Contents

2. Empirical research evaluating the effects of non-traditional approaches to enhancing sleep in typical and clinical children and young people.
3. Transcutaneous Electrical Acupoint Stimulation Improves the Outcomes of In Vitro Fertilization: A Prospective, Randomized and Controlled Study.
4. Neuronal Regeneration after Electroacupuncture Treatment in Ischemia-Reperfusion-Injured Cerebral Infarction Rats.
7. Effects of Acupuncture on 1-chloro-2,4-dinitrochlorobenzene-induced Allergic Contact Dermatitis in Mice.
8. Laser Acupuncture at HT7 Improves the Cerebellar Disorders in Valproic Acid-Rat Model of Autism.
10. An fMRI study of the effects on normal language areas when acupuncturing the Tongli (HT5) and Xuanzhong (GB39) acupoints.
Acupuncture plus Herbal Medicine for Alzheimer’s Disease: A Systematic Review and Meta-Analysis.

By Zhou S, Dong L, He Y, Xiao H.

Abstract

Alzheimer’s disease (AD) is associated with the unprecedented aging tendency in our world population and has become a significant health issue. The use of Traditional Chinese Medicine to treat AD has been increasing in recent years. The objective of this meta-analysis is to evaluate the effectiveness of combining acupuncture with herbal medicine to treat AD. Randomized controlled trials (RCTs) of acupuncture plus herbals versus treatment with western drugs for AD were retrieved from 11 databases. The data were extracted by two authors; dichotomous data were expressed as odds ratio (ORs) and 95% confidence intervals (CIs), while continuous data were calculated by mean differences (MDs) with 95% CIs. Although the combined analysis of the score of Activity of Daily Life (ADL) scale MD was [Formula: see text]3.59 (95% CI 7.18-0.01, [Formula: see text]), which indicates there was no statistically significant difference between the two treatments at reducing the ADL scale score, the pooled results of 12 trials indicated that acupuncture plus Chinese herbal medicine was better than western drugs at improving the effectiveness rate (OR 2.24, 95% CI 1.40-3.56), the combined evidence of 11 articles showed that acupuncture plus Chinese herbal medicine was more effective than western drugs at improving the scores for the Mini Mental State Examination (MMSE) scale (2.10, 95% CI 0.69-3.51, [Formula: see text]) and the traditional Chinese medicine symptom (MD 5.07, 95% CI 3.90-6.25, [Formula: see text]). From the current research results, acupuncture plus herbal medicine may have advantages over western drugs for treating AD. Nevertheless, well-designed RCTs with a larger sample size are required in the future.

Empirical research evaluating the effects of non-traditional approaches to enhancing sleep in typical and clinical children and young people.

By France KG, McLay LK, Hunter JE, France MLS.
Abstract
This paper examines the effects of non-traditional (non-behavioural and non-prescription pharmaceutical) approaches to sleep in children and young people (0-18 y). A systematic search identified 79 studies that met inclusion criteria. Seventeen percent of the studies were rated as having a conclusive level of evidence, forty-two percent with preponderant evidence and forty-one percent with only suggestive evidence. There were promising indications, with certain populations only, for aromatherapy, ketogenic diets, an elimination diet (few foods diet), elimination of cow's milk, avoidance of caffeine, tryptophan with adenosine and uridine, omega-3 and omega-6, valerian, music, osteopathic manipulation and white noise. Bright light therapy and massage returned some positive results. All of these interventions warrant further, more rigorous research. There was limited or no evidence to support acupressure or acupuncture, other diets or dietary supplements, exercise or weighted blankets. Caution is needed in interpreting some studies because poorer quality studies were more likely to return positive results. Suggestions are made for the improvement of large and smaller scale research, especially conceptualization around multiple physiological measures of sleep and the adoption of research methods which are of use in clinical settings.

Transcutaneous Electrical Acupoint Stimulation Improves the Outcomes of In Vitro Fertilization: A Prospective, Randomized and Controlled Study.

Abstract
OBJECTIVES:
To explore whether transcutaneous electrical acupoint stimulation (TEAS) can improve the outcomes of in vitro fertilization (IVF).

SETTING:
IVF center in a university hospital.

