Effect of thermal stress on the vestibulosympathetic reflexes in humans

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Wilson, Thad E., and Chester A. Ray Effect of thermal stress on the vestibulosympathetic reflexes in humans. J Appl Physiol 97: 1367–1370, 2004. First published May 28, 2004; 10.1152/japplphysiol.00403.2004.—Both heat stress and vestibular activation alter autonomic responses; however, the interaction of these two sympathetic activators is unknown. To determine the effect of heat stress on the vestibulosympathetic reflex, eight subjects performed static head-down rotation (HDR) during normothermia and whole body heating. Muscle sympathetic nerve activity (MSNA; peroneal microneurography), mean arterial blood pressure (MAP), heart rate (HR), and internal temperature were measured during the experimental trials. HDR during normothermia caused a significant increase in MSNA (Δ5 ± 1 bursts/min; Δ53 ± 14 arbitrary units/min), whereas no change was observed in MAP, HR, or internal temperature. Whole body heating significantly increased internal temperature (Δ3.9 ± 0.1°C), MSNA (Δ10 ± 3 bursts/min; Δ152 ± 44 arbitrary units/min), and HR (Δ25 ± 6 beats/min), but it did not alter MAP. HDR during whole body heating increased MSNA (Δ16 ± 4 bursts/min; Δ233 ± 90 arbitrary units/min from normothermic baseline), which was not significantly different from the algebraic sum of HDR during normothermia and whole body heating (Δ15 ± 4 bursts/min; Δ205 ± 55 arbitrary units/min). These data suggest that heat stress does not modify the vestibulosympathetic reflex and that both the vestibulo-sympathetic and thermal reflexes are robust, independent sympathetic nervous system activators.

ORTOSTATIC TOLERANCE IS REDUCED during heat stress compared with normothermia (1, 14, 15, 27). Sympathetic nervous system reflexes are imperative in maintaining blood pressure during orthostatic stress. The role of the baroreflexes during orthostasis and heat stress has been systematically examined (3, 10, 24). Baroreflex responses are largely preserved in the heat, albeit at a higher level of sympathetic activation level relative to normothermia (3, 5). If the baroreflexes are operational during heat stress, another mechanism(s) must be involved to account for the reduced orthostatic tolerance. One potential candidate is the vestibular system, because it is heavily involved in autonomic and cardiovascular responses to postural changes.

Doba and Reis (8) demonstrated the important role of the vestibular system during postural change. This study observed that, on denervation of the vestibular nerve, tilted cats were unable to maintain arterial blood pressure (8). Later studies reported that stimulation of the otolith organs increases sympathetic outflow and vascular resistance in the cat (12, 32, 33).

In humans, head-down rotation (HDR), which activates the otolith organs, has been shown to increase muscle sympathetic nerve activity (MSNA) and limb vascular resistance (17, 22). Increases in MSNA have also been observed during off-vertical axis rotation, which engages the otolith organs (11).

The vestibulosympathetic reflex in human experiments is independent of other postural reflexes, such as the baroreflexes (20). Currently, the role of heat stress on the vestibulosympathetic reflex is unknown because only the role of baroreceptors has been adequately investigated during orthostasis and heat stress. Heating also has direct effects on endolymph and vestibular hair cell firing characteristics (19, 28). Therefore, it is possible that elevations in body temperature during heat stress will alter afferent feedback from the vestibular sensory organs, modifying autonomic responses. Thus a diminished sympathetic response and subsequent reduction in peripheral resistance may be elicited by the vestibulosympathetic reflex during heat stress and may contribute to the orthostatic intolerance observed during heat stress. On the basis of the finding that the baroreflexes function adequately during heat stress and that heating may have direct effects on the vestibular system, we hypothesize that the vestibulosympathetic reflex would be attenuated during heat stress.

METHODS

Subjects. Eight healthy subjects (5 men, 3 women) participated in this study. The subjects’ physical characteristics were age of 23 ± 1 yr, height of 173 ± 4 cm, and weight of 69 ± 4 kg. Subjects were not taking medications and were free of any known cardiovascular, neurological, or metabolic diseases. All subjects refrained from caffeine, alcohol, and exercise 24 h before the study. Written, informed consent from each subject was obtained before participation, and the study was approved by The Pennsylvania State University College of Medicine Institutional Review Board.

