Intensity-dependent thermoregulatory responses at the onset of dynamic exercise in mildly heated humans

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Humans have an excellent ability to regulate their internal and skin temperatures by sweating during dynamic exercise. The sweating response during dynamic exercise is controlled by changes in thermal factors, such as internal and skin temperatures. However, the initiation of dynamic exercise and brief isometric exercise under warm environmental conditions can increase the sweating rate without marked changes in the thermal factors. This indicates that sweating responses are due mainly to alterations in nonthermal factors associated with mental stress, central command, or metabolic mechanisms.

Van Beaumont and Bullard showed for the first time that the sweating rate increases concomitantly with a sinusoidal change in the workload when the internal temperature is constant. Neither of these experiments evaluated a quantitative manner how the nonthermal sweating response at the onset of dynamic exercise changed with increasing exercise intensity. We concluded that nonthermal and cutaneous blood flow responses are exercise intensity dependent but directionally opposite at the onset of dynamic exercise in mildly heated humans. Furthermore, cutaneous blood flow responses to increased exercise intensity are greater in glabrous (palm) than in nonglabrous (chest and forearm) skin.

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In contrast to the sweating response, cutaneous vascular conductance (CVC), which is also associated with nonthermal factors, decreases at the beginning of dynamic exercise (6, 13, 30). Reflex cutaneous vasoconstriction occurs in the chest, forearm, foot, palm, and finger (2, 6, 11, 13, 24, 30, 35), and vasoconstriction is greater in glabrous (hairless) than in nonglabrous (hairy) skin at a given exercise intensity (24). Furthermore, there is a relatively high correlation between the reduction in CVC on the forearm and increases in exercise intensity at the onset of dynamic exercise under normothermic conditions (30). However, the potential differences in the effects of exercise intensity on cutaneous vasoconstriction between nonglabrous and glabrous skin at the onset of dynamic exercise remain to be verified, because nonglabrous skin is regulated by an active vasodilator system and a noradrenergic vasoconstrictor system, whereas glabrous skin is controlled entirely by a noradrenergic vasoconstrictor system (5, 12).

The purpose of the present study was to investigate quantitatively the effects of changing exercise intensity (nonthermal factors) on sweating response and to determine whether this quantitative sweating response was due to changes in ASG and/or SGO at the onset of dynamic exercise in humans who were mildly heated. Moreover, we determined the different effects of exercise intensity on cutaneous blood flow response at the onset of dynamic exercise in nonglabrous and glabrous skin.

METHODS

Subjects. Eighteen healthy male subjects were recruited for the study. Their age, height, weight, and maximal O$_2$ uptake (V$_{O2 \text{max}}$) were as follows: 20.6 ± 1.1 yr, 1.69 ± 0.01 m, 56.7 ± 1.1 kg, and 49.9 ± 2.4 ml·kg$^{-1}$·min$^{-1}$, respectively. The purpose and procedures of the study were explained to the subjects before their informed consent was obtained. The study was approved by the Human Subjects Committee of our department at Kobe University.

Procedures. Before the experiments, V$_{O2 \text{max}}$ of each subject was measured using a ramped exercise protocol (15–30 W/min, pedaling frequency set at 60 rpm) on a cycle ergometer, which was modified so that the subjects sat in a contoured chair behind the pedals (semisupine position). At least two of the following criteria were used to evaluate the V$_{O2 \text{max}}$ test: 1) maximal or near-maximal values of rating of perceived exertion (RPE), 2) respiratory gas exchange ratio (>1.05, 3) heart rate (HR) within 10 beats/min of the age-predicted maximal HR, and 4) inability to maintain a pedaling frequency of 40 rpm.