PARTICIPANTS:
Four hundred and eighty-one infertile patients with bilateral tubal blockage who were referred for IVF. Patients were randomized into four groups.
**INTERVENTION:**
TEAS was administered for 30 min, respectively, at 24h before TVOR and two hours before ET. The acupoints included SP10 (Xuehai, bilateral), SP8 (Diji, bilateral), LR3 (Taichong, bilateral), ST36 (Zusanli, bilateral), EX-CA1 (Zigong, bilateral), RN4 (Guanyuan), PC6 (Neiguan, bilateral), and RN12 (Zhongwan). Based on different frequencies of TEAS, patients were grouped into a TEAS-2Hz group, a TEAS-100Hz group and a TEAS-2/100Hz group. Patients in the control group only received routine IVF treatment and no TEAS was applied on them.

**PRIMARY AND SECONDARY OUTCOME MEASURES:**
The number of mature oocytes, normally fertilized oocytes and good-quality embryos were used to evaluate oocyte developmental competence of the patients. Data of clinical pregnancy rate (CPR), implantation rate (IR), and live birth rate (LBR) were also obtained.

The levels of neuropeptide Y (NPY), transforming growth factor alpha and granulocyte colony-stimulating factor in the follicular fluids were measured with enzyme-linked immunosorbent assay (ELISA).

**RESULTS:**
No significant differences were found between the control, TEAS-2Hz, TEAS-100Hz and TEAS-2/100Hz groups on the numbers of metaphase II oocytes, normally fertilized zygotes, early cleavage embryos or good quality embryos (P > .05). However, the CPR, IR and LBR of the TEAS-2/100Hz group were significantly higher than those of the other groups, respectively (P < .05). The NPY levels in the follicular fluids of TEAS-2/100Hz group were significantly higher than those of the other groups (P < .05).

**CONCLUSION:**
TEAS using a frequency of 2/100Hz could help to improve the IVF outcomes partly by increasing NPY levels in the follicular fluids.

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**Neuronal Regeneration after Electroacupuncture Treatment in Ischemia-Reperfusion-Injured Cerebral Infarction Rats.**


By Liao SL, Lin YW, Hsieh CL.

**Abstract**
Adult neuronal cells which can regenerate have been reported. The present study investigated whether acupuncture enhances neuronal regeneration in ischemic stroke rats. We established an
ischemic stroke rat model by occluding the cerebral blood flow of the right middle cerebral artery for 15 minutes and then allowing reperfusion in Sprague-Dawley rats. The results indicated that, in these rats, 2 Hz electroacupuncture (EA) at both Zusanli (ST36) and Shangjuxu (ST37) acupoints reduced the infarction/hemisphere ratio 8 days after reperfusion and reduced the modified neurological severity score (mNSS) and increased the rotarod test time 4 and 8 days after reperfusion, respectively. In addition, 2 Hz reduced nestin immunoreactive cells in the penumbra area and the ischemic core area; 2 Hz EA also reduced Ki67 immunoreactive cells and increased glial fibrillary acidic protein immunoreactive cells in the penumbra area. These findings suggest that 2 Hz EA at the ST36 and ST37 acupoints has a neuroprotective role. However, additional studies are needed to further investigate these preliminary results.

Manual Acupuncture Suppresses the Expression of Proinflammatory Proteins Associated with the NLRP3 Inflammasome in the Hippocampus of SAMP8 Mice.

Abstract

OBJECTIVE:
To investigate the effect of manual acupuncture (MA) on NLRP3 inflammasome-related proteins.

METHODS:
SAMP8 mice were randomly divided into Alzheimer's disease (AD) group, the MA group, and the medicine (M) group. Mice in the M group were treated with donepezil hydrochloride at 0.65 μg/g. In the MA group, MA was applied on Baihui (GV20) and Yintang (GV29) for 20 min and then pricked at Shuigou (GV26). The Morris water maze was applied to assess spatial learning and memory. Immunohistochemical staining and western blot analysis were used to observe the expression of NLRP3 inflammasome-related proteins.

RESULTS:
Compared with the normal (N) control group, spatial learning and the memory capabilities of the AD group significantly decreased ($p < 0.01$). The number of NLRP3, ASC, Caspase-1, and IL-1β positively stained cells in the AD group was higher than the N group, and the relative expression levels of
The above proteins were significantly higher than those in the N group ($p < 0.01$). These changes were reversed by both MA and donepezil ($p < 0.01$).

