Transient Increase in Human Muscle Sympathetic Nerve Activity during Manual Acupuncture

Yoshiki SUGIYAMA, Ye-Xiang XUE, and Tadaaki MANO

Department of Autonomic and Behavioral Neurosciences, Division of Higher Nervous Control, Research Institute of Environmental Medicine, Nagoya University, Chikusa-ku, Nagoya, 464-01 Japan

Abstract To clarify the effects of manual acupuncture on the autonomic nervous system, we measured efferent muscle sympathetic nerve activity (MSNA) from the right peroneal nerve while simultaneously recording blood pressure and heart rate both during the resting period and after manual acupuncture applied to the Tsusanli acupoint of the same limb. The needle was rotated intermittently for 30 s at 5-min intervals. MSNA increased transiently with the suppression of heart rate during rotation of the acupuncture needle. No consistent change in blood pressure was found throughout the acupuncture session. After removal of the needle, both the MSNA and heart rate returned to the initial control values, and the mean blood pressure showed an increase over the resting value. MSNA showed a negative correlation with heart rate in four out of five subjects who received acupuncture. These results suggest that the coactivation of cardiac vagal and muscle sympathetic nerves is evoked by the acupuncture maneuver.

Key words: acupuncture, autonomic nervous system, muscle sympathetic nerve activity, Tsusanli acupoint.

Clinically, acupuncture therapy is given to patients who have various pathological conditions that produce such common symptoms as pain or muscle soreness. There are several theories as to the mechanism of action of acupuncture, and involvement of the autonomic nervous system has been suggested. In previous reports, two opposite sympathetic responses were found when acupuncture was applied to human subjects [1–3]. The sympathomimetic response, also described as the short-term response, consists of a cooling sensation followed by decreased skin temperature in the same spinal segment. In contrast, the sympatholytic response, or long-term effect, lasts for hours and is expressed as a warm sensation. Other reports suggest the possibility of parasympathetic cholinergic involvement [4, 5].

Using microneurography, muscle sympathetic nerve activity (MSNA) can be

recorded as postganglionic sympathetic nerve activity from human peripheral nerves [6,7]. This activity has a major role in increased peripheral vascular resistance, releasing norepinephrine from the nerve endings that innervate the blood vessels in muscles. MSNA is under the control of the vasomotor center in the medulla oblongata which receives negative feedback signals from arterial and cardiopulmonary baroreceptors [8]. Because of the negative feedback characteristic of the baroreflex via arterial baroreceptors, MSNA discharge is considered to be synchronized in part to the heartbeat and in part to fluctuations in blood pressure [9, 10].

The physiological responses of the cardiovascular system during acupuncture appear to be complex. Many factors may be responsible for the changes seen; e.g., cardiac or vasomotor, skin or muscle, and sympathetic or parasympathetic nerve activities. The relation between change in MSNA and systemic blood pressure during acupuncture, however, has yet to be clarified. We describe the changes found in MSNA associated with changes in heart rate and in systemic blood pressure during acupuncture.

SUBJECTS AND METHODS

Healthy young volunteers, 8 men and 2 women, aged 25 to 37 years, who were familiar with acupuncture, were studied. The subjects were divided into two groups, the acupuncture group (4 men and 1 woman) and the control group (4 men and 1 woman). The subjects lay supine on a bed in a room with the temperature controlled between 28 and 32°C. MSNA was recorded microneurographically from the right peroneal nerve simultaneously with an electrocardiogram as well as with a pneumogram recorded by a hyperventilation detector (Nihon Kohden MZE-6100), and arterial blood pressure was recorded by mass compensatory photoplethysmography (Ohmeda Finapres 2300).

An epoxy-insulated tungsten microelectrode with a tip diameter of 1 μ m and an impedance of 2 to 5 M Ω (Federick Haer & Co 26-05-1) was inserted percutaneously without anesthesia in the muscle nerve fascicles of the right peroneal nerve at the popliteal fossa. After amplification with a high input-impedance preamplifier (WP Instruments DAM-6A), the nerve signals were passed through two active filters between 500 and 5,000 Hz (NF Corporation E-3201A) and monitored on a cathode-ray oscilloscope (Tektronix 5113) equipped with a loudspeaker. The identification of MSNA was based on the following criteria: 1) efferent activity recorded from the muscle nerve fascicle, 2) spontaneous discharge synchronous with heartbeat, 3) marked enhancement by Valsalva's maneuver, and 4) no response to arousal stimuli [6, 7].

