Eur J Appl Physiol (1994) 68:460–464

European Journal of Applied Physiology and Occupational Physiology

Different thermal dependency of cutaneous sympathetic outflow to glabrous and hairy skin in humans

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Accepted: 16 February 1994

Abstract. We investigated the effects of ambient temperature on the sudomotor and vasoconstrictor components of skin sympathetic nerve activity (SSNA). The sympathetic traffic was measured by simultaneous microneurographic recording from post-ganglionic nerve fibres in the tibial and the peroneal nerves. When the ambient temperature was raised from 25° C to 34° C, both sudomotor and vasoconstrictor components of SSNA were enhanced in the peroneal nerve but were suppressed in the tibial nerve. The sudomotor and vasoconstrictor sympathetic outflows were elevated in both nerves when the temperature was lowered from 34° C to 18° C. Our results suggested that the sudomotor and the vasoconstrictor components of SSNA are differently modulated by ambient temperature. The difference in sudomotor and vasoconstrictor components of SSNA in the tibial and the peroneal nerves at different ambient temperature may have been responsible for the differences observed in sweating and vasoconstriction in glabrous and hairy skin.

Key words: Skin sympathetic nerve activity – Sweating – Skin blood flow – Ambient temperature

Introduction

It has been shown that the sympathetic outflows from the central nervous system are distributed to different effector organs according to regional differentiation (Kullman et al. 1970; Hales and Iriki 1975; Hales et al. 1978, 1979). In addition to animal studies, simultaneous microneurographic recording from skin and muscle sympathetic nerves in human subjects has enabled differentiation between the sympathetic outflow efferents to muscle and skin in human subjects (Wallin 1986). In humans, two components of the sympathetic outflow to the skin, sudomotor and vasoconstrictor nerves, can also be differentiated by changes in the effector responses induced in the skin electric potential and the photo-electric plethysmography, respectively (Bini et al. 1980a, b). In particular, Bini et al. (1980b) have recorded skin sympathetic nerve activity (SSNA) from two nerves simultaneously and have discussed the regional differentiation. However, they did not analyse SSNA by classifying sudomotor and vasoconstrictor bursts quantitatively. The qualitative and quantitative relationships between sweating and SSNA, as well as between vasoconstriction and SSNA have been extensively studied (Iwase et al. 1988, 1990; Sugenoya et al. 1990; Mano 1990) but regional differences have not yet been investigated.

Ambient temperature is known to alter SSNA, and modulate thermal sweating and vasoconstriction in glabrous and hairy skin. Previously, we have reported an ambient temperature-dependent difference in reflex sympathetic bursts in the tibial and peroneal nerves (Iwase et al. 1990) but differences in resting activity have not yet been analysed. The aim of the present study was to elucidate the ambient temperature-dependence of the sudomotor and vasoconstrictor responses of SSNA to glabrous and hairy skin. In the present study, SSNA was recorded simultaneously from skin nerve fascicles of the tibial nerve that innervate mainly glabrous skin and the peroneal nerve that innervates mainly hairy skin using the double recording technique of microneurography.

Methods

Subjects. Five healthy male volunteers (aged 23–30 years, mean 27.8 years) were fully informed about the aims of the study and gave their written consent to participate in the experiment. This study was approved by Human Research Committee, Research Institute of Environmental Medicine, Nagoya University, Japan.

Recordings and identification of skin sympathetic nerve activity. All experiments were performed with the subjects in the supine position. Micro-electrodes with an impedance of 3–5 MΩ and a tip diameter of 1 μm were inserted percutaneously without