**CONCLUSION:**
MA can improve the learning and memory capabilities of SAMP8 mice.

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**Manual Acupuncture at PC6 Ameliorates Acute Restraint Stress-Induced Anxiety in Rats by Normalizing Amygdaloid Noradrenergic Response.**


**Abstract**
Acupuncture improves ethanol withdrawal-induced anxiety in rats in an acupoint-dependent manner. Thus, the present study investigated the effects of acupuncture on acute restraint stress- (ARS-) induced anxiety. Male rats were exposed to ARS for 3 h followed by acupuncture at either PC6 (Neiguan), HT7 (Shenmen), or a nonacupoint (tail) once a day for three consecutive days. Five minutes after the third acupuncture treatment, anxiety-like behavior was evaluated in an elevated plus maze (EPM). Additionally, plasma corticosterone (CORT) levels were measured by radioimmunoassay and the concentrations of norepinephrine (NE) and 3-methoxy-4-hydroxy-phenylglycol (MHPG) in the central nucleus of the amygdala (CeA) were determined using high-performance liquid chromatography. Acupuncture at PC6, but not HT7 or a nonacupoint, attenuated anxiety-like behavior, but this attenuation was abolished by a postacupunctural intra-CeA infusion of NE. Acupuncture at PC6 also reduced the oversecretion of plasma CORT and inhibited increases in amygdaloid NE and MHPG induced by ARS. Further, Western blot analyses and real-time polymerase chain reaction assays revealed that acupuncture at PC6 prevented ARS-induced enhancements in the protein and mRNA expressions of tyrosine hydroxylase in the CeA. These results suggest that acupuncture performed specifically at acupoint PC6 reduces ARS-induced anxiety-like behavior by dampening amygdaloid noradrenergic responses.
Effects of Acupuncture on 1-chloro-2,4-dinitrochlorobenzene-induced Allergic Contact Dermatitis in Mice.


Abstract
Allergic contact dermatitis (ACD) is a chronic inflammatory skin disease. Topical corticosteroids are the first-line therapy for ACD despite their significant adverse effects. Acupuncture has been widely used in the treatment of various skin diseases, but its underlying mechanism remains unrevealed. In this study, we investigated the characteristics of acupuncture treatment based on effectiveness and mechanism. BALB/c mice received 1-chloro-2,4-dinitrobenzene (DNCB) application to build AD-like model. Results showed that acupuncture was an effective treatment method in inhibiting inflammatory conditions, serum IgE levels, and expression of proinflammatory cytokine Th2 (IL-4, IL-6), and Th2 (IL-1β, TNF-α) mRNA compared with DNCB treatment. Acupuncture treatment also inhibited nuclear factor-κB p65, phosphorylation of IκBα, and phosphorylation of occludin proteins expression. Furthermore, it could improve the expression of epidermal growth factor in both mRNA and protein levels. These results suggest that acupuncture, as an alternative therapy treatment for its no significant side effects, was effective in alleviating ACD by reducing proinflammatory cytokines and changing proteins’ expression.

Laser Acupuncture at HT7 Improves the Cerebellar Disorders in Valproic Acid-Rat Model of Autism.


Abstract
The novel therapeutic strategy against autism is essential due to the limited therapeutic efficacy. Based on the benefit of laser acupuncture at HT7 acupoint on the neurological disorders related with oxidative stress and inflammation, its benefit on oxidative stress, neuroinflammation, and GABAergic/glutamatergic imbalance in cerebellum of autism have been considered. To elucidate this issue, male rat pups were induced autistic-
like conditions by valproic acid (VPA) and treated with laser acupuncture at HT7 acupoint once daily between postnatal Day 14 and Day 40. At the end of study, the changes of oxidative stress markers, the expressions of cytokines interleukin 6 (IL-6) and glutamic acid decarboxylase (GAD) proteins (65 kDa and 67 kDa) together with gamma-aminobutyric acid transaminase (GABA-T) activity and density of Purkinje cell in the cerebellum were assessed. The results showed that laser acupuncture HT7 decreased oxidative stress, IL-6 expression, and GABA-T activity but increased the expressions of GAD 65 kDa together with the density of Purkinje cells in the cerebellum. Therefore, laser acupuncture at HT7 is the potential strategy to improve the cerebellar disorders in VPA-rat model of autism. The mechanism may occur partly via the decrease of oxidative stress status, inflammation, and the improved GABAergic function.

