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RESEARCH ARTICLE

# Link Between Electroacupuncture Stimulation near the Sympathetic Trunk and Heart Rate Variability

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**Background:** The cardiovascular system and airway smooth muscles are regulated by the autonomic nervous system.
**Objectives**: This study investigated the effect of electrical acupuncture stimulation near the cervical sympathetic ganglia on heart rate variability and respiratory function.
**Methods:** This prospective, single-center study at Teikyo Heisei University recruited 24 healthy adults randomly assigned to no-stimulation and electroacupuncture (EA) groups in a crossover trial with a 2-week washout period. After 5 min of rest, a 5-min rest or acupuncture stimulus was delivered, followed by a further 5 min of rest for both groups. EA, at 2-Hz (level of no pain), was delivered near the left cervical ganglia at the level of the sixth cervical vertebra in the EA group.
**Results:** The high-frequency component of the heart rate variability was significantly higher in the EA group than that in the no-stimulation group. Further, there was a significant increase in the high-frequency component of the heart rate in the EA group during the stimulation compared to before and after stimulation. Heart rate decreased significantly during EA compared to before stimulation in the EA group. Regarding respiratory function, forced vital capacity, forced expiratory volume in 1 s, and peak flow significantly increased in the EA group compared with the no-stimulation group, and after stimulation compared with before stimulation.
**Conclusion:** Stimulation with 2-Hz EA near the cervical sympathetic trunk increased parasympathetic nerve activity and reduced heart rate. However, the respiratory function was activated via increased sympathetic nerve activity. Therefore, 2-Hz EA may be effective for autonomic nerve regulation in bronchial stenosis.

**Keywords:** Cervical sympathetic ganglion, Nasal mucosa, Sympathetic vasoconstrictors

## INTRODUCTION

Cardiac and respiratory rhythms are associated with the activity of the phrenic postganglionic sympathetic neurons [1]. In addition to postganglionic sympathetic axons, the phrenic nerve contains mechanically sensitive afferents of the pericardium [2,3]. The physiological activity of the cardiovascular system is controlled by the autonomic nervous system. The heart is dually innervated; it receives parasympathetic input via the vagus nerve from both the dorsal motor nucleus and the nucleus ambiguus and sympathetic input from the cervical sympathetic ganglion. The cervical sympathetic ganglion comprises the superior cervical ganglion, middle cervical ganglion, vertebral artery ganglion, and stellate ganglion. It sends postganglionic fibers to the organs and blood vessels in the head, neck, and upper chest regions. The heart is innervated by branches from the upper, middle, and stellate ganglia (the upper, middle, and lower cardiac nerve branches, respectively).

In our previous studies, 2-Hz electroacupuncture (EA) stimulation delivered near the cervical sympathetic trunk acted on the airway smooth muscle by engaging internal somatic reflexes such as the sensory and autonomic nerves, increasing the peak expiratory flow (PEF) [4]. PEF monitoring is also recommended as an objective way to assess patients' daily airflow limits. Diurnal variation of PEF correlates with airway hypersensitivity, suggesting that sizable diurnal variation increases airway hypersensitivity, and this is considered an indicator of control status [5-9]. This suggests that 2-Hz EA stimulation near the cervical sympathetic trunk

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may be an intervention for respiratory symptoms that cause airflow limitation. In addition, this stimulus demonstrated that the contraction of blood vessels in the nose lowers the skin temperature [10] and increases the maximal respiratory mouth pressure [11]. Notably, the phrenic nerve contains sympathetic nerve fibers [1] that increase respiratory mouth pressure by acting on the diaphragm. Studies conducted on animals have also found that direct acupuncture of the stellate ganglia increases porcine heart rate (HR) [12]. In addition, in clinical studies on human stellate ganglion acupuncture, acupuncture stimulation of the stellate ganglia regulates the sympathetic–vagus nerve balance and protects vertebral–posterior basilar artery vasospasm and vascular endothelium; this reportedly improves blood flow and arteriosclerosis [13].

The effects of acupuncture on the autonomic nervous system have been investigated with HR as an index. Respiration is also the main rhythm that induces HR variability (HRV), and respiratory rate affects the magnitude of HRV [14]. HRV analysis is another established method of assessing cardiovascular risk [15]. Conventional acupuncture and acupuncture by low-frequency stimulation suppress sympathetic nerve activity and strengthen parasympathetic nerve activity [16,17]; this reaction is triggered by the upper spinal reflex via the brainstem. In addition, acupuncture can stimulate and activate the sympathetic nerve. However, the neck has sensory receptors and sensory nerves distributed in the skin and muscle tissue; HR may decrease as a response to acupuncture. The effects of EA stimulation near the human neck sympathetic trunk on heart rate variability (HRV) have not yet been investigated. This study further evaluates the effect of 2-Hz EA stimulation delivered in the vicinity of the neck sympathetic trunk on HRV and respiratory function.