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anaesthesia into the skin nerve fascicles of the tibial and peroneal nerves at the popliteal fossa to record SSNA. The spontaneous SSNA from these nerves was recorded simultaneously. The SSNA was identified using the criteria of previous studies (Hagbarth et al. 1972; Iwase et al. 1988, 1990; Mano 1990; Wallin 1992). The four criteria for identification of SSNA were:
1. Non-synchronous with heart beat, and irregular burst activity with a duration of 300–500 ms
2. Generation of reflex bursts during mental or somatosensory (sound, pain, light, or electrical) stimuli
3. To be followed by sweating or a reduction in skin blood flow
4. Dependence on ambient temperature.
The sympathetic nerve signals from the tibial and peroneal nerves were fed into two high impedance input pre-amplifiers (WP Instruments DAM-6A), with band-pass filters set at 500–5000 Hz. During the experiment, the filtered neurogram was monitored with a cathode-ray oscilloscope (Tektronix-5113) and an audio amplifier, and stored on magnetic tape for later analysis. Nerve signals were fully rectified, integrated with a time constant of 0.1 s and displayed by a thermal pen recorder (NEC-San-ei Recti-Horiz) as a mean-voltage neurogram. The SSNA was quantified by the integrated value of the mean voltage neurogram, and expressed as SSNA bursts per minute (burst rate).

Identification and quantification of sudomotor and vasoconstrictor nerve activities. An occurrence of SSNA burst activity followed by sweat expulsion with a latency of 2.4–3.0 s was classified as a sudomotor burst, while that followed by a reduction in skin blood flow with a latency of about 6.3 s was classified as a vasoconstrictor burst (Iwase et al. 1988, 1990; Mano 1990). Any SSNA bursts followed by both sweat expulsion and reduction in skin blood flow were classified as mixed activity (Sugenoya et al. 1990). Any SSNA bursts that induced no effector response were classified as unidentified activity (Sugenoya et al. 1990).

Quantification of sweating. The ventilated capsule method (Fourtion: Hidrograph AMU-2) was employed for determination of the sweat expulsion. Two plastic capsules, each with an open surface area of 1 cm^2, were fixed on the sole of the foot and the dorsum pedis ipsilateral to the microneurographic recording. Dry nitrogen was allowed to flow into the capsules at a rate of 0.2 $l \cdot min^{-1}$, and was withdrawn into highly sensitive capacitance hygrometers to determine the humidity change. Sweat expulsion (Ogawa and Sugenoya 1993) was used for the identification of sudomotor nerve activities.

Measurement of skin blood flow. Laser Doppler flowmetry (Advance: ALF 21) was employed to measure skin blood flow. Two probes were attached to the skin of the sole of the foot and the dorsum pedis ipsilateral to the microneurographic recording. Reduction in skin blood flow was used to identify vasoconstrictor activities.

Experimental protocol. The subjects reclined on a bed in a sound- and light-proof room. Initially, ambient temperature was maintained at 25° C for 30 min, during which spontaneous SSNA from the two nerves were recorded for 20 min. Ambient temperature was then raised to 34° C; simultaneously, in some cases, water blankets (Blanketrol) were applied to warm the subjects. After body heating for 30 min, the spontaneous SSNA was recorded for 20 min, after which the ambient temperature was lowered to 18° C, and in some subjects their bodies were simultaneously cooled using the water blankets. The SSNA were recorded for 20 min after 30 min of cold exposure.

Data analysis. The data obtained were quantified as the burst number per minute (burst rate) since there was no way to guarantee that the tip of the electrode would not become dislodged and thus alter the signal : noise ratio during the long period of the experiment. They were compared among the ambient temperatures in tibial or peroneal nerves using Student's paired *t*-test. Any *P* values less than 0.05 were considered significant.

Results

Resting skin sympathetic nerve activity at various ambient temperatures

The tibial and peroneal SSNA discharges were fairly synchronous under different ambient temperatures.

Tibial SSNA was moderately active [21.2 (SEM 4.5) $bursts \cdot min^{-1}$] at the thermoneutral ambient temperature of 25° C, and was suppressed to 10.9 (SEM 5.6) $bursts \cdot min^{-1}$ ($P < 0.05$, vs 25° C) when the ambient temperature was raised to 34° C. On the other hand, an increase was observed to 29.4 (SEM 3.0) $bursts \cdot min^{-1}$ ($P < 0.05$, vs 25° C) when the ambient temperature was lowered to 18° C.

