



Short communication

An alternative method to enhance vagal activities and suppress sympathetic activities in humans

J.D. Wang^{a,b}, Terry B.J. Kuo^c, Cheryl C.H. Yang^{d,*}^aDepartment of Traditional Chinese Medicine, Tzu-Chi General Hospital, Dalin 622, Taiwan^bDepartment of Thoracic Medicine, Tzu-Chi General Hospital, Dalin 622, Taiwan^cInstitute of Neuroscience, Tzu Chi University, Hualien 970, Taiwan^dDepartment of Physiology, Tzu Chi University, Hualien 970, Taiwan

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Abstract

Vagal withdrawal and/or sympathetic overactivity is always accompanied by various kinds of stress and is dangerous to the body. We proposed that mild acupuncture on the Sishencong points may effectively enhance vagal activities but suppress sympathetic regulations of the heart in humans. Experiments were carried out on nine healthy male volunteers, while they were lying in a quiet room during 2–4 P.M. Acupuncture was applied 2 mm deep into the skin using standard stainless acupuncture needles at the Sishencong points, which are located on the vertex of the head, each 1 cm away from Baihui (GV 20) in four directions. Four points around the temporal area were selected as control points. Forty minutes of precordial ECG signals before, during, and after acupuncture were recorded continuously. Frequency-domain analysis of the stationary RR intervals was performed to evaluate the total variance, high-frequency power (HF, 0.15–0.40 Hz) and low-frequency power (LF, 0.04–0.15 Hz) in normalized units (LF%). Acupuncture on the Sishencong points resulted in an increased HF but a decreased LF% compared with the before acupuncture stage. Such effects did not occur when manual acupuncture was applied to the control points. The differences in the heart rate dynamics between Sishencong and the control groups took place 10 min after initiation of acupuncture and persisted even after the removal of the needles. Based on these results, we concluded that manual acupuncture on the Sishencong points enhanced cardiac vagal and suppressed sympathetic activities in humans. The underlying mechanisms and potential applications warrant further investigations.

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It is well known that the autonomic nervous system (ANS) monitors and controls many aspects of the body functions almost every second of our lives. Nowadays, more and more researchers take into account the ANS changes on varied physiological situations or on the cause and effect of some pathological conditions. When humans were under varied kinds of stress, ANS disturbances were frequently induced, which consisted of suppressed vagal and/or enhanced sympathetic functions. For example, ANS changes were always accompanied with systemic disorder such as fatigue (Pagani et al., 1994), gastrointestinal problems (Bichet et al., 1982), cardiac dysfunctions (Esler, 1992;

Manolis et al., 1998), and stress responses (Gallo et al., 1988; Sloan et al., 1991). People with vagal withdrawal were prone to enter a vicious cycle that may result in a tendency of lethal tachyarrhythmia (Huikuri et al., 1996). Appropriate restoration of the ANS functions is demanded and necessary to maintain a balanced life. Unfortunately, there are still no effective and safe maneuvers to enhance the vagal output while suppressing the sympathetic functions.

Investigators have made many efforts to stimulate the vagal and/or lower sympathetic activities using various methods, including physical and chemical maneuvers for the improvement of such cardiac dysfunction. For example, electric stimulation of vagal activity has been used to relieve myocardial infarction (Sneddon et al., 1993) and epilepsy (Neufeld and Korczyn, 1996). Lowering sympathetic activity using clonidine or β -adrenergic blocking drugs has been used for treatment of congestive heart failure (Manolis et al.,

* Corresponding author. Tel.: +886-3-8565301x7096; fax: +886-3-8580639.

E-mail address: cchiang@mail.tcu.edu.tw (C.C.H. Yang).

1998), myocardial ischemia (Uchida and Murao, 1974), and prevention of sudden death (Esler, 1992). However, because of the invasiveness of these methods, they are not used as routine treatment.