## MATERIALS AND METHODS

### 1. Participants

This was a randomized crossover study with a two-week washout period. This study adhered to the tenets of the Declaration of Helsinki. The purpose, methods, and potential outcomes of this study were explained to all participants and written informed consent was then obtained.

Twenty-four healthy adults with no respiratory symptoms or smoking history were recruited (19 males and five females; age: 21.12 ± 1.42 years; body mass index: 22.39 ± 2.91 kg/$m^2$). A random number table assigned individuals to the no-stimulation and 2-Hz EA stimulation groups in a 1:1 ratio.

Participants were required to abstain from consuming alcohol and caffeine (coffee, tea, etc.) on the day before and the day of the study to avoid influencing the autonomic nervous system. They were also required to abstain from eating and drinking (other than water) 2 h before the experiment. Experiments were performed from 9:00 to 14:00 and the room temperature was standardized at 24-27℃.

### 2. Intervention method

The stellate ganglion of the cervical sympathetic trunk lies on the 7th cervical and 1st thoracic vertebrae near the vertebral artery and dome of the pleura. To avoid the danger of puncturing these structures, EA was delivered by inserting a needle at the level of the 6th cervical vertebra in the vicinity of the middle cervical (and vertebral) sympathetic ganglia. Each participant was placed in a supine position with a rolled-up towel under the neck. Just lateral to the cricoid cartilage, a finger was used to pull the left carotid sheath laterally to palpate the anterior tubercle of the left transverse process of the 6th cervical vertebra. To avoid puncturing the carotid artery, an acupuncture needle was inserted directly into the anterior tubercle.

The acupuncture equipment was two stainless steel needles (length: 50 mm; diameter: 0.20 mm; SEIRIN, Shizuoka, Japan). Each needle was inserted to a depth of approximately 1.5 mm. Furthermore, they were inserted near the 6th cervical vertebra on the left side and the cervical ganglion at the level of the vertebral artery nodule. In the EA group, the EA stimulation intensity was set to a pain-free level (0.01-0.06 mA) using a current-carrying device (Ohm Pulser LFP-2000e; Zen Iryoki, Fukuoka, Japan). The 2-Hz EA stimulation was only delivered to the left side for 5 min. The participants who received 2-Hz EA stimulation were stimulated continuously for 5 min without breaks.

Patients were monitored for adverse events such as anemia, internal bleeding, and pneumothorax.

### 3. Respiratory function and HRV measurement protocol

The participants' respiratory function was measured after resting for 10 min in a sitting position. Next, resting (5 min) and intervention stimulation (5 min) were performed in a supine position and the patient rested again (5 min). Afterward, the respiratory function was then re-measured. HRV was measured continuously for 2 min after resting in the supine position for 3 min. The needle was then inserted into the transverse process of C6 and HRV was measured during 5 min of EA stimulation for the EA group or resting for the non-stimulation group. Next, the needle was withdrawn and the patient was asked to rest for another 5 min to record the HRV. To avoid the effects of respiratory function, HR was measured from 3 min after the supine position to 2 min in the second half (Fig. 1). Furthermore, we wanted to confirm the HRV during 2-Hz EA stimulation, so we referred to the HRV after stimulation (Table 1).

