Vestibular activation does not influence skin sympathetic nerve responses during whole body heating

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Vestibular activation does not influence skin sympathetic nerve responses during whole body heating. J Appl Physiol 97: 540–544, 2004. First published April 9, 2004; 10.1152/japplphysiol.00174.2004.—The cutaneous vasculature and eccrine sweat glands are modified by both thermal and nonthermal factors. To determine the effect of thermal stress on the vestibulosympathetic reflex, skin sympathetic nerve activity (SSNA) and cutaneous end-organ responses were measured in 10 subjects during static head-down rotation (HDR) and dynamic yaw and pitch (30 cycles/min) to activate the otolith organs and semicircular canals. SSNA (microneurography) and skin temperature were collected during normothermia and after whole body heating. Body temperature was controlled by perfusing neutral (34–35°C) or warm (44–46°C) water through a tube-lined suit. During normothermia, HDR did not alter SSNA (−0.4 ± 4.4% change), CVC (4.2 ± 6.9% change), or sweat rate (−2.7 ± 12.2% change) within the innervated area of skin. Dynamic yaw and pitch also did not elicit significant changes in SSNA, CVC, or sweat rate during normothermia. Whole body heating significantly increased internal temperature (0.8 ± 0.1°C), mean skin temperature (4.1 ± 0.2°C), CVC (322 ± 109% control), and sweat rate (0.35 ± 0.08 mg·cm−2·min−1). After whole body heating, HDR did not significantly alter SSNA (3.2 ± 7.6% change), CVC (−7.3 ± 3.9% change), or sweat rate (−3.3 ± 1.9% change). Dynamic yaw and pitch also did not produce significant changes in SSNA, CVC, or sweat rate after whole body heating. These data suggest that vestibular activation by head movements is not a nonthermal factor affecting SSNA and cutaneous end-organ responses in humans.

skin blood flow; sweat rate; otolith organs; semicircular canals; microneurography; skin sympathetic nerve activity

WHOLE BODY HEATING RESULTS in large increases in skin sympathetic nerve activity (SSNA), skin blood flow, and sweating. Nonthermal factors can also stimulate or modulate these responses (5, 9, 11, 30, 31, 34). Examples of these nonthermal factors include age, circadian and menstrual cycles, arousal state, hydration and heat acclimation status, exercise, and posture. Although posture has been identified to affect cutaneous end-organ responses, only baroreceptor-mediated cutaneous end-organ responses have been adequately investigated. These studies have not assessed other posture-related mechanisms, such as the vestibular system, in the modulation of SSNA and cutaneous end-organ responses. Vestibular activation elicits pronounced effects on the autonomic nervous system in animals and humans (15, 25, 28, 41). Sympathetic outflow responses to vestibular activation are dependent on the specific sensory organ (i.e., semicircular canals and otolith organs) engaged. It is well established that activation of otolith organs increases muscle sympathetic nerve activity (MSNA) and decreases limb blood flow in humans (8, 10, 13, 18, 33). Cui et al. (4) observed alterations in SSNA during stimulation of the semicircular canals with warm and cold water irrigation of the ear. During this procedure, they observed decreases in SSNA during nystagmus and increases in SSNA after nystagmus, as well as alterations in both vasomotor and sudomotor indexes during this procedure (4). In contrast, other studies suggest that neither stimulation of the otolith organs nor the horizontal semicircular canals alters SSNA and cutaneous vascular responses (26, 27). However, the above studies were only conducted in normothermic conditions. Thermal condition is a potent stimulator and modulator of SSNA and cutaneous end-organ responses. Modulation of these responses to a particular perturbation is often not apparent without a certain level of cutaneous activation such as an increase in temperature (7). No previous investigations have been undertaken to determine the effect of vestibular activation on SSNA and cutaneous end-organ responses during a heightened state of SSNA elicited by whole body heating.