Acupuncture has gained its popularity for its effect of analgesia (Ulett et al., 1998). Besides, evidences also support that acupuncture has beneficial effects for patients with visceral diseases (Sodipo and Falaiye, 1979) and cardiovascular dysfunction (Tam and Yiu, 1975). For example, acupuncture at the particular sites called Sishencong, which are around the vertex of the head (Fig. 1), may produce a sedative effect and has been prescribed to relieve insomnia for a long time in Chinese medicine. Xie et al. (1994) reported that gentle acupuncture on the Sishencong points is effective in relieving insomnia in over 88% of treated patients. Since people with high vagal and low sympathetic activity have a tendency to sleep (Furlan et al., 1990), we suspected that the Sishencong acupuncture plays a role in the regulation of the ANS functions.

Frequency-domain analysis of heart rate variability (HRV) is a sophisticated albeit noninvasive tool for the detection of ANS regulation of the heart. It has been well established that HRV can be categorized into high-frequency (HF, 0.15–0.40 Hz) and low-frequency (LF, 0.04–0.15 Hz) components according to its oscillating frequency and developing mechanism (Kuo et al., 1999; Yang et al., 2000). The HF is equivalent to the well-known respiratory sinus arrhythmia and represents vagal control of heart rate (Fouad et al., 1984). The LF is jointly contributed by both sympathetic and vagal nerves (Berger et al., 1989). The LF% is considered by some investigators to mirror sympathovagal balance (Montano et al., 1994) or to reflect the sympathetic modulations (Malliani et al., 1991; Mon-

tano et al., 1994; Task Force of the European Society of Cardiology and the North American Society of Pacing and Electrophysiology, 1996; Pagani et al., 1997). Since it is accessible, frequency-domain analysis of HRV has gained in popularity with its broad application as a functional indicator of the ANS. Previous work from our laboratory has demonstrated that this technique has the sensitivity to detect the effects of gender, aging, and even critical illness on the changes of ANS activities (Yien et al., 1997; Kuo et al., 1999; Yang et al., 2000).

This experiment was carried out to test the hypothesis that acupuncture on the Sishencong points may have a facilitative effect on cardiac vagal regulation and/or a suppressive effect on sympathetic regulation. Since HRV analysis is virtually noninvasive and produces almost no stress on the study subjects, we particularly used such technique to monitor the effects of Sishencong acupuncture on the ANS.

Nine healthy subjects (mean age, 27 ± 5 years) were enrolled in this study. The exclusion criteria included diabetic neuropathy, cardiac arrhythmia, or other cardiovascular diseases, which affect HRV (Malliani et al., 1991). Written informed consent was obtained from each participant. The procedures used in this study were approved by the Protection of Human Subjects Institutional Review Board Tzu-Chi University and Hospital, Hualien, Taiwan. They were asked not to take any medication or acupuncture a week prior to the experiment. During the test days, they were not allowed to have any alcoholic or caffeinated beverages or do heavy exercise. Every subject was restricted from food intake at least one hour before the test. Each subject participated in two randomly distributed groups: the control group, and the Sishencong group. Sishencong is a group of four points which are located on vertex of head, each 1 cm away from Baihui (GV 20) at four directions (anterior, bilateral, and posterior, Fig. 1). Different sessions were performed at weekly intervals at the same time. Room temperature was kept at 25 ± 1 °C. Subjects were asked to lie on a comfortable bed in a quiet room for at least 20 min. The experiment lasted for 40 min during which the precordial ECG was recorded. For subjects in the Sishencong group, stainless needles (diameter 270 μ m) were inserted in Sishencong points at the sixth minute in a clockwise sequence (posterior, left lateral, anterior, and then right lateral). Four needles were just gently inserted in the scalp to 2 mm deep without any manipulations. The average time for insertion was 1 min. In the control group, the procedure was the same as Sishencong group except for the point locations (Fig. 1). At the 30th minute, the needles were removed. The ECG signals were recorded continuously until 40 min had passed.