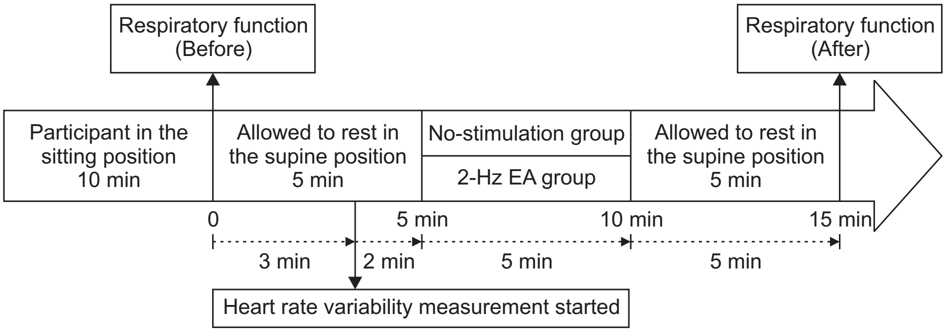


**Fig. 1.** Schematic of the time course. EA = electroacupuncture; HRV = heart rate variability.

## 4. Respiratory function test (spirometry)

Forced vital capacity (FVC) and forced expiratory volume in 1 s (FEV 1.0) were measured using a spirometer (SP-3700 COPD lung Per/lung Per plus; Fukuda Electronics Co., Tokyo, Japan). PEF and vital capacity (VC) were also determined according to the American Society of Respiratory Surgery guidelines [18]. Up to five measurements were taken when the results were not consistent. For FVC measurement, it was assumed that the difference between the two best FEV 1.0 values and between the two best FVC values would be within 200 ml and the largest total value of FVC and FEV 1.0 was adopted. The respiratory function measurements showing the maximum values were adopted. Since PEF can be measured simultaneously with FVC, we adopted the PEF value at which the sum of the FVC and FEV 1.0 was the maximum for analysis.

## 5. HRV

Autonomic nerve activity was obtained by attaching electrodes (Vitrode Bs 150; NIHON KOHDEN, Tokyo, Japan) to the sternum and the lateral chest, located on the left and right papillary lines, and was recorded by an electrocardiograph (LRR-03; GMS, Tokyo, Japan). The obtained HRV was frequency-analyzed by the modified maximum entropy method using HRV waveform analysis software (Crosswell, Tokyo, Japan). The LF component of 0.05-0.15 Hz and the high frequency (HF) component of 0.15-0.4 Hz were extracted, and the value of the LF component divided by the HF component was defined as the index of the sympathetic nerve activity.

## 6. Statistical analysis

HRV results are expressed as mean ± standard deviation (SD). To check the HRV during 2-Hz EA stimulation, the groups (no-stimulation and 2-Hz EA groups) and measurement period (before and during intervention) were set as independent variables and the values of each endpoint were set as dependent variables. Respiratory function results were expressed as mean ± SD. Two-way analysis of variance was used for comparison between groups and the significance level was set at 5%. JMP® 15 (SAS Institute Inc., Cary, NC, USA) was used for statistical data analysis.

## 7. Ethics approval

The study design was approved by the Ethics Review Committee of Teikyo Heisei University (Tokyo, Japan) (approval number: 29-126) and was conducted in accordance with the provisions of the Declaration of Helsinki, as revised in 2013.

# RESULTS

## 1. Changes in HR and autonomic activity

Table 1 presents the measured values of HR, LF/HF, HF, PEF, FVC, and FEV 1.0. A significant decrease ($p = 0.0163$) in HR was confirmed in the EA group during the intervention compared with that before stimulation. Additionally, HR revealed a significant decreasing trend in the EA group ($p = 0.0556$) compared to that in the no-stimulation group (Fig. 2) [1]. However, no significant differences were noted in the changes in LF/HF between the groups during the intervention (Fig. 2) [2].

A significant increase in HF ($p = 0.0030$) was confirmed in the EA group during the intervention compared to that before stimulation. In addition, the increase in the EA group was significantly prominent ($p = 0.0003$) compared to that in the no-stimulation group (Fig. 2) [3].

## 2. Changes in respiratory function

There was a significant increase ($p = 0.0131$) in PEF in the EA group after the intervention compared to before stimulation. Furthermore, the increase in PEF in the EA group was significantly greater ($p = 0.0005$) than that in the no-stimulation group (Fig. 3) [1]. However, no significant differences were noted in FVC changes between or within the groups after intervention (Fig. 3) [2].

There was a significant increase ($p = 0.0131$) in FEV 1.0 in the EA group after the intervention compared to before the intervention. Additionally, the increase in FEV 1.0 in the EA group was significantly greater ($p = 0.0005$) than that in the no-stimulation group (Fig. 3) [3]. Moreover, there was a