The SSNA burst rate in the peroneal nerve increased from 17.8 (SEM 6.1) $bursts \cdot min^{-1}$ to 36.6 (SEM 6.5) $bursts \cdot min^{-1}$ when the ambient temperature was raised from 25° C to 34° C (Fig. 1). During air cooling from 34° C to 18° C, the peroneal SSNA burst rate decreased to 24.7 (SEM 6.4) $bursts \cdot min^{-1}$, which was still significantly higher than the basal value at 25° C ($P < 0.05$).

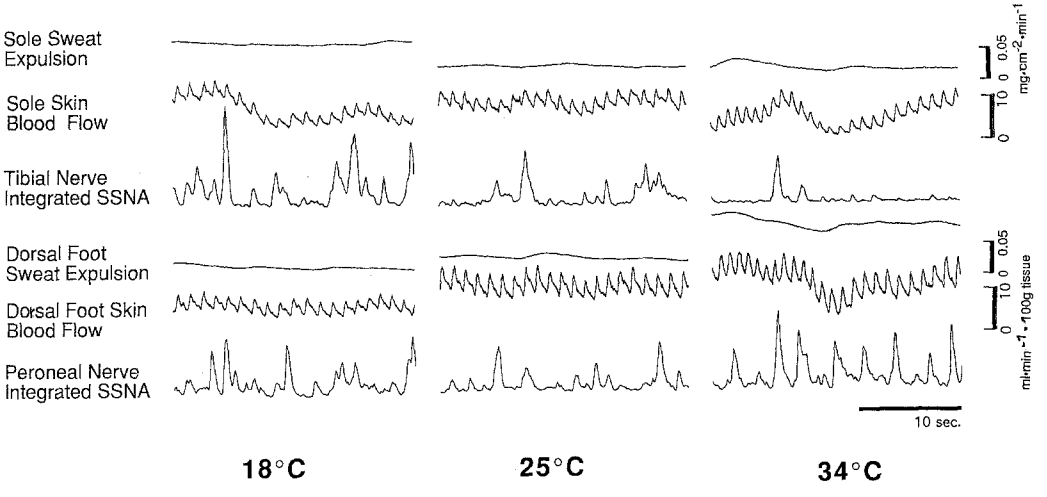

Fig. 1. Changes in skin sympathetic nerve activity (*SSNA*) from the tibial and the peroneal nerves at various ambient temperatures. Tibial and peroneal *SSNA* discharged almost synchronously, while the activity was different at different ambient temperatures

Changes in sudomotor and vasoconstrictor components of SSNA under various ambient temperatures

Figure 2 shows changes in the sudomotor and vasoconstrictor components of SSNA as well as mixed and unidentified bursts at various temperatures in the tibial and the peroneal nerves.

In the tibial nerve, both sudomotor and vasoconstrictor components showed reduced activities with an increase in ambient temperature (25 to 34° C) and enhanced activities upon cooling (34 to 18° C). The sudomotor component showed a tendency to decrease from 4.6 (SEM 1.6) bursts·min^{-1} at 25° C to 2.1 (SEM 3.6) bursts·min^{-1} at 34° C ($0.15 < P < 0.1$, NS). Upon cooling from 34° C to 18° C, sudomotor activity increased to a value of 6.7 (SEM 1.1) bursts·min^{-1} ($P < 0.01$ vs 25° C). The vasoconstrictor component of tibial SSNA decreased from 9.6 (SEM 1.9) to 3.7 (SEM 1.2) bursts·min^{-1} ($P < 0.001$ vs 25° C) with warming (25 to 34° C) and increased to 14.2 (SEM 2.0) bursts·min^{-1} ($P < 0.05$ vs 25° C) while cooling from 34° C to 18° C.