The detailed procedures for HRV analysis have been reported previously (Kuo et al., 1999; Yang et al., 2000). In brief, precordial ECG was taken in the daytime from each subject for 40 min while lying quietly and breathing normally. To avoid circadian variation effects, HRV meas-

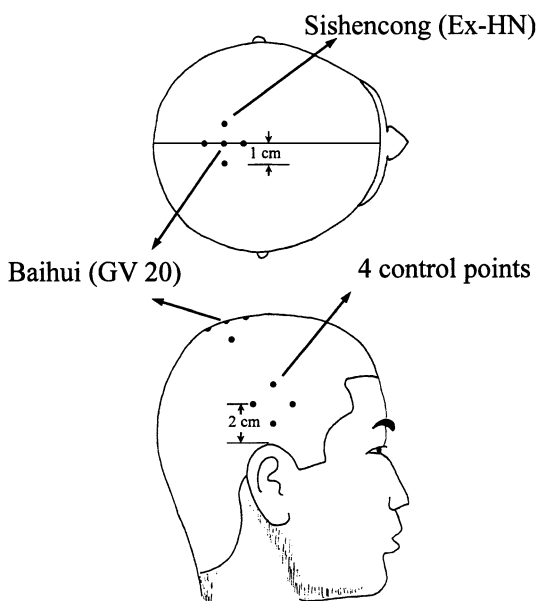


Fig. 1. The locations of Sishencong (Ex-HN), Baihui (GV 20) (upper panel), and the four control points (lower panel).

urements were always performed between 2:00 and 4:00 P.M. The raw ECG signals were recorded using an analog-to-digital converter with a sampling rate of 256 Hz. The digitized ECG signals were analyzed on-line, and were simultaneously stored on a hard disk for off-line verification. The signal acquisition, storage, and processing were performed using an IBM-PC compatible computer. Our computer algorithm then identified each QRS complex and rejected each ventricular premature complex or noise according to its likelihood in a standard QRS template. The stationary RR values were resampled and interpolated at the rate of 7.11 Hz to accomplish the continuity in time domain.

Every 5 min, frequency-domain analysis was performed using a nonparametric method of fast Fourier transform (FFT). The DC component was deleted, and a Hamming window was used to attenuate the leakage effect (Kuo and Chan, 1993). For each time segment (288 s, 2048 data points), our algorithm estimated the power spectral density based on FFT. The resulting power spectrum was corrected for attenuation resulting from the sampling and the Hamming window (Kuo et al., 1999). The power spectrum was subsequently quantified into standard frequency-domain measurements as defined previously (Task Force of the European Society of Cardiology and the North American Society of Pacing and Electrophysiology, 1996), including total variance, high-frequency power (HF, 0.15–0.40 Hz), and low-frequency power (LF, 0.04–0.15 Hz) in normalized units (LF%). Variance and HF were logarithmically transformed to correct the skewness of distribution (Kuo et al., 1999).

The values are expressed as means \pm S.E. Data between groups were compared using Student's *t* test or two-way analysis of variance (ANOVA) with repeated measures, followed by Fisher's least significant difference test for a posteriori comparison of individual means. Differences were considered statistically significant at $P < 0.05$.

Sample recordings of RR interval and power spectral analysis of HRV before and after acupuncture in two different groups are showed in Fig. 2. We found that in both the control (Fig. 2A) and experimental (Fig. 2C) groups, the mean values of RR interval were around 700–1000 ms. In addition, the spectral patterns of HRV showed that there were three spectral components in lower frequency ranges (< 0.5 Hz) of heart rate before acupuncture. Mild stimulation of the control points had a trend to decrease HF and increase LF% (Fig. 2B). In contrast, mild stimulation of the Sishencong points significantly exaggerated variability of RR intervals, enhanced HF, and suppressed the percentage of LF (Fig. 2D).