Heating also has direct effects on endolymph and vestibular hair cell-firing characteristics (22, 35, 40). Therefore, it is possible that elevations in body temperature will alter afferent feedback from the vestibular sensory organs, modifying autonomic responses. The purpose of this study is to examine the effects of heat stress on the vestibulosympathetic reflex in the skin. We hypothesized that 1) SSNA would not be affected by activation of the otolith organs or the semicircular canals in normothermia, but increases would be observed during whole body heating; 2) sweat rate would be unaffected by activation of the otolith organs or the semicircular canals in normothermia because the system is not activated, but increases would be observed during whole body heating; and 3) skin blood flow would not be affected by activation of the otolith organs and semicircular canals during normothermia because of tonic vasoconstrictor tone, but decreases in skin blood flow would be observed during whole body heating.

METHODS

Subjects. Ten healthy subjects (7 men, 3 women), with mean age of 23 ± 1 yr, height of 177 ± 2 cm, and weight of 71 ± 3 kg, participated in this study. Subjects reported 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. Heat acclimation status was not assessed in subjects, although all studies were performed during the summer months. 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 in the prone position in a dimly lit, quiet, normothermic (21–23°C) laboratory to minimize environmental influences on SSNA. To determine the role of the otolith organs on SSNA and cutaneous end-organ responses, static head-down rotation (HDR) was performed. HDR was completed by passively moving the head from a neck extension position to the point of maximal flexion. To determine the role of the semicircular canals on SSNA and cutaneous end-organ responses, dynamic yaw was performed by having one of the investigators rotate the subject’s head in the horizontal axis at 30 cycles/min (0.5 Hz). To determine the role of combined semicircular canals and otolith organs on SSNA and cutaneous end-organ responses, dynamic pitch was performed by having one of the investigators rotate the subject’s head while whole body heating was completed by perfusing warm water (model DRT 4, Moor Instruments, Wilmington, DE) on a portion of the back not covered by the tube-lined suit and from the area within the innervation field of the SSNA being recorded (i.e., dorsal foot). Cutaneous vascular conductance (CVC) was calculated from the ratio of skin blood flow flux to mean arterial pressure. CVC was normalized to a percent of a 5-min normothermia control period performed before vestibular or thermal interventions. To verify that baseline levels of skin blood flow did not influence CVC responses, in a subset of the participants (n = 4) CVC data were also expressed as a percentage of maximum flow induced via local heating. To induce maximal cutaneous vasodilation, small local heaters housing the laser-Doppler flow probes (model SH02, Moor Instruments) were engaged for 30 min to elevate local skin temperature to 42°C (36). Sweat rate was measured via capacitance hygrometry (HMP235, Viasala, Woburn, MA) by means of perfusing 100% nitrogen at a flow rate of 500 ml/min through a ventilated capsule (surface area = 3.94 cm²) attached to the surface of the skin.

Data analysis and statistics. Data were sampled at 40–200 Hz via an analog-to-digital converter and data-acquisition system (16SP PowerLab, ADInstruments). To assess total SSNA, the area of the integrated neurogram was calculated for each segment via computer software (Chart 5, ADInstruments) and normalized as a percentage of baseline before each vestibular intervention. Segments with aberrant electrical noise were excluded from the calculation. Average values during the final 60 s of each data segment were obtained and statistically analyzed. We did not statistically compare absolute SSNA

| Table 1. Thermal, hemodynamic, and sweating responses to whole body heating |
|---------------------------|---------------------------|---------------------------|
| Normal thermoregulation | Heat Stress | P Value |
| Tsk, °C               | 36.3±0.1 | 37.1±0.1 | <0.001 |
| Tsk, °C               | 33.5±0.4 | 37.7±0.3 | <0.001 |
| MAP, mmHg             | 74±3 | 75±2 | 0.447 |
| HR, beats/min         | 63±3 | 86±6 | <0.001 |
| Back CVC, %control   | 100 | 386±41 | <0.001 |
| Back SR, mg·cm⁻²·min⁻¹ | 0.35±0.08 | 0.023 |
| Foot CVC, %control   | 100 | 422±109 | 0.008 |
| Foot SR, mg·cm⁻²·min⁻¹ | 0.41±0.08 | 0.001 |

Values are means ± SE. Tsk, sublingual temperature; Tsk, mean skin temperature; MAP, mean arterial pressure; HR, heart rate; CVC, cutaneous vascular conductance; SR, sweat rate. Percent control refers to CVC during a 5-min normothermia period performed before vestibular interventions. P value represents significance between normothermia and heat-stress conditions.