**Table 1.** Patient demographics, heart rateand autonomic activity, and respiratory function

| Characteristics | Group | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| | [×] No-stimulation group (n = 24) | | | | [●] 2-Hz EA group (n = 24) | | | |
| Age (yrs)[a] (mean ± SD) | 21.12 ± 1.42 | | | | 21.12 ± 1.42 | | | |
| BMI[a] (mean ± SD) | 22.39 ± 2.91 | | | | 22.39 ± 2.91 | | | |
| Heart rate and autonomic activity[b] | Rest before[d] (2 min) | Stimulation (5 min) | Level of change[e] (Stimulation-Rest before) | After stimulation[f] (5 min) | Rest before[d] (2 min) | Stimulation (5 min) | Level of change[e] (Stimulation-Rest before) | After stimulation[f] (5 min) |
| HR (bpm) (mean ± SD) | 68.54 ± 8.78 | 68.28 ± 8.88 | −0.26 ± 2.57 | 65.05 ± 7.83 | 64.73 ± 8.08 | 63.47 ± 7.58 | −1.26 ± 2.36 | 62.67 ± 8.63 |
| LF/HF (ratio) (mean ± SD) | 1.95 ± 1.55 | 2.20 ± 1.51 | 0.25 ± 1.14 | 1.70 ± 1.05 | 2.02 ± 2.12 | 1.37 ± 0.96 | −0.65 ± 2.16 | 1.62 ± 0.89 |
| HF ($m^2$) (mean ± SD) | 723.52 ± 788.91 | 683.89 ± 693.68 | −0.39 ± 294.51 | 745.17 ± 822.01 | 598.27 ± 702.33 | 762.17 ± 762.17 | 175.42 ± 255.31 | 727.03 ± 692.53 |

| Lung-function test[c] | Before | After | Level of change (After-Before) | Before | After | Level of change (After-Before) |
|---|---|---|---|---|---|---|
| PEF (L/s) (mean ± SD) | 8.10 ± 2.01 | 7.90 ± 2.07 | −0.19 ± 0.52 | 7.53 ± 1.81 | 8.14 ± 1.69 | 0.60 ± 0.78 |
| FVC (L) (mean ± SD) | 4.51 ± 0.74 | 4.53 ± 0.75 | 0.02 ± 0.11 | 4.45 ± 0.79 | 4.53 ± 0.73 | 0.04 ± 0.14 |
| FEV 1.0 (L) (mean ± SD) | 3.91 ± 0.74 | 3.94 ± 0.73 | 0.03 ± 0.12 | 3.85 ± 0.76 | 3.94 ± 0.73 | 0.08 ± 0.27 |
| VC (L) (mean ± SD) | 4.19 ± 0.74 | 4.19 ± 0.74 | −0.00 ± 0.15 | 4.20 ± 0.74 | 4.27 ± 0.78 | 0.07 ± 0.10 |

[a]Owing to the crossover study design, the participants had an average (SD) age of 21.12 ± 1.42 years and a BMI of 22.39 ± 2.91 in both groups; [b]The heart rate and autonomic activity is the actual value before and during, which is the value during minus the value before stimulation. [c]The respiratory function test is the actual value before and after stimulation, and the value after stimulation minus before stimulation; [d]To avoid the effects of respiratory function, HR was measured from 3 min after the supine position to 2 min in the second half; [e]To confirm the effect of electric acupuncture stimulation on HRV, evaluation was performed before and during stimulation; [f]The post-stimulation HRV was used as a reference.

HR = heart rate; LF/HF = low frequency/high frequency; HF = high frequency; PEF = peak expiratory flow; FVC = forced vital capacity; FEV 1.0 = forced expiratory volume in 1 second; SD = standard deviation; BMI = body mass index; min = minutes.

