Whole body heat stress attenuates baroreflex control of muscle sympathetic nerve activity during postexercise muscle ischemia

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Cui J, Shibasaki M, Davis SL, Low DA, Keller DM, Crandall CG. Whole body heat stress attenuates baroreflex control of muscle sympathetic nerve activity during postexercise muscle ischemia. J Appl Physiol 106: 1125–1131, 2009. First published February 12, 2009; doi:10.1152/japplphysiol.00135.2008.—Both whole body heat stress and stimulation of muscle metaboreceptors activate muscle sympathetic nerve activity (MSNA) through nonbaroreflex pathways. In addition to stimulating muscle metaboreceptors, exercise has the potential to increase internal temperature. Although we and others report that passive whole body heating does not alter the gain of the arterial baroreflex, it is unknown whether increased body temperature, often accompanying exercise, affects baroreflex function when muscle metaboreceptors are stimulated. This project tested the hypothesis that whole body heating alters the gain of baroreflex control of muscle sympathetic nerve activity (MSNA) and heart rate during muscle metaboreceptor stimulation engaged via postexercise muscle ischemia (PEMI). MSNA, blood pressure (BP, Finometer), and heart rate were recorded from 11 healthy volunteers. The volunteers performed isometric handgrip exercise until fatigue, followed by 2.5 min of PEMI. During PEMI, BP was acutely reduced and then raised pharmacologically using the modified Oxford technique. This protocol was repeated two to three times when volunteers were normothermic, and again during heat stress (increase core temperature ~ 0.7°C) conditions. The slope of the relationship between MSNA and BP during PEMI was less negative (i.e., decreased baroreflex gain) during whole body heating when compared with the normothermic condition (−4.34 ± 0.40 to −3.57 ± 0.31 units·beat−1·mmHg−1, respectively; P = 0.015). The gain of baroreflex control of heart rate during PEMI was also decreased during whole body heating (P < 0.001). These findings indicate that whole body heat stress reduces baroreflex control of MSNA and heart rate during muscle metaboreceptor stimulation.

sympathetic nervous system; muscle metaboreceptors

EXERCISE evokes the activation of the sympathetic nervous system, which contributes to increases in heart rate, cardiac output, peripheral vasoconstriction, and blood pressure (1, 25, 35). In addition to central mechanisms (i.e., central command) (13, 25, 48), inputs from mechanically and chemically sensitive afferents in the exercising muscle are important in evoking sympathetic activation (20, 21, 23, 24, 40, 47). During vigorous exercise, the baroreceptors remain functional in modulating blood pressure (27, 28, 32, 33, 41). Most data suggest that exercise resets the baroreflexes, while a number of studies have demonstrated that baroreflex gains are modulated during exercise and/or postexercise occlusion (10, 22, 31, 39). For example, postexercise occlusion elevates carotid sinus baroreflex gain during positive neck pressure application and reduced the gain during negative neck pressure (31), and baroreflex control of muscle sympathetic nerve activity (MSNA) is more effective during static muscle contraction (39). Consistent with these observations, we showed that the sensitivity of baroreflex modulation of MSNA is elevated during postexercise muscle ischemia (PEMI) of normothermic individuals (7).

Exercise increases not only metabolites in the exercising muscles, but when prolonged also increases muscle and internal temperatures. However, most studies investigating the effects of exercise on baroreflex control of blood pressure have done so in normothermic volunteers. Heat stress itself (i.e., in the absence of exercise) is a potent activator of the sympathetic nervous system (36), as evidenced by large increases in MSNA (5, 6, 17, 26). Although we and others demonstrated that passive whole body heat stress does not alter integrated baroreflex control of MSNA (6, 17) or heart rate (4, 6, 17, 49), the effects of heat stress in altering baroreflex function during exercise is unknown. Put another way, it is unknown whether the effects of metaboreceptor stimulation in altering baroreflex function is affected by the thermal status of the individual.

Although body temperature regulation can occur through central and low-level regulatory loops (38), the hypothalamus is the primary neural structure governing thermoregulation. Previous studies revealed that electrical stimulation of the hypothalamus alters baroreflex function (12). Moreover, components of the circuitry that comprises the exercise pressor reflex arc, such as the ventrolateral medulla in the brain stem (2, 3), have connections with the hypothalamus (16). Sympathetic activation evoked by either muscle metaboreceptor stimulation (20, 47) or heat stress (5, 37) occurs presumably via nonbaroreflexes pathways. When both of these sympathetic activation mechanisms are engaged, baroreflex control of sympathetic outflow may be altered. Therefore, we hypothesized that passive whole body heat stress alters baroreflex control of MSNA and heart rate, relative to normothermia, during muscle metaboreceptor stimulation evoked by PEMI.