The main experiments were conducted in an environmental chamber (model SR-3000, Nagano Science, Osaka, Japan) maintained at an ambient temperature of 35°C and a relative humidity of 50% with minimal air movement. We selected these environmental conditions to produce a slight increase in sudomotor activation and skin blood flow (SkBF), with withdrawal of sympathetic vasoconstrictor activation at rest by raising the skin temperature without markedly changing the internal temperature (17, 18). After entering the chamber, each subject rested in the semisupine position on the modified cycle ergometer for ~60 min until the SR and SkBF levels reached a steady state. During this period, the instruments for measuring various parameters were affixed. After this rest period, the baseline data were recorded for 5 min before the commencement of the cycle exercise. The subjects cycled (60 rpm) at three relative intensities of 30% (58 ± 4.8 W), 50% (112 ± 7.2 W), and 70% V$_{O2 \text{max}}$ (168 ± 9.6 W) for 60 s in random order. We controlled the respiratory frequency at 30 breaths/min during 120-s rest, 60-s cycle exercise, and 120-s recovery periods using an auditory signal, because breathing frequency influences skin sympathetic nerve activity (4). The exercise bouts were separated by rest periods of ≥10 min to make the hemodynamic and thermoregulatory responses return to the baseline levels and to minimize muscle fatigue.

On a different day, the subjects performed the cycle exercise under the same conditions and procedures used in the main experiment to measure O$_2$ uptake (V$_{O2}$) during the exercise.

Measurements. V$_{O2}$ was estimated from the measurements of ventilation volume and expired fraction of O$_2$ and CO$_2$ production (Aeromonitor AE-300S, Minato, Osaka, Japan). In the main experiment, esophageal temperature (T$_{es}$), local skin temperature at nine body sites (forehead, chest, abdomen, forearm, hand, palm, thigh, lower leg, and foot), SR on the chest, forearm, thigh, and palm, ASG on the forearm, SkBF on the chest, forearm, and palm, HR, arterial blood pressure (systolic and diastolic pressure), and RPE were measured.

The temperature variables were measured with a copper-constantan thermocouple. One thermocouple with a silicone-lubricated tip was placed at a distance of one-fourth of the standing height from the external nares. The mean skin temperature (T$_{sk}$) was estimated according to the method of Hardy and DuBois (9).

The SR on the chest, forearm, thigh, and palm were measured continuously using the ventilated capsule method (17, 22), in which dry nitrogen gas was supplied to four capsules (1.54 cm$^3$) at a flow rate of 600 ml/min, and the humidity and temperature of the nitrogen gas flowing out of each capsule were measured using a capacitance hygrometer (model HMP 133Y, Vaisala, Helsinki, Finland). The time delay for measuring the SR was 1 s, which was taken into account when the SR was calculated.

The number of ASG was measured at a site adjacent to the ventilated capsule on the forearm using the starch-iodine technique (16). The ASG and SGO were identified in 14 subjects during a 10-s window, and the SGO was calculated by dividing the SR by the number of ASG observed over the same period.

The SkBF on the chest, forearm, and palm were monitored continuously using laser-Doppler velocimetry (model ALF21, Advance, Tokyo, Japan), which is specific for the skin and is not influenced by the underlying skeletal muscle blood flow (26). The probes for measuring SkBF were located within 1 cm of the ventilated capsules. The CVC on each site of the body was calculated from the ratio of the SkBF to the mean arterial blood pressure (MAP). Although the laser-Doppler flow signal does not provide an absolute measurement of blood flow, it does provide a reliable index of relative changes in SkBF and CVC from the resting levels before the commencement of each exercise bout.
The various temperature, SR, and SkBF values were recorded every second and stored in a personal computer (model PC9801RA, NEC, Tokyo, Japan) using a data logger (model HR2300, Yokogawa, Tokyo, Japan). We also calculated the mean SR from three sites (chest, forearm, and thigh) and the mean CVC from two sites (chest and forearm) to evaluate the responses from nonglabrous regions.

The HR was measured continuously from the R-R interval of the electrocardiogram. The arterial blood pressure from the right radial artery was measured continuously in a non-invasive manner using arterial tonometry (JENTOW-7700, Colin, Aichi, Japan). The blood pressure was corrected for systolic and diastolic pressure by brachial auscultation, which was measured with an autosphygmomanometer during the respective rest periods. The MAP was calculated as the diastolic pressure plus one-third of the pulse pressure. Each subject was asked to rate his perceived exertion on a scale of 6–20 (1) as an index of central command (34) at the end of each cycle exercise.