Protocol. All experiments were performed with the subjects in the prone position in a dimly lit, quiet, normothermic (20–22°C) laboratory to minimize environmental influences on autonomic responses. To determine the role of the otolith organs on MSNA responses, static HDR was performed as previously described (26). Briefly, HDR involves the head being extended and supported in the baseline condition; the support is subsequently removed, and the head is allowed to passively rotate to the point of maximal rotation. Subjects performed this maneuver with their eyes closed. Head rotation was measured by means of an electrogoniometer (13). HDR was completed for 3 min during normothermia and then subsequently during whole body heating. Temperature was controlled in normothermia by perfusing neutral temperature water (34–35°C) through a custom-designed high-density tube-lined suit (Med-Eng Systems, Ottawa.

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ON, Canada). Whole body heating was accomplished by perfusing warm (44–46°C) water through the suit to increase mean skin temperature. Once sublingual temperature increased (~0.5–0.7°C), the temperature of the water was reduced in an attempt to reduce the rate of rise of internal temperature during the HDR data collection period.

Instrumentation and measurements. Internal temperature was measured via a thermistor placed in the sublingual sulcus. Skin temperature was measured via the weighted average of three thermocouples attached to the skin (25) and routed through a thermocouple meter (TC-1000, Sabel Systems, Henderson, NV).

Multifiber recordings of MSNA were obtained with a tungsten microelectrode inserted in the common peroneal nerve. A reference electrode was placed subcutaneously 2–3 cm from the recording electrode. The recording electrode was adjusted until a site was found in which MSNA bursts were clearly identifiable. The nerve signal was amplified, passed through a band-pass filter with a bandwidth of 700–2,000 Hz, and integrated with a time constant of 0.1 s (Iowa Bioengineering, Iowa City, IA). Mean voltage neurograms were visually displayed and recorded on a data acquisition system. The nerve signal was also routed to a loudspeaker for monitoring throughout the study.

Arterial blood pressure and heart rate were measured continuously by a finger cuff (Finapres, Ohmeda, Englewood, CO). Cuff blood pressure was also recorded by auscultation of the brachial artery (Dinamap XL, Critikon/GE Medical Systems, Tampa, FL). Skin blood flow was indexed via laser-Doppler flowmetry (model DRT 4, Moor Instruments, Wilmington, DE) from two areas on the back not directly exposed to the water-perfused suit. Back sweat rate was measured via the weighted average of three thermocouples attached to the skin. Respiratory frequency was monitored through a band-pass filter with a bandwidth of 700–2,000 Hz, and integrated with a time constant of 0.1 s (Iowa Bioengineering, Iowa City, IA). Mean voltage neurograms were visually displayed and recorded on a data acquisition system. The nerve signal was also routed to a loudspeaker for monitoring throughout the study.

Data analysis and statistics. Data were sampled at 40–200 Hz via an analog-to-digital converter and data acquisition system (8S, AD-Instruments, New Castle, Australia). MSNA was quantified both as burst frequency (burst/min) and total activity calculated via the sum of areas of all the sympathetic bursts in 1 min (arbitrary units/min).

Table 1. Temperature and thermoregulatory effector responses to whole body heating

<table>
<thead>
<tr>
<th>Condition</th>
<th>Temperature (°C)</th>
<th>CVC, %baseline</th>
<th>SR, mg·cm⁻²·min⁻¹</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normothermia</td>
<td>36.2 ± 0.1</td>
<td>100</td>
<td>0.43 ± 0.10</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Heat Stress</td>
<td>34.1 ± 0.2</td>
<td>307 ± 28</td>
<td>0.7 ± 0.4</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td></td>
<td>36.2 ± 0.1</td>
<td>100</td>
<td>0.43 ± 0.10</td>
<td>0.016</td>
</tr>
</tbody>
</table>

Values are means ± SE. T_{sl}, sublingual temperature; T_{sk}, mean skin temperature; CVC, cutaneous vascular conductance; SR, sweat rate.

RESULTS

Whole body heating significantly increased internal temperature (~0.9°C) and mean skin temperature (~4.4°C) compared with normothermia (Table 1). However, no further increase in internal temperature was observed during the HDR intervention (pre-HDR 37.1 ± 0.1 and post-HDR 37.0 ± 0.1°C; P = 0.403). Whole body heating significantly increased CVC and sweat rate (Table 1).

MSNA expressed as burst frequency and total activity increased during both whole body heating and HDR (Fig. 1). HDR during whole body heating elicited an increase in MSNA of 16 ± 4 bursts/min and 233 ± 90 arbitrary units/min from normothermic baseline. However, these values were not significantly different from the algebraic sum of HDR during normothermia and whole body heating (Δ15 ± 4 bursts/min and Δ205 ± 55 arbitrary units/min) (Fig. 1). To demonstrate increases in MSNA associated with HDR and whole body heating, representative neurograms from one subject during thermal and vestibular perturbations are presented in Fig. 2.