METHODS

Subjects. Eleven volunteers (5 men, 6 women) participated in this study. The average age was 31 ± 9 (SD) yr, and all were of normal height (168 ± 16 cm) and weight (71 ± 15 kg). The volunteers were

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normotensive (supine blood pressures <140/90 mmHg), were not taking medications, and had no known cardiovascular disease. The volunteers refrained from caffeine, alcohol, and intensive exercise 24 h before the study. This study was approved by the Institutional Review Boards of the University of Texas Southwestern Medical Center and the Presbyterian Hospital of Dallas, and a written informed consent was obtained from each volunteer.

**Measurements.** Internal temperature (Tcore) was measured from intestinal temperature via telemetric temperature pill (HQ, Palmetto, FL) that was swallowed by each volunteer ~90–120 min before the onset of data collection. This method provides an accurate measurement of internal temperature (29). Mean skin temperature (Tsk) was obtained from the weighted electrical average of six thermocouples attached to the skin (45). Each volunteer was dressed in a tube-lined suit that permitted the control of Tsk by changing the temperature of water perfusing the suit. Skin blood flow (SkBF) was indexed from dorsal forearm skin of the nonexercising arm using laser-Doppler flowmetry with integrating flow probes (Perimed, North Royalton, OH). Forearm sweat rate was measured adjacent to this area via capacitance hygrometry (Vaisala, Woburn, MA). A ventilated capsule (surface area = 2 cm²) is attached to the skin. Dry nitrogen is passed through the capsule at a rate of 300 ml/min. Sweat rate was calculated from the nitrogen flow rate and effluent gas absolute humidity. These measures of SkBF and sweat rate were only used as additional indexes, with internal and skin temperatures, of the magnitude of the heat stress. Heart rate was monitored from the electrocardiogram interfaced with a cardiographometer (1,000-Hz sampling rate; CWE, Ardmore, PA).

Beat-by-beat blood pressure was recorded from a finger (Finometer, Finapres Medical Systems, Amsterdam, The Netherlands) with resting values verified by auscultation of the brachial artery (SunTech, Medical Instruments Raleigh, NC). Respiratory frequency was monitored using piezoelectric pneumography. Multifiber recordings of MSNA were obtained with a tungsten microelectrode inserted in the peroneal nerve. A reference electrode was placed subcutaneously 2–3 cm from the recording electrode. The signal was amplified, filtered with a bandwidth of 500–5,000 Hz, and integrated with a time constant of 0.1 s (Iowa Bioengineering, Iowa City, IA). The recording electrode was adjusted until a site was found in which muscle sympathetic bursts were clearly identified using previously established criteria (46). Mean voltage neurograms were displayed on a chart recorder. The nerve signal was also routed to an oscilloscope and a loudspeaker for monitoring throughout the study.

**Protocols.** All studies were conducted with the volunteers in a supine position in a room with an ambient temperature of ~25°C. Before data collection, force generation from a maximal voluntary handgrip contraction (MVC) was determined from the nondominant arm using a handgrip dynamometer (TKK5401 GRIP D, Takei Scientific Instruments). Neither the exercising limb nor the limb from which SkBF and sweat rate were measured was covered by the water-perfused suit.

While normothermic, the volunteers rested quietly, during which time baseline thermal and hemodynamic data were obtained. The volunteers then performed isometric handgrip exercise at 40% MVC until fatigue followed by 2.5 min of PEMI. Identification of fatigue was dependent on the inability of the volunteer to maintain the desired force production, coupled with subjective reporting of the volunteers. PEMI was initiated 5 s before the end of exercise by rapidly infusing a pneumatic cuff (Hokanson, Bellevue, WA) placed on the upper portion of the arm to 250 mmHg. During the subsequent period of ischemia, baroreflex modulation of MSNA and heart rate were assessed via the modified Oxford technique, which has been previously described (6, 7, 9, 15). In brief, ~20 s after cuff inflation, 100 μg of sodium nitroprusside was administered intravenously via a catheter placed in the nonexercising arm, followed ~60 s later by 150 μg of phenylephrine HCl. These drugs induced a decrease, followed by an increase, in blood pressure (see Fig. 2). In the normothermic condition, this protocol was repeated two to three times separated by 20-min intervals. This duration was sufficient for arterial blood pressure, heart rate, and MSNA to return to the baseline levels. The gain of baroreflex control of MSNA and heart rate during PEMI from these trials was averaged and is reported as the normothermic trial.