Fig. 3. shows the changes in RR interval, variance, LF%, and HF in the different experimental stages of these two groups. To manifest the time–sequence changes after acupuncture, the data were normalized by their initial value at NB and were expressed as percentage of NB. In the control group, acupuncture at the control points at the N_0 stage was followed by increases in LF% and decreases in HF. And these effects persisted during (N_0 – N_4) and after (R_1 – R_2) the

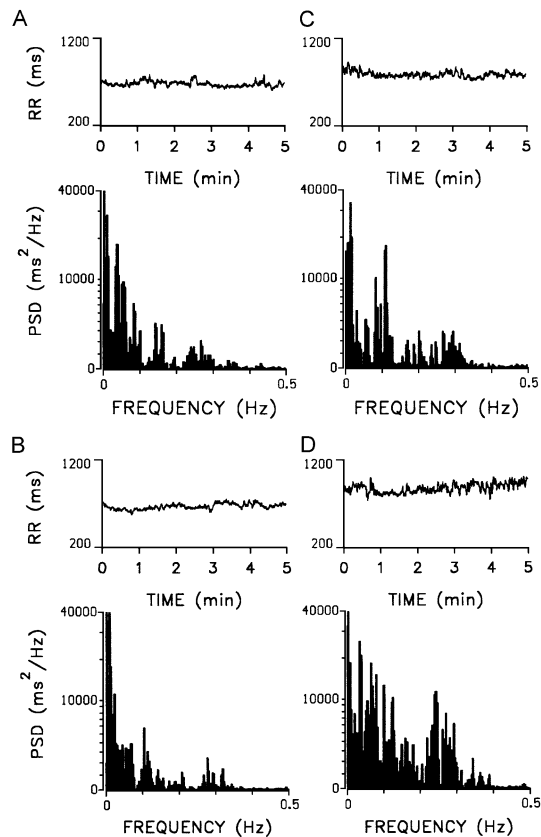


Fig. 2. Sample recordings of 5-min RR interval and average periodograms showing power density of the heart rate before and after acupuncture in two different groups in the same person. The left panel represented before (A) and 15 min after (B) acupuncture in the control group. The right panel represented before (C) and 15 min after (D) acupuncture in Sishencong group. RR indicates mean of RR interval; PSD, power spectral density.

acupuncture manipulation. In the Sishencong group, acupuncture at N_0 stage was followed by significant decreases in LF% and increases in RR interval and HF. These effects were also sustained during (N_0 – N_4) and after (R_1 – R_2) the acupuncture manipulation. When we made a comparison between the control and Sishencong groups at each stage, we noted they were statically different in LF% and HF ($P < 0.05$) at N_1 , N_2 , N_3 , and N_4 stage when the needles were still in place. These differences persisted even at R_1 and R_2 after the needles had been removed. The maximal disparity of LF% between the control and Sishencong groups occurred at N_2 stage (15th to 20th minutes) where disparity of HF occurred at the N_3 stage (20th to 25th minutes).

Using the standard procedure of frequency-domain HRV analysis, the results of this study revealed that manual acupuncture on the Sishencong point may enhance cardiac vagal as well as suppress sympathetic activities in healthy humans. In addition, the above mentioned effects persisted even after cessation of the treatment. We suggest that this method is a potentially applicable adjuvant for the prevention or treatment of cardiac autonomic disturbance.