Statistical analysis. The data for the 60-s preexercise period and the final 30 s of the exercise period were collected. The changes in SR and CVC were calculated by subtracting the value of the 60-s preexercise period from the value of the final 30 s of the exercise period. Values are means ± SE. Two-way analysis of variance was performed using the Student’s paired t-test when the F values were significant to compare the data from all exercise intensities. Linear regression analysis was performed between SR or CVC and exercise intensity. The slopes of the regression lines were represented as the average of the slopes for each individual. Two-way analysis of variance was also performed to test for regional differences in sweating and cutaneous blood flow responses. P < 0.05 was considered to be statistically significant.

RESULTS

Figure 1 illustrates the average responses of all subjects with respect to T es, T sk, HR, MAP, SR on the chest, forearm, thigh, and palm, and CVC on the chest, forearm, and palm during the cycle exercise at 50% VO2 max. The physiological response patterns (time courses) of these variables during the exercise periods were similar, irrespective of the exercise intensity.

T es and T sk were essentially constant throughout the rest (36.88 ± 0.05°C and 35.33 ± 0.08°C, respectively) and exercise periods and did not change significantly with increasing exercise intensity (Fig. 2). The HR increased abruptly just after the initiation of exercise and increased gradually thereafter. After a brief delay, MAP increased throughout the exercise period. Moreover, HR and MAP increased proportionally with increasing exercise intensity (Fig. 2; P < 0.05). RPE and VO2 during exercise also increased significantly with increasing exercise intensity (P < 0.05).

The local skin temperatures on the chest (0.06 ± 0.03°C) and forearm (0.07 ± 0.03°C) at 70% VO2 max increased significantly above the preexercise values. The skin temperatures on the chest, forearm, thigh, and palm did not change across the exercise intensities, with the exception of the forearm at 30–70% VO2 max. Skin temperature was significantly higher on the forearm than on the chest and thigh (P < 0.01) and was higher on the chest than on the thigh (P < 0.05) at each exercise intensity. Skin temperature was highest on the palm.

The SR on the palm increased abruptly from the preexercise level just after the beginning of exercise and subsequently reached a steady state at all exercise intensities.
intensities, although the SR values were not significantly different for the various exercise intensities (Fig. 3). The SR on the chest, forearm, and thigh increased rapidly after a period of latency and increased progressively after somewhat of a plateau during each exercise period. The time delays in onset of sweating on the chest and forearm were significantly shorter with increasing exercise intensity, with the exception of exercise at 30–50% $\dot{V}O_2\text{max}$ ($P < 0.05$), although that on the thigh was not markedly different across the exercise intensities. The respective time delays for onset of sweating were 16.4 $\pm$ 4.9, 9.6 $\pm$ 2.9, and 5.4 $\pm$ 1.9 s on the chest, 14.7 $\pm$ 4.2, 9.3 $\pm$ 2.7, and 5.4 $\pm$ 1.6 s on the forearm, and 8.4 $\pm$ 2.7, 7.6 $\pm$ 2.2, and 7.2 $\pm$ 2.1 s on the thigh at 30%, 50%, and 70% $\dot{V}O_2\text{max}$. The SR on the chest, forearm, and thigh were significantly higher than the preexercise values at all exercise intensities and increased linearly with increasing exercise intensity (Fig. 3; $P < 0.05$), and the SR was greater on the chest than on the forearm, thigh, and palm at 50% and 70% $\dot{V}O_2\text{max}$ ($P < 0.01$). The increase in the mean SR of the chest, forearm, and thigh was 0.05 mg·cm$^{-2}$·min$^{-1}$ with an increase in exercise intensity equivalent to 10% $\dot{V}O_2\text{max}$. Furthermore, significant relations were found between the SR and RPE on the chest ($r = 0.522$), forearm ($r = 0.570$), and thigh ($r = 0.518$) and on the mean value of the chest, forearm, and thigh ($r = 0.571$, $P < 0.01$). The number of ASG on the forearm rose linearly with increasing exercise intensity, as did the SR on the forearm; a similar relation was not noted for the SGO (Fig. 4; $P < 0.05$).