After normothermic data collection was complete, Tsk was increased to ~38°C by perfusing the tube-lined suit with 46°C water. Once Tcore was elevated ~0.7°C, the temperature of the waster perfusing the suit was slightly reduced to attenuate further increases in Tcore. Baseline thermal and hemodynamic data were once again obtained after the desired Tcore was achieved. Thereafter, the handgrip exercise followed by the PEMI protocol was repeated, including the administration of the aforementioned drugs. Approximately 17 min after the end of the first handgrip exercise plus PEMI procedure during heating, another 3 min of baseline data were collected following by repeating the exercise + PEMI procedure. Baroreflex gain for MSNA and heart rate during PEMI from these two trials during heating was averaged and is reported as the whole body heating trial.

**Data analysis.** Data were sampled at 200 Hz through a commercial data-acquisition system (Biopac System, Santa Barbara, CA). MSNA bursts were first identified in real time by visual inspection of data plotted on the chart recorder, coupled with the burst sound from the audio amplifier. These bursts were further evaluated via a computer software program that identified bursts based on fixed criteria, including an appropriate latency following the R-wave of the electrocardiogram (6, 7). Integrated MSNA in both thermal conditions was normalized by assigning a value of 100 to the mean amplitude of the largest 10% of the bursts during the 6-min normothermic baseline period (15). Normalization of the MSNA signal was performed to reduce variability between the volunteers attributed to factors including needle placement and signal amplification. Total MSNA was identified from burst area of the integrated neurogram that was evaluated on a beat-by-beat basis. If no MSNA burst was detected for a particular cardiac cycle, a value of zero was assigned to that cardiac cycle. Beat-by-beat systolic and diastolic blood pressures as well as heart rate were obtained from the arterial blood pressure waveform and the electrocardiogram, respectively.

Averaged responses were obtained during the 3-min period before exercise (baseline) and the last minute of exercise. Thermal and cardiovascular responses from repeated bouts within each thermal condition were averaged.

To calculate the slope of the MSNA vs. diastolic blood pressure, MSNA values were averaged over 3-mmHg diastolic blood pressure bins for the linear regression analysis as described previously (6, 7). Diastolic blood pressure was used because MSNA correlates closely with diastolic pressure, but not with systolic blood pressure (44). The gain of baroreflex modulation of heart rate was identified from the slope of the relationship between beat-by-beat heart rate vs. systolic blood pressure during pharmacologically induced changes in diastolic blood pressure. Beat-by-beat heart rates were also pooled over 3-mmHg systolic blood pressure bins, followed by linear regression analysis of these data.

Statistical analyses were performed using commercially available software (SigmaStat 3.0, SPSS). Baseline values between the normothermic and whole body heating trials were compared via paired t-tests. The effects of the whole body heating on the responses to handgrip exercise were evaluated via a two-way repeated-measures ANOVA, with main factors of thermal status and exercise, followed by multiple comparison post hoc analyses where appropriate. The effects of the whole body heating on baroreflex gains during PEMI were compared with the normothermic trials via paired t-tests. All values are reported as means ± SE. P values < 0.05 were considered statistically significant.
Whole body heating increased Tcore from normothermic baseline (36.97 ± 0.10°C) to 37.79 ± 0.09°C before the second exercise trial in the heat. The mean increase in Tcore during resting baseline before the two heat stress exercise trials was 0.72 ± 0.05°C. The increased Tcore, SkBF, and sweat rate indicate that the volunteers were sufficiently heat stressed. Whole body heating increased resting heart rate and MSNA, while mean arterial blood pressure was not significantly changed (Table 1). Neither Tsk nor Tcore significantly changed during isometric handgrip exercise, regardless of the thermal condition.