Vagal enhancement and sympathetic suppression have been correlated with some physiological functions, includ-

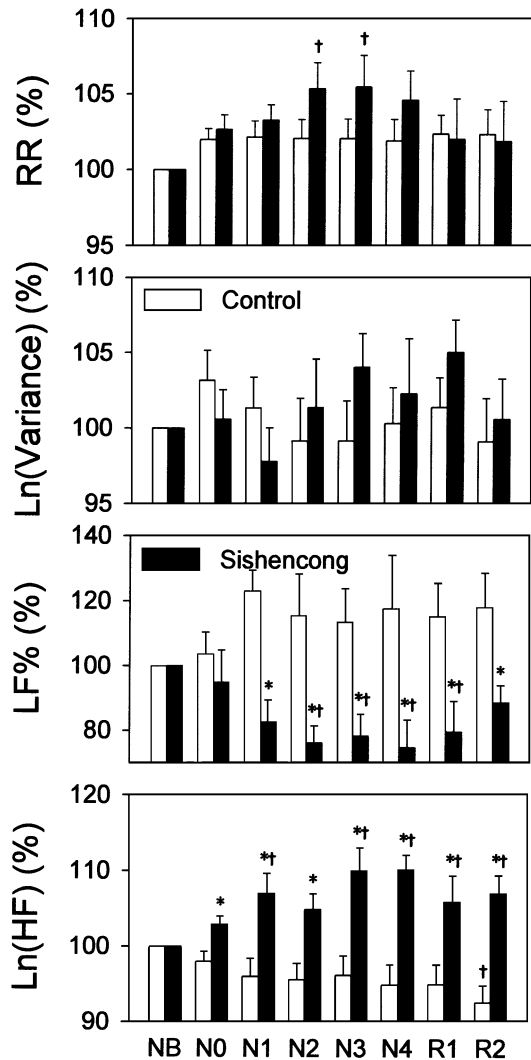


Fig. 3. Temporal changes in mean of RR interval (RR), variance of RR interval (Variance), normalized low-frequency power (LF%) and high-frequency power (HF) during the eight time intervals (NB, N_0 – N_4 , R_1 – R_2) of nine cases after acupuncture in two different sessions. Values are normalized by NB and were expressed as percentage of NB. Ln, natural logarithm. NB represents before-needle stage (zero to fifth minute). Needles were inserted at sixth minute. N_0 – N_4 represent after-needle stage (N_0 , 7th to 12th; N_1 , 10th to 15th; N_2 , 15th to 20th; N_3 , 20th to 25th; N_4 , 25th to 30th minutes). R_1 and R_2 represent after remove-needle stage (R_1 , 30th to 35th and R_2 , 35th to 40th minutes). Values are presented as means \pm S.E., * P <0.05 vs. control group using Student's t test, † P <0.05 vs. NB using Fisher's least significant difference.

ing sleeping (Furlan et al., 1990) and eating (Uijtdehaage et al., 1992). Vagal excitation may be achieved using pharmacological agents such as scopolamine (Vesalainen et al., 1997), morphine (DeSilva et al., 1978), and atropine (Julu, 1992), by mechanical stimulation using the cold face test (Khurana et al., 1977), or by direct stimulation (Sneddon et al., 1993; Neufeld and Korczyn, 1996) of the vagus nerve. In the hospital, doctors used electric stimulation to activate the vagus nerve for relieving epilepsy (Neufeld and Korczyn, 1996) or myocardial ischemia (Sneddon et al., 1993).

Sympathetic suppression can be produced by pharmacological agents such as clonidine (Manolis et al., 1998), nitroglycerine (Uchida and Murao, 1974), or steroid drug (Brown and Fisher, 1986). In clinical applications for prevention or treatment, investigators frequently suppressed sympathetic activity using central sympathetic blockade to relieve the risk of congestive heart failure (Manolis et al., 1998), or myocardial infarction (Uchida and Murao, 1974). Most of the published methods, however, have been difficult, stressful, or even dangerous. Thus, they are seldom used for relieving stress in healthy subjects or patients.