The overall sudomotor activity in the peroneal nerve (sudomotor and mixed activities) was similar at 25° C to that in the tibial nerve. The peroneal sudomotor burst rate at 25° C was 5.0 (SEM 3.1) bursts·min^{-1}, increased significantly upon warming to 34° C [12.7 (SEM 2.6) bursts·min^{-1}, $P < 0.01$ vs 25° C] and decreased to 4.1 (SEM 4.3) bursts·min^{-1} at 18° C (not significant vs 25° C). The vasoconstrictor component in the peroneal nerve was lower at the thermoneutral temperature (25° C) than that of the tibial nerve. Peroneal vasoconstrictor activity increased from of 5.0 (SEM 2.2) bursts·min^{-1} at 25° C with both cooling and warming, to 18° C [10.2 (SEM 1.0) bursts·min^{-1}, $P < 0.01$ vs 25° C] and 34° C [3.5 (SEM 2.7) bursts·min^{-1}, $P < 0.01$ vs 25° C], respectively.

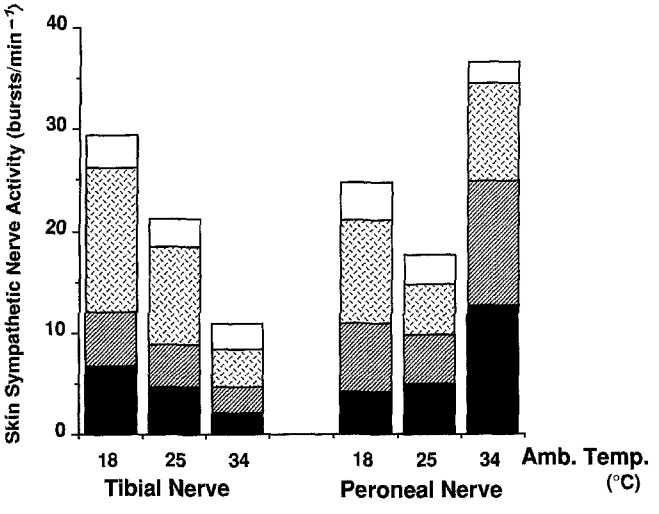

Fig. 2. Changes in the components of skin sympathetic nerve activity from the tibial and peroneal nerves at ambient temperatures of 18° C, 25° C, and 34° C. Sudomotor and vasoconstrictor components as well as mixed components of both in the tibial nerve were suppressed with an increase in ambient temperature, whereas only the sudomotor component in the peroneal nerve was increased with an increase in ambient temperature. Activity in the vasoconstrictor and mixed components in the peroneal nerve was highest at an ambient temperature of 34° C, but lowest at 25° C. The unidentified component in the figure corresponds to a sympathetic burst discharge which affected neither skin blood flow nor sweat rate. □ Unidentified; ⊠ Vasoconstrictor; ▨ Mixed; ■ Sudomotor

Discussion

Regional differentiation in sympathetic nerve activity was first reported by Dastré and Morat (1884). It was found that in animal experiments, visceral blood flow decreased, whereas skin blood flow increased in response to hypoxic stimulation (Dastré and Morat 1884). This phenomenon was also observed in humans by Bini et al. (1980b) who compared skin sympathetic nerve activities in the median and the posterior antebrachial nerves, and estimated that the variability was due to a qualitative difference in the fibre composition. The thermal dependency of sympathetic differentiation to the palm of the hand and the forearm has been investigated with regard to sweating by Ogawa 1975. Mental stimuli increased not only sweating in the glabrous skin of the palm of the hand and the sole of the foot, but also sweating in the general body surface of the skin. On the other hand, thermal stimuli enhanced not only sweating over the general body surface area, but also suppressed palmar sweating in some subjects. The tibial nerve innervates the glabrous skin of the sole of the foot, and it is conceivable that the sudomotor component of this nerve is influenced mainly by mental stimuli, contributing to mental sweating in this area of skin. The peroneal nerve that innervates hairy skin is affected mainly by thermal stimuli, and is thus involved in thermal sweating in the dorsum pedis.

In the present study, we investigated the differences in sympathetic outflow between two nerves that innervate glabrous and hairy skin. Simultaneous analysis of individual neural bursts and their effector organ responses allowed the evaluation of the differentiation of sudomotor and vasoconstrictor components of the SSNA traffic in these nerves. The assignment of sudomotor activity was performed by confirming sweating activity and that of the vasoconstrictor components by observing skin blood flow changes.