The duration of isometric handgrip exercise while volunteers were heat stressed (126 ± 9 s) was not significantly different from that in normothermia (155 ± 9 s, P = 0.07). Isometric handgrip exercise evoked significant increases in MSNA, heart rate, and blood pressure in both normothermic and heat-stressed conditions. At the end of the exercise bout, absolute heart rate and MSNA were significantly greater when the volunteers were heat stressed relative to when they were normothermic (Fig. 1). The two-way ANOVA revealed a significant interaction (P < 0.002) for heart rate, blood pressure, and both MSNA indexes, indicating that the magnitude of the increase in these variables to isometric exercise was influenced by the thermal status of the individual. Consistent with this finding, the increase (i.e., delta) in mean blood pressure (28.7 ± 1.8 vs. 34.8 ± 2.4 mmHg), heart rate (19.6 ± 3.7 vs. 30.5 ± 4.2 beats/min), and MSNA (16.6 ± 2.5 vs. 32.1 ± 3.0 bursts/min) during handgrip exercise was significantly greater when the volunteers were heat stressed.

Bolus injection of nitroprusside and phenylephrine during PEMI elicited a sequential fall and rise in blood pressure, respectively, that provoked reflex changes in heart rate and MSNA in both thermal conditions (Fig. 2). Peak responses to the drug infusions are showed in Table 2. A strong linear relationship between MSNA vs. diastolic blood pressure (Fig. 3) was observed for each volunteer (mean r² = 0.88 ± 0.02 for normothermia, mean r² = 0.85 ± 0.03 for the heat stress). The average slope of MSNA vs. diastolic blood pressure while the volunteers were heat stressed was significantly less negative relative to when the volunteers were normothermic (−4.34 ± 0.40 to −3.57 ± 0.31 units-beat⁻¹·mmHg⁻¹, P = 0.015, Fig. 4), indicating a reduced baroreflex gain during the heat stress.

A strong linear relationship between heart rate vs. systolic blood pressure was also observed for each volunteer (mean r² = 0.82 ± 0.04 for normothermia, mean r² = 0.70 ± 0.07 for the heat stress). Heat stress significantly shifted the relationship between heart rate and systolic pressure upward (Fig. 3). The average slope of the heart rate vs. systolic blood pressure while the volunteers were heat stressed was also significantly less negative compared with when the volunteers were normothermic (−0.80 ± 0.10 to −0.49 ± 0.07 beats/mmHg, P < 0.001, Fig. 5).

**DISCUSSION**

Numerous studies have sought to identify the effects of static and dynamic exercise on arterial baroreflex responsiveness (8,
Related studies have investigated the effects of responses associated with exercise, such as central command, muscle mechanoreceptor stimulation, and muscle metaboreceptor stimulation, in modulating baroreflex responsiveness \cite{7, 8, 10, 22, 30, 31, 33, 39, 41}. In many cases the outcome and conclusions from those studies were mixed. Conflicting findings, with respect to the effects of exercise on baroreflex gain, could originate from the different effectors examined, different methods utilized, as well as different study conditions. For example, differences in body temperatures, due perhaps to differing exercise protocols, could be one of the factors contributing to those conflicting findings. However, the potential for elevations in temperature to alter baroreflex function during exercise has not been studied. To that end the present study was performed to identify whether whole body heat stress modifies baroreflex function during muscle metaboreceptor stimulation.

Whole body heating significantly increased mean skin and core temperatures, skin blood flow, sweat rate, and heart rate. These data indicate the volunteers were sufficiently heat stressed by the heating protocol. Whole body heating reset the baroreflex curve and reduced the gain of MSNA during muscle metaboreceptor stimulation (see Fig. 3 and Table 2) compared with muscle metaboreceptor stimulation while the volunteers were normothermic. This heat stress-induced change in baroreflex gain during PEMI occurred despite the absence of an effect of heat stress alone (i.e., without exercise or PEMI) in changing baroreflex control of MSNA \cite{6, 17}. With respect to baroreflex control of heart rate, neither whole body heating alone \cite{4, 6, 49} nor metaboreceptor stimulation alone \cite{7} alters the gain of baroreflex control of heart rate. However, the present data show that the baroreflex curve governing heart rate was shifted upward (see Fig. 3 and Table 2) and the gain of baroreflex control of heart rate during PEMI was significantly decreased while the volunteers were heat stressed relative to the same perturbation while the volunteers were normothermic. Since whole body heating alone does not alter baroreflex control of MSNA \cite{6, 17} or heart rate \cite{4, 6, 49}, the decreases in the gains of baroreflex control of MSNA and heart rate in the present study are due to the combined effect of heat and metaboreceptor stimulation.