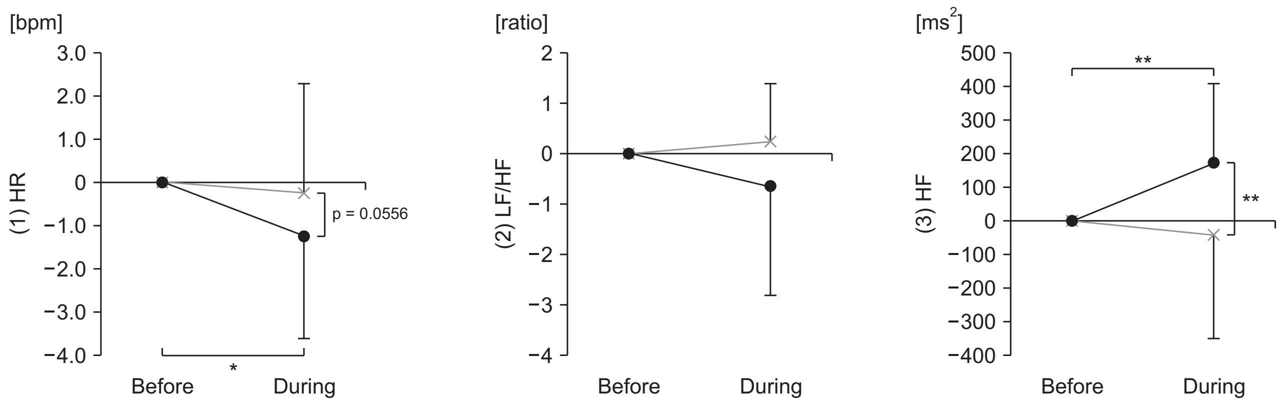


**Fig. 2.** EA effects on HR and autonomic activity. bpm = beat per minute; HR = heart rate; HF = high frequency; LF = low frequency.

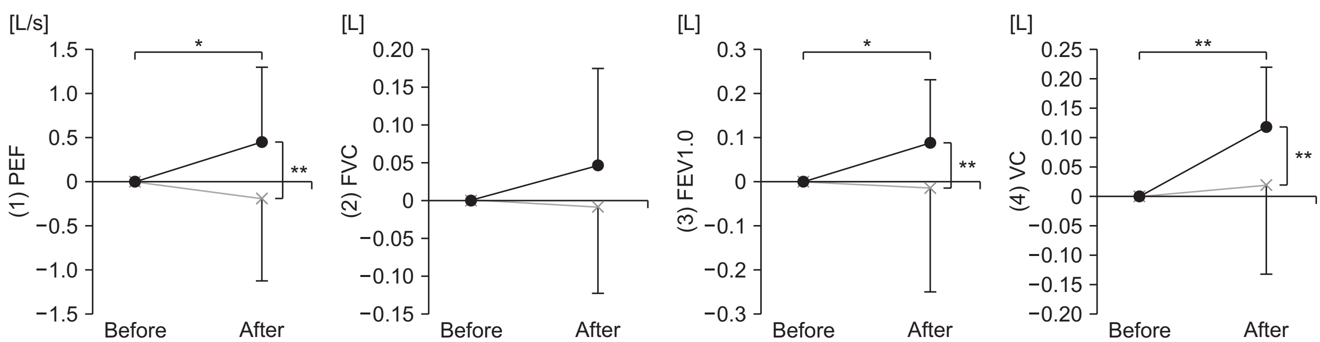


**Fig. 3.** EA effects on Respiratory function. PEF = peak expiratory flow; FVC = forced vital capacity; FEV1.0 = forced expiratory volume in 1 s; VC = vital capacity.

significant increase ($p$ = 0.0063) in VC in the EA group after the intervention compared to before stimulation. Furthermore, the increase in VC in the EA group was significantly greater ($p$ = 0.0038) than that in the no-stimulation group (Fig. 3) [4].

## DISCUSSION

This study investigated the effects of 2-Hz EA stimulation near the cervical sympathetic trunk on HRV and respiratory function. HR decreased and the HF component of HRV increased in the EA stimulation group. Moreover, pulmonary function testing revealed increased PEF and FEV 1.0 in the EA stimulation group. Since these results were crossover designs, it is possible that individual differences did not affect the results. No adverse events—such as pneumothorax, anemia, or internal bleeding—were observed during or after the experiment. Therefore, the safety of EA stimulation near the cervical sympathetic trunk was confirmed.

The heart is doubly innervated by the cardiac sympathetic nerve from the cervical sympathetic ganglion and by the vagus nerve from the dorsal motor nucleus and nucleus ambiguus. Decreased HR during acupuncture stimulation has been reported to result from mutual coordination between increased cardiac vagal activity and decreased cardiac sympathetic activity [5]. We observed that—at the time of EA stimulation—the HF component of HRV, which is an index of parasympathetic nerve activity, increased more than the LF/HF ratio, which is an index of sympathetic nerve activity. Thus, 2-Hz EA stimulation near the cervical sympathetic nerve did not activate the cardiac sympathetic nerve. This finding suggests that the upper spinal reflex was activated, thereby suppressing the sympathetic nerve activity of the heart and enhancing the vagal reflex centered in the brainstem. Indeed, respiratory function tests depicted increased PEF, FVE 1.0, and VC, which suggests that sympathetic nerves might have been activated.

