminary research helps us understand the neurophysiological mechanisms of acupuncture when following clinical guidelines on ACs, as well as provides an important opportunity to develop better treatment strategies for reducing, or even preventing pain.



Acupuncture and standard emergency department care for pain and/or nausea and its impact on emergency care delivery: a feasibility study

<http://aim.bmj.com/content/early/2014/03/07/acupmed-2013-010501.short>

Acupunct Med doi:10.1136/acupmed-2013-010501, Published Online First 7 March 2014.

By Anthony L Zhang.

Objective To evaluate the feasibility of delivering acupuncture in an emergency department (ED) to patients presenting with pain and/or nausea.

Methods A feasibility study (with historical controls) undertaken at the Northern Hospital ED in Melbourne, Australia, involving people presenting to ED triage with pain (VAS 0–10) and/or nausea (Morrow Index 1–6) between January and August 2010 (n=400). The acupuncture group comprised 200 patients who received usual medical care and acupuncture; the usual care group comprised 200 patients with retrospective data closely matched from ED electronic health records.

Results Refusal rate was 31%, with ‘symptoms under control owing to medical treatment before acupuncture’ the most prevalent reason for refusal (n=36); 52.5% of participants responded ‘definitely yes’ for their willingness to repeat acupuncture, and a further 31.8% responded

‘probably yes’. Over half (57%) reported a satisfaction score of 10 for acupuncture treatment. Musculoskeletal conditions were the most common conditions treated n=117 (58.5%), followed by abdominal or flank pain n=49 (24.5%). Adverse events were rare (2%) and mild. Pain and nausea scores reduced from a mean±SD of 7.01±2.02 before acupuncture to 4.72±2.62 after acupuncture and from 2.6±2.19 to 1.42±1.86, respectively.

Conclusions Acupuncture in the ED appears safe and acceptable for patients with pain and/or nausea. Results suggest combined care may provide effective pain and nausea relief in ED patients. Further high-quality, sufficiently powered randomised studies evaluating the cost-effectiveness and efficacy of the add-on effect of acupuncture are recommended.