After the 15-min resting period recording, a sterile Chinese acupuncture needle with a shaft diameter of 320 μ m was inserted in the right Tsusanli acupoint (2 cm below the lateral condyle of the tibia and 1 cm outside the tibial crest, ST36: WHO) in the acupuncture group and was kept in place for 20 min at a depth of 25 to 30

Fig. 1. Typical changes in mean blood pressure (upper trace), instantaneous heart rate (middle trace), and MSNA (lower trace) induced by acupuncture to the Tsusanli acupoint in one subject. Bar: period of acupuncture application; thick bars: periods of needle rotation.

Fig. 2. Typical example of changes in heart rate (ECG and instantaneous HR), MSNA (original and integrated traces) and the blood pressure wave recorded by Finapres during rotation of the acupuncture needle. Bar: period of acupuncture application; thick bar: period of needle rotation. Note: a decrease in heart rate is associated with an increase in MSNA.

mm. Since three kinds of techniques such as rotating needles, tapping needles, supplying electricity are empirically known to intensify the clinical effects of acupuncture therapy compared with the conventional method; retaining needles in acupoints, the needle was rotated manually for 30 s immediately after insertion and then at 5-min intervals. At the end of the fifth rotation, the needle was removed, and post-stimulus resting recordings were taken for 15 min. The subjects who participated as the control group were placed on a bed for 50 min without acupuncture.

Nerve signals were rectified at full wave and integrated using a resistance-capacitance integrating circuit with a time constant of 0.1 s to obtain a mean voltage neurogram. Since MSNA discharges synchronously with the heartbeat, sympathetic bursts were identified by inspecting the mean voltage neurogram with the help of a sound monitor. For the quantitative analysis of MSNA, the number of pulse-synchronous bursts per minute and the number of bursts per 100 heartbeats respectively were measured as the burst rate and burst incidence. Using the burst rate or burst incidence for the quantification of MSNA fails to take account of burst amplitude. However, burst rate and burst incidence have been shown to be reproducible and reliable when quantifying MSNA [10, 11]. Instantaneous heart rate was computed beat by beat from the R-wave on the electrocardiogram. Mean blood pressure was also calculated beat by beat from the systolic and diastolic blood pressure, following the formula: mean blood pressure = (systolic blood pressure + $2 \times$ diastolic blood pressure)/3. Mean values of the burst rate, burst incidence, heart rate, and mean blood pressure were measured every minute from the beat-to-beat data. In the period of needle rotation, these values were measured from the data of 30 s. Values were compared using Student's *t*-test between the two groups, and compared with resting values in the acupuncture group. A probability of less than 0.05 was considered significant. Values are expressed as means $\pm$ SE.

This study was approved by the Human Research Committee of the Research Institute of Environmental Medicine, Nagoya University. It was conducted under the guidelines of the Japan Microneurography Society. Written informed consent was obtained from each person studied.

RESULTS

Figures 1 and 2 show representative recordings of the MSNA in one of the subjects together with blood pressure and instantaneous heart rate throughout the

Fig. 3. Changes in heart rate (A), mean blood pressure (B), and MSNA as assessed by the burst rate (C) and burst incidence (D). Dotted lines indicate mean $\pm$ SD (upper line) and mean $-$ SD (lower line) of each variable in the control group. Acupuncture was applied to the Tsusanli point. Abscissa: time course of the experiment. Bar: period of application; thick bars: periods of needle rotation. Statistical significance: $^{\dagger}p < 0.05$ vs. control group, $*p < 0.05$ vs. resting value.

Fig. 3.