Effects of acupuncture at the ST-36 point on muscle sympathetic nerve activity and blood pressure in normal adults.
By Kimura K, Ishida K, Takahashi N, Toge Y, Tajima F.

Abstract
The aim of the present study was to determine the effects of acupuncture on post-ganglionic muscle sympathetic nerve activity (MSNA) in humans. MSNA was measured in 8 healthy adult males by microneurography evaluation of the left peroneal nerve. Blood pressure (BP) and heart rate (HR) were simultaneously recorded. MSNA was evaluated as the burst rate, with total MSNA, BP and HR normalized to their respective baseline values. After 10min of rest in the supine position, acupuncture was applied to the right ST-36 point in the tibialis anterior muscle for 15min, with recovery then monitored over a 20-min period. While the burst rate and total MSNA remained constant throughout the study, there was a significant decrease in BP during the real but not sham acupuncture procedure (p<0.05). HR did not significantly change throughout the study. The results rule out the role of MSNA in the BP fall during acupuncture at the ST-36 point, and suggest possible involvement of other factors in the fall of BP.
An fMRI study of the effects on normal language areas when acupuncturing the Tongli (HT5) and Xuanzhong (GB39) acupoints.  

Abstract  
Objective Functional magnetic resonance imaging (fMRI) analysis of the effects of acupuncturing the Tongli (HT5) and Tongli (HT5)-Xuanzhong (GB39) acupoints on the normal language areas with a view to providing a theoretical basis for using acupuncture to treat patients with aphasia. Methods This study enrolled healthy volunteers. The following acupoints were stimulated: right Tongli (HT5), right Tongli (HT5)-Xuanzhong (GB39), right Tongli (HT5) sham acupuncture, left Tongli (HT5), and left Tongli (HT5)-Xuanzhong (GB39) acupoints. Acupuncture stimulation was delivered whilst fMRI scanning of the brain was undertaken. Results Ten healthy volunteers (five males) were included in this study (mean age 44.5 ± 2.5 years; range 40-55 years). Based on the statistical analyses, only acupuncturing the right Tongli (HT5) acupoint resulted in activation of multiple regions of the bilateral cerebral hemisphere that were closely related to the language regions. The right Tongli (HT5) stimulation had a laterality index of 0.0952; with the activated voxels on the left side language-related areas being greater than those on the right side. Conclusions Acupuncturing the right Tongli (HT5) acupoint results in activation of the bilateral language-related areas, so this acupoint might be useful for the acupuncture treatment of aphasia caused by cerebral infarction.  

Effect of Electro-Acupuncture on Neuroplasticity of Spinal Cord-Transected Rats.  

Abstract  
BACKGROUND This study aimed to evaluate the effects of electro-acupuncture (EA) on neuroplasticity associated with the expressions of neurotrophic factors (NTFs) and their receptors in rats subjected to spinal cord transection (SCT). MATERIAL AND METHODS A total of 144 rats were randomly divided into 3 groups (n=48 per group): sham-operated
group, SCT group, and EA (electro-acupuncture) group. Rats in SCT and EA groups received spinal cord transection at T10-T11 vertebral levels. Then, EA group rats received EA treatment. Reverse transcription polymerase chain reaction was used to detect NTFs and receptors at the mRNA level. In situ hybridization (ISH) and immunohistochemistry (IHC) were used to detect the expression of NTFs and their receptors. Basso, Beattie, Bresnahan (BBB) scores and cortical somato-sensory evoked potentials (CSEP) were evaluated to assess the recovery of motor and sensory functions. We also measured BDA (Biotinylated dextran amine) axonal tracing, CGRP (Calcitonin gene-related peptide), GAP-43 (Growth-associated protein), and synaptophysin immunohistochemistry (IHC). RESULTS EA treatment led to obvious improvement in hindlimb locomotor and sensory functions. CNTF, FGF-2, and TrkB mRNA were significantly upregulated, while NGF, PDGF, TGF-β1, IGF-1, TrkA, and TrkC mRNA were concomitantly downregulated in the caudal spinal segment (CSS) following EA. Immunohistochemistry demonstrated an increased number of CGRP fibers, GAP-43, and synaptophysin profiles in the CSS in the EA rats. CONCLUSIONS EA may promote the recovery of neuroplasticity in rats subjected to SCT. This could be attributed to the systematic regulation of NTFs and their receptors after EA.