The effects of ambient temperature on nerve traffic and its components were tested by warming (to 34° C) or cooling (18° C) from the thermoneutral ambient environment (25° C). Raising the ambient temperature from 25° C to 34° C caused a marked reduction in the sudomotor component of the tibial nerve, with a concomitant increase in the same component of the peroneal nerve. This behaviour was consistent with previous observations of enhanced thermal sweating and suppressed mental sweating in the general body surface with warming (Ogawa 1975). It would be expected that sudomotor nerve activity in the peroneal nerve would be stimulated by exposure to heat in the environment to facilitate sweat excretion. On the other hand, re-

duced activity in the tibial nerve may be a good mental adjustment to a temperature of 34° C, leading to a marked reduction of sweating in glabrous skin.

Lowering the ambient temperature to 18° C caused similar sudomotor reactions in both nerves. The slightly higher sudomotor activity in the tibial nerve at 18° C would indicate enhanced mental sweating in the sole of the foot, whereas the sudomotor response in the peroneal nerve to the same ambient temperature appears to reflect the mental responses in the general body surface (Kuno 1956) since the thermal stimuli would have been totally removed under such ambient conditions.

The vasoconstrictor component in the two nerves showed variable activity in reaction to temperature changes. The peroneal nerve showed enhanced vasoconstrictive activity at both 18° C and 34° C compared to the thermoneutral (25° C) state, while the tibial nerve showed a marked increase in activity responding to cooling, and a marked suppression responding to warming. Under cold environmental conditions, the overall tendency was for vasoconstriction in the peripheral skin vasculature to prevent heat loss from the skin surface. The parallel course of the reactions in the two nerves at 18° C would indicate poor differentiation of vasoconstrictive activity between those peripheral nerves in a cold environment.

On the other hand, differentiation of vasoconstrictor activity in the tibial and peroneal nerves was marked in a warm environment, being higher in the peroneal nerve. In hairy skin, active vasodilatation occurred when the subject was heated. With regard to this vasodilatation, two causative mechanisms can be postulated. One possibility is the involvement of sudomotor nerve activity. Some co-transmitters, such as vasoactive intestinal polypeptide, have been postulated to be released at the cholinergic sudomotor nerve endings around eccrine sweat glands to dilate the peripheral vasculature (Lundberg et al. 1980). Another possible mechanism of active vasodilatation could be the involvement of vasodilator nerve fibres, although vasodilator nerve activity has not been sufficiently demonstrated in humans (Sugenoya et al. 1991). Increased vasoconstrictive activity in the peroneal nerve in the warm environment may have been associated with the observed active vasodilatation in the hairy skin. This may be a mechanism for sustaining cutaneous vascular tone and maintaining the systemic circulation in warm/hot environments. In fact, the heat-induced vasoconstriction as has been suggested to be caused in the finger by extreme thermal stress (Nagasaka et al. 1990) could be a highly probable cause of increased vasoconstrictive activity in the hairy skin at high ambient temperatures. Otherwise, the possibility must be considered that the vasodilator bursts in the peroneal nerve were largely misidentified as being vasoconstrictor bursts under warm environmental conditions, since we do not have a method of identifying cutaneous vasodilator nerve activity.

In conclusion, our study would indicate that skin sympathetic nerve activity changes its sudomotor and vasoconstrictor components differently in the tibial and peroneal nerves depending on ambient thermal conditions, and that regional differentiation exists in sudomotor and vasoconstrictor components of SSNA leading to glabrous and hairy skin, respectively.

Acknowledgements. We would like to thank Dr. A. J. Banes, Professor in the Division of General Surgery, Dr. J. Faber, Associate Professor in the Division of Physiology at the University of North Carolina, and Dr. N. Askenasy, Visiting Researcher to Research Institute of Environmental Medicine, Nagoya University, for their help in preparing the manuscript.

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