The CVC on the chest, forearm, and palm decreased just after the onset of exercise and reached a plateau during the exercise period (Fig. 1). The early reduction in CVC was more pronounced on the palm than on the chest and forearm. The CVC on the chest, forearm, and palm were significantly different from the preexercise values at each exercise intensity (except for the forearm at 30% $\dot{V}O_2\text{max}$) and decreased proportionally with increasing exercise intensity (Fig. 5; $P < 0.05$). The
slope of the regression line between the CVC and relative exercise intensity tended to dip more sharply on the palm than on the mean value of chest and forearm ($P = 0.072$); the reduction in the mean CVC of the chest and forearm was $5.5\%$, whereas that on the palm was $8.0\%$, with an increase in exercise intensity equivalent to $10\% \dot{V}O_2\text{max}$ (Table 1). In addition, the slope of the regression line was significantly steeper on the palm than on the chest ($P < 0.05$). The reduction in CVC was significantly greater on the palm than on the chest and forearm at $30\%$, $50\%$, and $70\% \dot{V}O_2\text{max}$ ($P < 0.01$). Moreover, there was a significant correlation between the CVC on the palm and RPE ($r = 0.616$, $P < 0.01$).

### DISCUSSION

Three new observations of nonthermal sweating and cutaneous vascular responses at the onset of dynamic exercise in mildly heated humans emerge from this study: 1) significant increases occur in the SR from nonglabrous, but not glabrous, skin, with an increase in exercise intensity from $30\%$ to $70\% \dot{V}O_2\text{max}$, in the absence of marked changes in $T_{es}$ and $T_{sk}$ across these exercise intensities. The mean SR of the three body sites (chest, forearm, and thigh) increased quantitatively $0.05 \text{mg cm}^{-2} \text{min}^{-1}$ with an increase in exercise intensity equivalent to $10\% \dot{V}O_2\text{max}$; 2) the exercise intensity-dependent nonthermal sweating response is due to changes in ASG, but not SGO; and 3) the intensity-dependent cutaneous blood flow responses were different for glabrous and nonglabrous skin at the onset of the exercise. The mean CVC of the two body sites (chest and forearm) and the CVC on the palm decreased $5.5\%$ and $8.0\%$, respectively, with an increase in exercise intensity equivalent to $10\% \dot{V}O_2\text{max}$, and the slope of the regression line between the CVC and relative exercise intensity on the palm tended to be steeper than on the chest and forearm. These results suggest that the exercise intensity-dependent responses (linear relation) of nonthermal sweating and cutaneous blood flow show directionally opposite responses. Furthermore, the cutaneous vasoconstrictor responses were more pronounced in glabrous than in nonglabrous skin with increasing exercise intensity.

### Table 1. Slope of regression line between SR or CVC and relative exercise intensity

<table>
<thead>
<tr>
<th>Slope of Regression Line</th>
<th>SR, mg cm$^{-2}$ min$^{-1}$ %\dot{V}O_2\text{max}$</th>
<th>CVC, %/%\dot{V}O_2\text{max}$</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chest</td>
<td>$0.007 \pm 0.001$</td>
<td>$-0.43 \pm 0.15$</td>
</tr>
<tr>
<td>Forearm</td>
<td>$0.004 \pm 0.001^*$</td>
<td>$-0.59 \pm 0.21$</td>
</tr>
<tr>
<td>Thigh</td>
<td>$0.004 \pm 0.001^*$</td>
<td>$-0.80 \pm 0.16^*$</td>
</tr>
<tr>
<td>Palm</td>
<td>$0.002 \pm 0.001^*$</td>
<td>$-0.55 \pm 0.15$</td>
</tr>
<tr>
<td>Mean</td>
<td>$0.005 \pm 0.001$</td>
<td></td>
</tr>
</tbody>
</table>