Electroacupuncture serum inhibits TNF-α-mediated chondrocyte inflammation via the Ras-Raf-MEK1/2-ERK1/2 signaling pathway.


By Chen H, Shao X, Li L, Zheng C, Xu X, Hong X, Li X, Wu M.

Abstract

The Ras-Raf-mitogen-activated protein kinase kinase (MEK)1/2-extracellular signal-regulated kinase (ERK)1/2 signaling pathway contributes to the release of chondral matrix-degrading enzymes and accelerates the degradation of articular cartilage. Electroacupuncture (EA) treatment has been widely used for the treatment of osteoarthritis (OA); however, the mechanism underlying the effects of EA on OA remains unclear. Therefore, the present study evaluated the anti-inflammatory effects and potential underlying mechanisms of EA serum (EAS) on tumor necrosis factor (TNF)-α-mediated chondrocyte inflammation. A total of 30 Sprague Dawley rats were randomly divided
into three groups: The blank group; experimental group I, which received 15 min of EA treatment; and experimental group II, which received 30 min of EA treatment. Subsequently, serum samples were obtained. Chondrocytes were isolated from the knee cartilage of Sprague Dawley rats, and were identified using collagen type II immunohistochemistry. TNF-α-treated chondrocytes were used as a cell model, and subsequently the cells were treated with EAS from each group for various durations. The results demonstrated that EAS treatment significantly promoted the viability and inhibited the apoptosis of TNF-α-treated chondrocytes. In addition, interleukin (IL)-1β concentration was significantly increased in the model group compared with in the control group, whereas EAS significantly reduced IL-1β concentration in TNF-α-treated chondrocytes. Furthermore, the protein expression levels of Ras, Raf and MEK1/2 were reduced in the EAS groups compared with in the model group. EAS also significantly inhibited the phosphorylation of ERK1/2, and the expression of downstream regulators matrix metalloproteinase (MMP)-3 and MMP-13. In conclusion, these results indicated that EAS may inhibit TNF-α-mediated chondrocyte inflammation via the Ras-Raf-MEK1/2-ERK1/2 signaling pathway in vitro, thus suggesting that EAS may be considered a potential therapeutic strategy for the treatment of OA.

Electroacupuncture Promotes Recovery of Motor Function and Reduces Dopaminergic Neuron Degeneration in Rodent Models of Parkinson's Disease.


Abstract

Parkinson's disease (PD) is a common neurodegenerative disease. The pathological hallmark of PD is a progressive loss of dopaminergic neurons in the substantia nigra (SN) pars compacta in the brain, ultimately resulting in severe striatal dopamine deficiency and the development of primary motor symptoms (e.g., resting tremor, bradykinesia) in PD. Acupuncture has long been used in traditional Chinese medicine to treat PD for the control of tremor and pain. Accumulating evidence has shown that using electroacupuncture (EA) as a complementary therapy ameliorates motor symptoms of PD. However, the
most appropriate timing for EA intervention and its effect on dopamine neuronal protection remain unclear. Thus, this study used the 1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine (MPTP)-lesioned mouse model (systemic-lesioned by intraperitoneal injection) and the 1-methyl-4-phenylpyridinium (MPP⁺-)lesioned rat model (unilateral-lesioned by intra-SN infusion) of PD, to explore the therapeutic effects and mechanisms of EA at the GB34 (Yanglingquan) and LR3 (Taichong) acupoints. We found that EA increased the latency to fall from the accelerating rotarod and improved striatal dopamine levels in the MPTP studies. In the MPP⁺ studies, EA inhibited apomorphine induced rotational behavior and locomotor activity, and demonstrated neuroprotective effects via the activation of survival pathways of Akt and brain-derived neurotrophic factor (BDNF) in the SN region. In conclusion, we observed that EA treatment reduces motor symptoms of PD and dopaminergic neurodegeneration in rodent models, whether EA is given as a pretreatment or after the initiation of disease symptoms. The results indicate that EA treatment may be an effective therapy for patients with PD.

Mast cell activation in the acupoint is important for the electroacupuncture effect against pituitrin-induced bradycardia in rabbits.
By Zhu H, Wang X, Huang M, Jing Y, Zhang D, Ding G.