Whole body heating significantly increased heart rate (~25 beats/min) but did not significantly alter arterial blood pressure (Table 2). HDR did not significantly change heart rate or arterial blood pressure in either thermal condition. The combination of HDR and whole body heating increased heart rate by 29 ± 6 beats/min, and this value was not significantly different from the algebraic sum of HDR during normothermia and during whole body heating (Δ25 ± 6 beats/min). Mean arterial blood pressure was also not significantly different between combined trial and algebraic sum of whole body heating and HDR (Table 2).

![Fig. 1. Change (Δ) in muscle sympathetic nerve activity [in bursts/min (A) and in arbitrary units/min (B)] during 3 min of head-down rotation (HDR) during normothermia and heat stress. Values are means ± SE. NS, not significant. Significant increases in muscle sympathetic nerve activity were observed during HDR and heat stress when performed independently. Sum of HDR and heat stress trials (Sum) were comparable to the combination trial (HDR + Heat). *P < 0.05 compared with baseline. †P < 0.05 compared with either heat stress or HDR.](http://jap.physiology.org/)
DISCUSSION

The major finding of the present study is that MSNA increases are similar during HDR in normothermia and heat stress. These findings indicate that heat stress does not modify the vestibulosympathetic reflex in humans and that both the vestibulosympathetic and thermal reflexes are robust independent sympathetic nervous system activators. Thus our results suggest that it is unlikely that a diminished vestibulosympathetic reflex contributes to heat-related decreases in orthostatic tolerance.

Increases in internal and mean skin temperature resulted in increases in MSNA. This is a consistent finding in humans (4, 5, 18). HDR caused similar increases in MSNA during both normothermia and heat stress. Although increases in MSNA with HDR are well established during normothermia (9, 17, 23, 26), this is the first report of MSNA responses during otolith activation during heat stress.

Comparable increases in MSNA during HDR in both normothermia and heat stress indicate that these sympathetic activators are independent effectors of MSNA. The combination of HDR and heat stress was not significantly different from the algebraic sum of HDR and heat stress, thus suggesting that the vestibulosympathetic reflex when combined with thermal reflexes is additive and not augmented or attenuated. The independent and additive MSNA response during HDR has been observed with other sympathetic maneuvers, such as isometric exercise, mental stress, hypoxia, and baroreceptor unloading (2, 16, 20, 21). Having multiple independent sympathetic reflexes is not surprising and likely contributes to coarse and fine homeostatic adjustments of the regulation of blood pressure during orthostasis.

Orthostatic tolerance is reduced during heat stress compared with normothermia (1, 15, 27). The precise mechanism for this increased intolerance is currently unknown, but the vestibular system could be contributing to this intolerance if heat stress altered autonomic responses to the engagement of the otolith organs. We observed that thermal state did not influence the MSNA responses during HDR. This indicates that, contrary to our hypothesis, the MSNA response during activation of otolith organs is not impaired during heat stress. However, even with maintained sympathetic outflows, it is possible that the vasculature is less responsive to vasoconstriction during heat stress compared with normothermia. Experimental evidence supports this assertion (6, 30). Hence, it is possible that a greater MSNA response is necessary during orthostatic stress to elicit a similar end-organ response during heat stress compared with normothermia. However, this does not appear to be possible through activation of the vestibulosympathetic reflex.

Another factor that must be considered when discussing orthostatic tolerance during heat stress is that activation of the otolith organs does not contribute to skin vascular resistance during normothermia (23) and whole body heating (31). This could be problematic for orthostatic tolerance in the human, because large amounts of blood flow are being directed to the skin and reductions within this vascular space would be important to maintain arterial blood pressure, whereas the further constriction of an already vasoconstricted vascular bed (i.e., muscle) would be less essential.

One potential limitation of this study is not having a direct measure of temperature within the otolith organs (i.e., sacculus and utricle). Previous studies have identified direct effects of temperature on endolymph and vestibular hair cell function.
(19, 28). These heat-related effects may diminish autonomic responses to the vestibulosympathetic reflex. Our whole body heating protocol significantly increased internal and mean skin temperature, but these increases may have not caused changes in endolymph or vestibular hair cell function. Nonetheless, our whole body heating protocol was clearly sufficient to result in significant physiological changes (e.g., increases in heart rate, CVC, and sweat rate) typically associated with heat stress.

Summary. Whole body heating does not significantly alter MSNA responses to HDR. The engagement of the otolith organs via HDR increases MSNA during normothermia and heat stress. The algebraic sums of MSNA during whole body heating and HDR performed together. This finding indicates that the vestibulosympathetic reflex is not impaired during heat stress. These results suggest that the vestibulosympathetic and thermal reflexes are independent activators of the sympathetic nervous system.

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GRANTS

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REFERENCES