Values are means $\pm$ SE of $18$ subjects. \dot{V}O_2\text{max}, maximal $O_2$ uptake; mean, mean sweating rate (SR) value of chest, forearm, and thigh and mean cutaneous vascular conductance (CVC) value of chest and forearm. $^*P < 0.05$ vs. chest.
In this study, we used mildly heated conditions to induce slight increases in sweating rate and cutaneous blood flow without markedly increasing the internal temperature and to clearly investigate nonthermal sweating and cutaneous blood flow responses at the onset of dynamic exercise, because it was reported previously that increases in SR and decreases in CVC by nonthermal factors during exercise were attenuated by sufficient hyperthermia (11, 15). On the other hand, the skin temperatures on the chest and forearm rose significantly by 0.06°C and 0.07°C, respectively, above the preexercise values at 70% $\dot{V}O_2$max, without marked changes in $T_{es}$ and $T_{sk}$ throughout the experiment (Fig. 2). Although local skin temperature influences sweating (22) and cutaneous blood flow (12) responses, the observed increases in skin temperature on the chest and forearm were too low to have any physiological impact on thermoregulatory reflexes. Thus the environmental conditions selected in this study were appropriate for an investigation of nonthermal sweating and cutaneous blood flow responses at the onset of dynamic exercise.

It has been reported that an increase in muscle temperature, which activates thermoreceptors in deep veins and muscles, may facilitate the sweating response at the onset of dynamic exercise in warm environments (7). However, it is uncertain whether thermoreceptors actually exist in deep veins and muscles. If it is assumed that local thermoreceptors exist, doubts remain as to whether their activation would affect sweating and cutaneous blood flow responses (32), because changes in the SR and CVC showed opposite responses in this study (Figs. 3 and 5). These results suggest that thermal factors, which include muscle temperature, may not importantly affect sweating and cutaneous blood flow responses in this study.

Although the SR on the forearm due to nonthermal factors reached a plateau at ~45–60% MVC during the
isometric handgrip exercise (17), we observed a linear relation between the nonthermal SR on the forearm and exercise intensity from 30% to 70% \( \dot{V}O_2_{\text{max}} \). Also, the SR on the palm during dynamic exercise, which reflects psychological effects, did not show a clearly graded response to increasing exercise intensity, whereas that on the palm during the handgrip exercise depended on exercise intensity (17). In addition, the RPE and MAP were greater at 45% and 60% MVC than at 70% \( \dot{V}O_2_{\text{max}} \). Thus the differences in exercise intensity-dependent responses of nonthermal sweating between dynamic and isometric exercise may be due to the degree of physical strain, even when relative exercise intensity levels are compared.

As shown in Fig. 1, the SR on the palm increased rapidly just after the onset of dynamic exercise, but the SR on the chest, forearm, and thigh increased gradually at all exercise intensities. These patterns of sweating responses are consistent with those observed during isometric handgrip exercise (17). Furthermore, in this study, we found that the intensity-dependent response of nonthermal sweating was due to increases in ASG, but not SGO, at the onset of dynamic exercise, as well as during the isometric handgrip exercise (20). The result suggests that the effect of nonthermal factors on changes in the SR from nonglabrous skin may induce the recruitment of ASG during dynamic and isometric exercise routines.

It has been reported that the sweating response differs from one region of the body to another during dynamic exercise and that the SR is greater on the chest than on the forearm and thigh (10, 22, 29). In this study, the slope of the regression line between the SR and relative exercise intensity was significantly greater on the chest than on the forearm, thigh, and palm. Furthermore, the SR was significantly greater on the chest than on the forearm, thigh, and palm at 50% and 70% \( \dot{V}O_2_{\text{max}} \). The regional differences in sweating responses might be modulated by regional differences in ASG, rather than differences in local skin temperature, because the skin temperatures on the chest, forearm, thigh, and palm did not differ with exercise intensity, and the change in SR on the forearm was due to ASG, rather than SGO (Fig. 4). These results suggest that there are regional differences in nonthermal sweating responses at the onset of dynamic exercise, not only between nonglabrous and glabrous regions, but also across nonglabrous regions, with increasing exercise intensity.