Abstract
This research was conducted to verify the structural and functional characteristics of mast cells in the electroacupuncture (EA) effects on bradycardia. First, we examined the mast cell density at PC 6, adjacent acupoint LU 7, and a non-acupoint. We tested the effects of EA at PC 6 on heart rate (HR) and blood pressure (BP) in rabbits with pituitrin-induced bradycardia. We also injected sodium cromolyn (Cro), a mast cell membrane stabilizer, at PC 6 30 min before EA to investigate if it affected the EA effects. The results showed that in both PC 6 and LU 7, the mast cell densities were higher than in the non-acupoint (P < 0.05). EA could induce mast cell degranulation at PC 6, which could be suppressed by sodium cromolyn (P < 0.05). EA improved HR, though the change was relatively small in the initial stage with a significant change at 35 min after modelling (P < 0.05). BP significantly improved at 10 min after...
the onset of pituitrin-induced bradycardia (P < 0.05). The EA effects on both HR and BP were suppressed by sodium cromolyn (P < 0.05).

Therefore, we concluded that mast cells in the acupoint are important for the EA effects against pituitrin-induced bradycardia in rabbits.

Comprehensive evaluation of gene expression signatures in response to electroacupuncture stimulation at Zusanli (ST36) acupoint by transcriptomic analysis.


By Wu JS, Lo HY, Li CC, Chen FY, Hsiang CY, Ho TY.

Abstract

BACKGROUND:
Electroacupuncture (EA) has been applied to treat and prevent diseases for years. However, molecular events happened in both the acupunctured site and the internal organs after EA stimulation have not been clarified.

METHODS:
Here we applied transcriptomic analysis to explore the gene expression signatures after EA stimulation. Mice were applied EA stimulation at ST36 for 15 min and nine tissues were collected three hours later for microarray analysis.

RESULTS:
We found that EA affected the expression of genes not only in the acupunctured site but also in the internal organs. EA commonly affected biological networks involved in cytoskeleton and cell adhesion, and also regulated unique process networks in specific organs, such as γ-aminobutyric acid-ergic neurotransmission in brain and inflammation process in lung. In addition, EA affected the expression of genes related to various diseases, such as neurodegenerative diseases in brain and obstructive pulmonary diseases in lung.

CONCLUSIONS:
This report applied, for the first time, a global comprehensive genome-wide approach to analyze the gene expression profiling of acupunctured site and internal organs after EA stimulation. The connection between gene expression signatures, biological processes, and diseases might provide a basis for prediction and explanation on the therapeutic potentials of acupuncture in organs.
Effects of electroacupuncture to the trigeminal nerve area on the autonomic nervous system and cerebral blood flow in the prefrontal cortex.

https://www.ncbi.nlm.nih.gov/pubmed/28765118
By Waki H, Suzuki T, Tanaka Y, Tamai H, Minakawa Y, Miyazaki S, et al.,

Abstract

BACKGROUND:
The autonomic nervous system and trigeminal nerve are involved in adjusting flow through diverging cerebral arteries in the prefrontal cortex. The purpose of this study was to examine the effect of 100 Hz electroacupuncture (EA) to the trigeminal nerve area on cerebral blood flow and autonomic nervous system function.

METHOD:
This was a randomised crossover study of 16 healthy volunteers who were assigned to an EA or control group. Stimulation (in the EA group) was performed five times, each after 1 min of rest. Needles were inserted at the inner edge of the eyebrows and 1 cm from the front hairline midpoint. We used high-frequency (HF) and low-frequency (LF) components of heart rate (HR) variability to assess autonomic nervous system function. HF and LF/HF ratio were taken as indicators of parasympathetic and sympathetic nervous system activity, respectively. We measured cerebral blood flow using a two-channel near-infrared spectroscope.

RESULTS:
In the EA group, HR significantly decreased (p=0.004) and HF significantly increased (p=0.006) relative to baseline. By contrast, there were no significant changes in HR or HF within the control group (p>0.05). Accordingly, HR tended to be lower (p=0.087) and HF greater (p=0.071) in the EA group versus the control group. There were no significant differences in LF/HF ratio within/between groups. Compared with the control group, cerebral blood flow was significantly greater in the left (p=0.048) and right (p=0.016) prefrontal cortex in the EA group.

CONCLUSIONS:
Delivery of 100 Hz EA to the trigeminal nerve area reduces HR and increases parasympathetic nervous activity and cerebral blood flow.