Fig. 4. Relationship between heart rate and MSNA in the acupuncture group. There was a negative correlation in 4 out of 5 subjects.

experiment (Fig. 1) and during needle rotation (Fig. 2). The instantaneous heart rate decreased transiently with increases of the integrated MSNA trace both in the burst rate and burst amplitude during each needle rotation session.

Changes in the heart rate and mean blood pressure, and in MSNA in the burst rate and burst incidence are summarized as mean values ($\pm$ SE) for the five subjects in Fig. 3. Because of the large inter-individual variations and a small number of the subjects, none of the parameters showed statistically significant changes compared with the control group. The exceptions were the MSNA in burst incidence during the second and third needle rotation. There are two main findings: the cyclic behavior of the variables during the repeated sessions of rotation of the acupuncture needle, and the different behaviors following removal of the needle. Rotation of the acupuncture needle induced two simultaneous changes; a transient reduction in heart rate (Figs. 2 and 3A) and an increase in MSNA in both the burst rate and burst incidence (Figs. 2 and 3C, D). No significant change in mean blood pressure was detected throughout the procedure (Fig. 3B). There were no cumulative effects after the repeated rotations on the heart rate, mean blood pressure and on the MSNA in the burst rate and burst incidence (Fig. 3). Both the heart rate and MSNA returned to the control values 3–4 min before a new rotation session.

Following removal of the needle, the heart rate immediately returned to the control value obtained before acupuncture. Blood pressure, however, tended to remain at a somewhat higher level than that found before and during acupuncture. MSNA in the burst incidence tended to decrease in the first minutes after removal of the needle, then gradually returned to the control value.

To clarify the mechanism of the increased MSNA during acupuncture, we

analyzed a correlation between MSNA and heart rate. There was a negative correlation with heart rate in 4 out of 5 subjects (Fig. 4).

DISCUSSION

Acupuncture applied at different sites results in various hemodynamic and neurogenic responses [2, 12, 13]. The differences in response suggest that several regulatory pathways are involved in the acupuncture action mechanism. We examined the effects of manual acupuncture at the Tsusanli acupoint on the muscle vasomotor activity of the same extremity in relation to the systemic cardiovascular parameters of instantaneous heart rate and blood pressure as measured by a Finapres. When acupuncture was applied, MSNA showed a transient increase accompanied by a transient reduction in heart rate. Ernst and Lee [1, 2] using a thermal detection technique for skin found that skin vasomotor activity increases during acupuncture at the Hoku acupoint. A cooling tendency of the skin is interpreted as a short-term decrease in skin blood flow caused by the transient increase in skin vasomotor activity in response to acupuncture. Because of the parallel behaviors of muscle and skin vasomotor activities [11, 14], an increase in MSNA can be interpreted as the sympathomimetic effect of acupuncture on muscle vasomotor activity.

In contrast to the sympathomimetic effect of acupuncture, Ogawa *et al.* [15] found that segmental suppression of sweating was caused by electrical acupuncture to the lateral chest wall on the ipsilateral side. Because sweating is regulated by sudomotor nerve activity, a component of skin sympathetic nerve activity [6, 7], their finding suggests that acupuncture to the lateral chest has a sympathosuppressive effect similar to the skin pressure-sweating reflex, the so-called pressure hemihidrosis or hemihidrotic reflex [15–17]. Sato and Schmidt [18] reported complex visceral responses to cutaneous stimulation in animal experiments. These observations indicate that the site of acupuncture is an important factor in the different responses of internal organs.

To determine what the mechanism is of the increased MSNA in both the burst rate and burst incidence during acupuncture, in particular during needle rotation, we analyzed the relation of MSNA to heart rate. There was a negative correlation with heart rate in 4 out of 5 subjects. Acupuncture has been shown to be cardiosuppressive (slowing the heart rate), which we also found. Yazawa [5] studied heart rate variation during acupuncture at the Ximen point (PC4: WHO). He reported that atropine administration blocked the acupuncture-induced effect of reduced heart rate variability, and he suggested that the mechanism that slows the heart rate is activation of the parasympathetic cholinergic system. The negative correlation between MSNA and the heart rate observed in our study suggests that the transient increase in MSNA during needle rotations is attributable to the primary sympatho-excitatory effect of acupuncture.