Norton et al. \cite{28} reported that the maximal gain of carotid-cardiac baroreflex curves early during an exercise bout (10 min), as well as after prolonged exercise (50 min), were not

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**Fig. 2.** Representative tracing of handgrip force (HG), HR, MSNA, and mean arterial blood pressure (BP) during postexercise ischemia (PEMI). During PEMI, a bolus of 100 \(\mu\)g sodium nitroprusside (SNP) and 150 \(\mu\)g phenylephrine HCl (PE) were administrated sequentially with \(~1\)-min interval. A: normothermic condition. B: heat-stress condition.
significantly different relative to preexercise values. They also reported that dynamic exercise with varied intensity did not affect the maximal gains in carotid-cardiac baroreflex curve (27). Although internal temperature was not reported in those studies, given the workload (65% of maximal aerobic capacity) and climatic conditions (24°C) in that study, it is likely that internal temperature of those volunteers, after 50 min of exercise, was the same or perhaps higher than internal temperature of the present volunteers during passive heat stress. The present investigation evaluated the interactive effects of muscle metaboreceptor stimulation (i.e., PEMI) and heat stress on global baroreflex function. This is in contrast to the studies of Norton et al. (27, 28) that evaluated carotid baroreflex responsiveness during dynamic exercise. It may be that these differences in protocols contributed to the apparent differences in conclusions from the cited and the present studies.

The mechanism(s) by which heat stress attenuates baroreflex control of MSNA and heart rate during PEMI is unknown but can be speculated on. First, inputs from both thermoreceptors (43) and muscle afferents (19) are transmitted to the hypothalamus, and electrical stimulation of the hypothalamus has been shown to alter baroreflex function (12). The ventrolateral medulla of the brain stem is a component of the exercise pressor reflex arc (2, 3) and is also an essential part of the central baroreflex pathways (14), while this area is also connected with hypothalamus (16). Thus it is possible that the inputs from the afferents of thermoreceptors and metaboreceptors modulate the baroreflexes. Second, stimulation of muscle metaboreceptors evokes pronounced increases in sympathetic activity (20, 47), which occurs presumably via nonbaroreflex pathways. Whole body heat stress also causes pronounced increases in sympathetic activity (5, 6, 17, 26), which also is reported to be independent from baroreflexes (5, 37). The combination of these two stimulations induces pronounced

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<th>Preinjection</th>
<th>Nitroprusside</th>
<th>Phenylephrine</th>
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<tbody>
<tr>
<td><strong>Normothermia</strong></td>
<td></td>
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<tr>
<td>Mean arterial blood pressure, mmHg</td>
<td>110±3</td>
<td>95±4*</td>
<td>116±4†</td>
</tr>
<tr>
<td>Heart rate, beats/min</td>
<td>67±4</td>
<td>90±5*</td>
<td>61±3†</td>
</tr>
<tr>
<td>MSNA, bursts/min</td>
<td>33±3</td>
<td>76±7*</td>
<td>24±4†</td>
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<td>MSNA, units/min</td>
<td>610±80</td>
<td>1,391±112*</td>
<td>433±57†</td>
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<tr>
<td><strong>Heat stress</strong></td>
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<tr>
<td>Mean arterial blood pressure, mmHg</td>
<td>105±3</td>
<td>92±3*</td>
<td>114±4†</td>
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<tr>
<td>Heart rate, beats/min</td>
<td>91±5‡</td>
<td>113±4‡</td>
<td>87±5‡</td>
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<tr>
<td>MSNA, bursts/min</td>
<td>54±5‡</td>
<td>88±11*</td>
<td>46±7‡</td>
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<tr>
<td>MSNA, units/min</td>
<td>1,122±160‡</td>
<td>1,629±263*</td>
<td>983±172‡</td>
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Data for the preinjection period are mean values of −10 s during postexercise muscle ischemia (PEMI) and just before the infusion of sodium nitroprusside. Data for sodium nitroprusside are mean values of −10 s during the lowest blood pressure induced by this drug during PEMI. Data for phenylephrine HCl are mean values of −10 s during the highest blood pressure induced by phenylephrine HCl during PEMI. It should be noted that the data for the preinjection baseline period were obtained from a very short period, which only provides a reference for the operating range in the baroreflex and does not constitute stable responses during PEMI. *P < 0.05 compared with preinjection. †P <0.05 compared with sodium nitroprusside. ‡P <0.05 compared with normothermia.
increases in MSNA. Thus the capacity for MSNA to be further elevated during a hypotensive challenge would be reduced. Given large increases in heart rate by heat stress, despite the absence of metaboreceptor stimulation being a primary controller of heart rate, a similar response may occur for this variable. Reduced capacity to increase MSNA and heart rate during a hypotensive challenge could be reflective of reduced baroreflex responsiveness of these variables. On the other hand, because both heat stress and muscle metaboreceptor stimulation evoke MSNA activation via nonbaroreflex mechanisms, baroreceptor activation by a hypertensive challenge under this combined condition may not be able to thoroughly “override” heat stress and metaboreceptor-mediated stimulation of MSNA.