We observed that the reduction in CVC was significantly greater on the palm than on the chest and forearm at all exercise intensities. Yamazaki (35) noted that the amplitude of fluctuation in CVC during dynamic exercise, during which the workload was modified in a sinusoidal manner, was greater on the palm than on the forearm and dorsal hand because of differences in the baseline CVC levels. However, in this study, the regional differences in cutaneous blood flow response were probably not due to differences in the preexercise CVC levels, because the changes in CVC were normalized to 100% of the resting levels before commencement of the exercise bout. It has been reported that the cutaneous vascular response in nonglabrous skin is regulated by the noradrenergic vasoconstrictor and active vasodilator systems, whereas that in glabrous skin is regulated entirely by the noradrenergic vasoconstrictor system (5, 12). The decrease in CVC at the initiation of dynamic exercise is attributed entirely to enhanced active vasoconstrictor tone (13). On the other hand, it is possible that the active vasodilator system, which is activated mainly under hyperthermic conditions (14), was not activated under our experimental conditions, because we noted that the \( T_{es} \) did not increase markedly throughout the experiment. Therefore, the observed differences between nonglabrous and glabrous skin might be due to differences in sympathetic innervation of these skin regions. It is also possible that the presence or absence of arteriovenous anastomoses affects the cutaneous blood flow response, because the change in SkBF is much greater through arteriovenous anastomoses in the palm (12, 25, 35). Thus the cutaneous blood flow response from glabrous skin is more sensitive to changes in exercise intensity at the onset of dynamic exercise than that from nonglabrous skin.

The exercise intensity-dependent responses of nonthermal sweating and cutaneous blood flow did not result from psychic excitement, because the SR on the palm did not change with increasing exercise intensity. In this study, the RPE may be an index of central command (34), which correlated significantly with the SR on the chest, forearm, and thigh and with the CVC on the palm. Therefore, we suggest that the SR from nonglabrous skin and the CVC from glabrous skin may be determined by the magnitude of the central command with increasing exercise intensity. However, the effects of central command on nonthermal SR might be weaker at the onset of dynamic exercise than during the isometric handgrip exercise, because the correlation coefficient between the SR on the forearm and RPE was smaller in this study (\( r = 0.570 \)) than that reported (\( r = 0.728 \)) by Kondo et al. (17).

We cannot rule out the possibility that peripheral excitatory factors, such as the mechanoreflex (6, 7, 19, 31) and metaboreflex (3, 6, 18, 28) of contracting skeletal muscle, modulate the exercise intensity-dependent response of nonthermal sweating. In this study, the SR from nonglabrous skin increased rapidly after a period of latency and increased progressively after leveling off in the second half of the dynamic exercise period (Fig. 1). The sweating response just after the initiation of dynamic exercise may be modulated by the muscle mechanoreflex as well as by the central command, because the muscle metaboreceptors are probably not stimulated during the initial stages of mild or moderate dynamic exercise (33). On the other hand, the progressive increase in the SR during the second half of the exercise period, which is greater with increasing exercise intensity, may support involvement of the muscle metaboreflex.

In this study, the time delays of sweating onset on the chest and forearm were shorter with increasing
exercise intensity, which is consistent with the results of the isometric handgrip exercise (17). The exercise intensity-dependent time delays may not be attributed entirely to the central command and the muscle mechanoception, because the time delays (5.4–16.4 s) represent slow responses to the effects of these two factors. Because it has been suggested that acetylcholinesterase is capable of modulating the SR when sudomotor activity is low but is less effective when sudomotor activity is high (27), the time delay may also depend on the level of SR.

In conclusion, the sweating response from nonglabrous skin (chest, forearm, and thigh) increased linearly with increasing exercise intensity from 30% to 70% \( \dot{V}O_2 \text{max} \), whereas glabrous skin (palm) did not show a clearly graded response. The intensity-dependent response of nonthermal sweating is due to changes in ASG, but not SGO. On the other hand, there was a negative correlation between CVC and relative exercise intensity, with the slope being steeper in glabrous (palm) than in nonglabrous (chest and forearm) skin. These responses occur early during dynamic exercise, before there are any changes in body temperature, indicating their nonthermal nature.

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