After removal of the acupuncture needle, MSNA tended to be suppressed for

a few minutes concomitant with a relative increase in blood pressure, which suggests a sympatholytic response in vasomotor activity [1,2]. Such late sympathosuppressive effects may be partly due to the baroreflex mechanism.

In conclusion, the coactivation of cardiac vagal and muscle sympathetic nerves is evoked by the acupuncture maneuver.

REFERENCES

1. Ernst M and Lee MHM: Sympathetic vasomotor changes induced by manual and electrical acupuncture of the Hoku point visualized by thermography. *Pain* **21**: 25–33, 1985
2. Ernst M and Lee MHM: Sympathetic effects of manual and electrical acupuncture of the Tsusanli knee point: Comparison with the Hoku hand point sympathetic effects. *Exp Neurol* **94**: 1–10, 1986
3. Moriyama T: The effect of acupuncture stimulation on muscle nerve sympathetic activity in man. *J Jpn Assoc Phys Med Baln Clim* **49**: 95–102, 1986 (in Japanese)
4. Ionescu-Tirgoviste C, Pruna S, and Bajenaru O: The participation of autonomic nervous system in the mechanism of action of acupuncture. *Am J Acupun* **19**: 21–28, 1991
5. Yazawa K: Mechanism of the autonomic nervous system in acupuncture-stimulated bradycardia. *J Jpn Assoc Phys Med Baln Clim* **48**: 183–189, 1985 (in Japanese)
6. Mano T: Sympathetic nerve mechanisms of human adaptation to environment—Findings obtained by recent microneurographic studies. *Environ Med* **34**: 1–35, 1990
7. Vallbo ÅB, Hagbarth K-E, Torebjörk HE, and Wallin BG: Somatosensory, proprioceptive, and sympathetic activity in human peripheral nerves. *Physiol Rev* **59**: 919–957, 1979
8. Fagius J, Wallin BG, Sundlöf G, Nerhed C, and Englesson S: Sympathetic outflow in man after anaesthesia of the glossopharyngeal and vagus nerves. *Brain* **108**: 423–438, 1985
9. Hagbarth K-E and Vallbo ÅB: Pulse and respiratory grouping of sympathetic impulses in human muscle nerves. *Acta Physiol Scand* **74**: 96–108, 1968
10. Sundlöf G and Wallin BG: Human muscle nerve sympathetic activity at rest: Relationship to blood pressure and age. *J Physiol (Lond)* **274**: 621–637, 1978
11. Sundlöf G and Wallin BG: The variability of muscle nerve sympathetic activity in resting recumbent man. *J Physiol (Lond)* **272**: 383–397, 1977
12. Beachman WS and Perl ERL: Characteristics of a spinal sympathetic reflex. *J Physiol (Lond)* **173**: 431–438, 1964
13. Hoffmann P and Thorén P: Long-lasting cardiovascular depression induced by acupuncture-like stimulation of the sciatic nerve in unanaesthetized rats: Effects of arousal and type of hypertension. *Acta Physiol Scand* **127**: 119–126, 1986
14. Bini G, Hagbarth K-E, Hynninen P, and Wallin BG: Regional similarities and differences in thermoregulatory vaso- and sudomotor tone. *J Physiol (Lond)* **306**: 553–565, 1980
15. Ogawa T, Asayama M, and Ito Y: The extent of hemihidrosis caused by skin pressure and acupuncture. *Auton Nerv Syst* **18**: 246–253, 1981 (in Japanese)
16. Sugiyama Y, Watanabe T, Takeuchi S, Iwase S, and Mano T: Asymmetric discharges of skin sympathetic nerve in humans—With special reference to pressure hemihidrosis.

Environ Med 36: 207-210, 1992

17. Takagi K and Sakurai T: A sweat reflex due to pressure on the body surface. Jpn J Physiol 1: 22-28, 1950
18. Sato A and Schmidt RF: The modulation of visceral functions by somatic afferent activity. Jpn J Physiol 37: 1-17, 1987