Instrumentation and measurements. Internal temperature was measured from a thermistor placed in the sublingual sulcus. Mean skin temperature was measured via the weighted average of three thermocouples attached to the skin (29) routed through a thermocouple meter (model TC-1000, Sabel Systems, Henderson, NV).

Multifiber recordings of SSNA 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 placed and adjusted until a site was found in which SSNA bursts were clearly identified using previously established criteria (5, 37). In brief, these included J) light stroking of the skin within the innervated region resulted in afferent discharge, 2) deep inspiration and arousal stimuli resulted in non-pulse-synchronous activity, and J) signal-to-noise ratio was >3:1. 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 (16SP PowerLab, ADInstruments, New Castle, Australia) and 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). Arterial blood pressure was also recorded by auscultation of the brachial artery (Dinamap XL, Critikon/GE Medical Systems, Tampa, FL) to verify finger pressures. Skin blood flow was measured via laser-Doppler flowmetry (model DRT 4, Moor Instruments, Wilmington, DE) on a portion of the back not covered by the tube-lined suit and from the area within the innervation field of the SSNA being recorded (i.e., dorsal foot). Cutaneous vascular conductance (CVC) was calculated from the ratio of skin blood flow flux to mean arterial blood pressure. CVC was normalized to a percent of a 5-min normothermia control period performed before vestibular or thermal interventions. To verify that baseline levels of skin blood flow did not influence CVC responses, in a subset of the participants (n = 4) CVC data were also expressed as a percentage of maximum flow induced via local heating. To induce maximal cutaneous vasodilation, small local heaters housing the laser-Doppler flow probes (model SH02, Moor Instruments) were engaged for 30 min to elevate local skin temperature to 42°C (36). Sweat rate was measured via capacitance hygrometry (HMP235, Viasala, Woburn, MA) by means of perfusing 100% nitrogen at a flow rate of 500 ml/min through a ventilated capsule (surface area = 3.94 cm²) attached to the surface of the skin.
Significantly increased heart rate, CVC, and sweat rate. No significant differences in SSNA were observed during vestibular activation before and after heat stress.

Whole body heating also elicited significant CVC differences during normothermia. Whole body heating resulted in increases in SSNA and mean skin temperature. These combined thermal factors resulted in increases in SSNA, CVC, and sweat rate. The increase in SSNA with increasing ambient temperature is a well-documented phenomenon (1, 21, 39). These heating-induced increases in SSNA and cutaneous end-organ responses were important to adequately evaluate the vestibulosympathetic reflex on the skin. This condition is important because the modulation of cutaneous effenter responses is often not apparent without a certain level of SSNA activation. For example, sweating responses are often difficult to observe during a particular perturbation in normothermia, but the same perturbation might cause heightened sweating responses in a heated state (7).

We were unable to identify any change in SSNA or sweat rate responses with vestibular activation of the otolith organs and semicircular canals. The lack of a change in SSNA with vestibular activation in the heated state confirms previous observations in normothermia (26, 27). Nonetheless, the effect of vestibular activation on sweating had previously not been addressed. Dodd et al. (6) observed decreases in SSNA and an index of sweating with tilting and lower body negative pressure (LBNP) during mild heating. However, others have not observed these changes in SSNA of sweat function with baroreceptor unloading via LBNP or pharmacological interventions (38, 39). It is possible that some of the observations of Dodd et al. were because tilting activates both the baroreflex and vestibulosympathetic reflex, whereas LBNP and pharmacological methods only unload the baroreceptors. We did not observe any changes with vestibular activation in either thermal condition, indicating that the vestibular system does not explain discrepancies between the results of the above studies.