According to the literature (Xie et al., 1994) and our clinical experience, gentle acupuncture on the Sishencong points is effective in relieving insomnia. And such effect persists for several hours after the removal of needles. The underlying mechanism of Sishencong acupuncture, however, has not yet been understood. In the present study, we found that manual acupuncture on the Sishencong points promptly enhanced vagal and suppressed sympathetic influences on heart rate simultaneously. These effects on the ANS started during the first 10 min and persisted even after the needles were removed. It was just opposite to the stress response, indicating that the stress effect of the needle insertion was relatively insignificant in this condition. Nevertheless, the described effects of Sishencong acupuncture are in fact mild and reversible. Side effects related with excess vagal symptoms or with significant changes in heart rate and blood pressure were not noted in our participants. Although the linkage between acupuncture and ANS response is still ambiguous, we suggested that this acupuncture maneuver is a noteworthy adjuvant for reversing stress responses related to ANS involvement because of its convenience and efficacy.

To evaluate the effects of acupuncture, changes in heart rate (Nishijo et al., 1997), blood pressure (Sugiyama et al., 1995), pupil size (Ohsawa et al., 1997), and visceral functions (Sato et al., 1993; Noguchi and Hayashi, 1996) have been used as indexes of ANS functions. The above physiological functions, however, are simultaneously influenced by other modulations in addition to ANS, thus they are usually confounded. For example, skin temperature (Ernst and Lee, 1985, 1986) and blood catecholamines (Sato et al., 1996) usually represent sympathetic activity. However, skin temperatures vary in different areas in response to the same stimulation (Ernst and Lee, 1985). The validity of plasma catecholamine as sympathetic activity was also questioned (Kjeldsen, 1984). Direct recording of either vagal nerve activity in animals or muscular sympathetic nerve activity in humans is both difficult and stressful. In addition, their representative as cardiac autonomic functions is not satisfactory. An important advantage of the frequency-domain analysis of HRV is that it utilizes spontaneous fluctuations in heart rate to estimate the tonic ANS functions. Since the sympathetic and parasympathetic nerves have their specific or even the hormonal system and frequency ranges of operation, it is feasible that their effect can be delineated in the frequency

domain. A well-controlled environment and a noninvasive data acquisition technique, however, are required for an accurate estimation of ANS activity.

In the present study, the changes in ANS functions can be clearly demonstrated by frequency-domain analysis of HRV. An increase in the mean RR value was also observed in the same individuals although the magnitude was small and was possible to overlook. The high sensitivity of HRV spectral analysis to detect ANS function has been demonstrated elsewhere (Kuo et al., 1999). Since the changes induced by acupuncture were rather small, HRV is especially suitable to detect the subtle effect on ANS function produced by acupuncture.

Nishijo et al. (1997) applied a more intense (up and down about 5 mm at a frequency of about 1 Hz) and persistent (30–60 s) stimulation on the Ximen point in humans, and they found ANS responses similar to our findings. In our study, however, the needles were only inserted 2 mm below the scalp surface. After insertion, the needles were left in the scalp without any manipulation. These results indicated that the vagal tonic or sympatholytic effects of acupuncture were independent to rotation or movement of the needles although such maneuvers may potentate the effect.

Mechanisms underlying the effects of acupuncture on the ANS functions have been analyzed in anesthetized animals. Acupuncture-like stimulation on the somatosensory pathway has proved to activate the sympathetic system, which is also known as the somatosympathetic reflex (Sato et al., 1996). This mechanism has been successful in the explanation of many physiological responses induced by acupuncture, but it is not the case of Sishencong acupuncture. In addition, anesthetics may greatly influence the central nervous function including sensory and autonomic functions (Sato et al., 1997). However, there is some uncertainty with regard to the anatomical locus of acupuncture point, strength, and frequency of stimulation in animals. The mechanism defined in anesthetized animals may not extrapolate to the effect of acupuncture observed in conscious humans. The changes of ANS functions, including sympathetic and parasympathetic divisions, which occurred during acupuncture on the Sishencong points, may have resulted from the direct effects on nerve fibers, receptors, or they may be associated with latent central nervous system involvement. The detailed mechanisms warrant further investigation.

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