In various animal studies, electrical stimulation of the thoracic sympathetic chain has been demonstrated to evoke excitatory responses in the upper and lower phrenic nerves. Therefore, most of the unmyelinated fibers of the phrenic nerve may be postganglionic sympathetic axons. Systolic blood pressure is reportedly stable throughout the respiratory cycle due to phrenic nerve discharge [1]. In addition, the presence of pericardial receptors with the phrenic nerve afferents and significant cardiac rhythm during mechanical stimulation in dogs has been observed [3].

The diaphragm and intercostal muscles are respiratory muscles of the striated type. The movement of the respiratory muscles changes the volume of the chest, which indirectly expands and contracts. Further, the spontaneous striated muscle is innervated by the central nervous system. Since it is controlled by autonomic nerves, it can move autonomously and involuntarily [19]. We observed that 2-Hz EA stimulation activated the sympathetic nerves and thereby increased FEV 1.0, PEF, and VC. It is possible that the sympathetic nerve is activated during EA stimulation and that the pericardial receptor is mechanically stimulated via the phrenic nerve. Notably, somatic cells of phrenic nerve sympathetic neurons are reportedly located in the superior cervical ganglion of rats [20]. Furthermore, 2-Hz EA stimulation near the cervical sympathetic trunk exposed the cervical sympathetic ganglia without directly stimulating them.

In addition, as a general feature of sympathetic nerve stimulation, unlike the somatic nerve, the sympathetic nerve does not show a significant potential change when damaged or electrically stimulated; therefore, the potential generated by each fiber may be high [21]. Consequently, in a study measuring skin temperature in the nose [8], 5 min of 2-Hz EA stimulation near the cervical sympathetic trunk tended to lower the start of the effects of stimulation and promote the return to the temperature prior to the start of stimulation from the latter half of the course. Therefore, although the 2-Hz EA stimulation to the sympathetic nerve activated it, electrical stimulation was not found to deliver any damage.

In our previous study of nasal skin temperature [10], The vasoconstriction and skin temperature of the nasal mucosa, which originated from the sympathetic vasoconstrictor nerves of the superior cervical ganglion and were not controlled by parasympathetic nerve fibers, decreased. Therefore, it is possible that the sympathetic nerve neurons of the phrenic nerve located in the superior cervical ganglion and the pericardial receptors were stimulated. Notably, it has also been reported that respiratory sympathetic outflow limits respiratory sinus arrhythmia with fast and slow breathing frequencies and cannot be considered a vagal phenomenon [22]. In addition, the level of cardiac vagal activity in quietly breathing humans is non-zero during inspiration but is associated with excitatory stimuli during exhalation [23]. Therefore, autonomous respiration during stimulation causes vagal outflow through low inspiration and large expiratory reflexes. In the present study, EA led to a marked decrease in HR, and a increase in the HF component of HRV was detected using a common method of assessing cardiopulmonary interaction. Cardiopulmonary connections are considered useful indicators of good health because they reflect the components of the autonomic sympathetic and parasympathetic nerves that control homeostasis and visceral function [24].

However, this survey has some limitations. Participants were healthy adults with no autonomic imbalance or respiratory or cardiovascular problems. Since it targeted healthy adults, the mechanism remains inadequate for the treatment of morbidity and further research is warranted. For this, it would also be necessary to verify the efficiency of EA stimulation in the disease model. Measurements should be taken 5 min after stimulation and efficacy should be assessed 10 and 15 min after stimulation. To validate the clinical application of this stimulus, it is necessary to assess the effects of continuous and repetitive stimuli and the effects of load.

## CONCLUSIONS

In this study, 2-Hz EA stimulation near the cervical sympathetic trunk showed an increase in PEF, FEV 1.0, and VC 5 min after stimulation via the autonomic ganglion fibers. It was found that HR decreases and the HF component of HRV increases when sympathetic nerve stimulation is accompanied by cardiac rhythm at the pericardial receptor. Furthermore, current findings suggest a potential improvement in respiratory function after 2-Hz EA stimulation. However, this study was conducted on healthy participants; therefore, further studies that explore the mechanism of this phenomenon are needed to assess its effectiveness for diseases of the cardiovascular system, bronchial stenosis, and respiratory weakness.

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## AUTHORS' CONTRIBUTIONS

Research Ideas or Design: K.T, Data collection: K.T, Data analysis and interpretation: K.T, K.I, Treatise writing: K.T, Significant revision of the treatise: K.T, K.I, X.W, D.S, Final draft approval: K.T, K.I, X.W, D.S.

## CONFLICT OF INTEREST

The authors declare no conflict of interest.

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