After increasing local muscle temperature ~4.5°C by local heating, MSNA responses during the PEMI were not different relative to when muscle temperature was normothermic (34). This observation reduces the likelihood that slight increases in the temperature of the exercising muscle during whole body heat stress (presumably ~0.7°C) are responsible for the observed attenuation in baroreflex function in the present study. The present data show that the increases in MSNA, blood pressure, and heart rate due to fatiguing isometric exercise, just before PEMI, were significantly greater when volunteers were heat stressed. The mechanisms of this unexpected finding are not readily apparent but can be speculated on. Ray et al. (34) demonstrated that increasing local temperature of exercising muscles ~4.5°C augmented MSNA responses during handgrip exercise. Moreover, renal vasoconstriction to handgrip exercise was also accentuated after locally heating the exercising muscles (18). However, MSNA and renal vasoconstrictor responses during the PEMI were not different between muscle heated and nonheated conditions (18, 34). The investigators concluded that heat-induced sensitization of mechanically sensitive muscle afferents may be responsible for these heightened neural and cardiovascular responses (18, 34). In contrast to that study, in the present study the exercising forearm was not covered by the water-perfused suit and thus was not locally heated. The largest increase in the temperature of the muscle before exercise would be no greater than the increase in internal temperature, ~0.7°C. It is unknown whether this small increase in muscle temperature is sufficient to similarly sensitize skeletal muscle afferents. Second, central command to the exercise workload may be heightened when volunteers are heat stressed, resulting in elevated heart rate, and perhaps MSNA responses, compared with normothermic exercise. These and/or perhaps other mechanisms responsible for heightened neural and cardiovascular responses to isometric exercise while heat stressed warrant further investigation.

Limitations. The heat stress trials were always performed after the normothermic trials, so therefore we cannot exclude an order effect, although this is unlikely. We saw no evidence of an order effect within normothermic condition for the repeated trials. The gain of baroreflex control of either MSNA or heart rate in the second normothermic trial was not significantly different from the first trial, with the interval between these trials being ~20 min. Similarly, no order effect was observed in our previous study, which assessed baroreflex gains during PEMI in normothermic subjects (7). Given the absence of an order effect when exercise bouts were performed within a 20-min window, it is highly unlikely that heat stress responses performed 45–60 min after normothermic data collection were influenced by an order effect.

The present study focused on the combined effects of heat stress and muscle metaboreceptor stimulation on baroreflex function, in which PEMI was used to stimulate muscle metaboreceptors under both thermal conditions. This approach was taken to specifically investigate whether elevations in body temperature that may accompany relatively moderate exercise alter the baroreflex function during muscle metaboreceptor stimulation, which also occurs during exercise. This study was not designed to evaluate the effects of PEMI as an independent factor and therefore we did not evaluate baroreflex responsiveness with and without PEMI regardless of the thermal condition. Second, because of the requirement to infuse vasoactive drugs during PEMI to evaluate baroreflex responsiveness, the effects of heat stress on MSNA and cardiovascular responses during PEMI could not be evaluated. The data for the preinjection baseline period shown in Table 2 were obtained from a very short period (between the time of circulatory occlusion and subsequent drug infusion), which only provides a reference for the operating range in the baroreflex and does not constitute stable responses during PEMI. Thus further studies are necessary to verify the effects of heat stress on the cardiovascular responses exclusively during muscle metaboreceptor stimulation via PEMI.

In conclusion, the present study shows that whole body heat stress attenuates the gain of baroreflex control of MSNA and heart rate during muscle metaboreceptor stimulation via PEMI. These results suggest that body temperature can modulate the effects of muscle metaboreceptor stimulation in altering baroreflex responsiveness during exercise. The interactive effects of heat stress on other variables influencing blood pressure control during exercise (e.g., central command and muscle...
mechanoreceptor stimulation) on baroreflex responsiveness deserve further investigation.

GRANTS

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