Vestibular activation did not significantly decrease CVC during normothermia and heat stress. We hypothesized that vestibular activation would have less of an effect in normo-

Table 2. CVC and SR values during static HDR and dynamic yaw and pitch during normothermia

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<th>Static HDR</th>
<th>Dynamic Yaw</th>
<th>Dynamic Pitch</th>
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<td></td>
<td>Baseline</td>
<td>HDR</td>
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<tr>
<td>CVC, %control</td>
<td></td>
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<tr>
<td>Back</td>
<td>98±2</td>
<td>106±4</td>
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<tr>
<td>Dorsal Foot</td>
<td>98±4</td>
<td>101±5</td>
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Values are means ± SE. HDR, head-down rotation. Dynamic yaw and pitch were performed at frequencies of 30 cycles/min. Percent control refers to CVC during a 5-min normothermia period performed before vestibular interventions. No significant CVC differences were observed during normothermia.
thermia because of tonic vasoconstrictor tone but that it would be involved in withdrawal of active cutaneous vasodilatation in the heated state similar to that observed with baroreceptor unloading. The upright posture engages multiple reflexes and vestibulosympathetic reflexes in the reduction of skin blood flow observed during orthostasis (23, 35). Head-up tilt reduces skin blood flow in the heat (17, 32), but this maneuver engages both the baroreflexes and vestibulosympathetic reflex. In contrast, LBNP in the supine position unloads only baroreceptors without activating the vestibular system. Using LBNP, Johnson et al. (12) identified decreases in skin blood flow with baroreceptor unloading, which was determined to be via withdrawal of the cutaneous active vasodilator system during whole body heating (3, 14). However, these studies did not test the possible role of the vestibulosympathetic reflex in the reduction of skin blood flow during orthostasis. On the basis of our results, we believe that the decrease in skin blood flow observed during orthostasis is not because of the vestibulosympathetic reflex but rather due to the activation of the baroreflexes.

Motion sickness, often produced by the vestibular system, alters sympathetic outflow (vasomotor and sudomotor) to the skin, which results in pallor and sweating (20). Additionally, others have observed alterations in SSNA and cutaneous end-organ responses during galvanic vestibular stimulation (producing ocular responses and postural illusions, which results in pallor and sweating) (20). Additionally, others have observed alterations in SSNA and cutaneous end-organ responses during normothermia and heat stress. These data suggest that activation of the otolith organs and semicircular canals is not a nonthermal factor affecting SSNA and cutaneous end-organ responses. Our results combined with previous studies indicate that postural alterations in skin blood flow are not likely associated with the vestibulosympathetic reflex but rather the activation of the baroreflexes in humans.

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Table 3. Cutaneous vascular conductance and sweat rate values during static head-down rotation and dynamic yaw and pitch during heat stress

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<tr>
<td></td>
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<tr>
<td>CVC, % control</td>
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<tr>
<td>Back</td>
<td>386±41</td>
<td>381±44</td>
<td>390±46</td>
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<tr>
<td>Dorsal foot</td>
<td>422±109</td>
<td>371±87</td>
<td>395±91</td>
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<tr>
<td>SR, mg·cm⁻²·min⁻¹</td>
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<td></td>
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<tr>
<td>Back</td>
<td>0.35±0.08</td>
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<tr>
<td>Dorsal foot</td>
<td>0.40±0.08</td>
<td>0.39±0.07</td>
<td>0.49±0.10</td>
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Values are means ± SE. Dynamic yaw and pitch were performed at a frequency of 30 cycles/min. Percent control refers to CVC during a 5-min normothermia control period performed before vestibular interventions. No significant CVC or SR differences were observed during heat stress.
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