Heat stress alters hemodynamic responses during the Valsalva maneuver

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Heat stress alters hemodynamic responses during the Valsalva maneuver. J Appl Physiol 108: 1591–1594, 2010. First published March 18, 2010; doi:10.1152/japplphysiol.91642.2008.—The Valsalva maneuver can be used as a noninvasive index of autonomic control of blood pressure and heart rate. The purpose of this investigation was to test the hypothesis that sympathetic mediated vasoconstriction, as referenced by hemodynamic responses during late phase II (phase IIb) of the Valsalva maneuver, is inhibited during whole body heating. Seven individuals (5 men, 2 women) performed three Valsalva maneuvers (each at a 30-mmHg expiratory pressure for 15 s) during normothermia and again during whole body heating. Seven individuals (5 men, 2 women) performed three Valsalva maneuvers (each at a 30-mmHg expiratory pressure for 15 s) during normothermia and again during whole body heating. 

Beat-to-beat arterial mean blood pressure (MAP) and heart rate were measured during each Valsalva maneuver, and responses for each phase were averaged across the three Valsalva maneuvers for both thermal conditions. Baseline MAP was not significantly different at the end of phase IIa and IIb during heat stress (25°C) compared with normothermia (30°C). 

Heat stress alters hemodynamic responses during a Valsalva maneuver, specifically phase IIb, to test the hypothesis that sympathetic mediated vasoconstriction during heat stress conditions (19). Phase II can be divided into an early phase (phase IIa), where blood pressure is falling due to impeded venous return to the heart and partial blunting of vagal withdrawal, and a late phase (phase IIb), where blood pressure recovers primarily due to vasoconstriction, given the absence or pronounced attenuation of this recovery with α-adrenergic blockade (6, 19, 24). Thus beat-to-beat alterations in blood pressure during phase IIb, in particular, may provide an index of α-adrenergic function (19). Therefore, the objective of the present investigation was to evaluate hemodynamic responses during a Valsalva maneuver, specifically phase IIb, to test the hypothesis that sympathetic mediated vasoconstriction is inhibited during moderate whole body heating in resting humans.

METHODS

Participants. Seven individuals (5 men, 2 women) participated in this study. The subject’s mean ± SD age, height, and weight were 31 ± 5 yr, 171 ± 7 cm, and 68 ± 12 kg, respectively. The phase of the menstrual cycle was not controlled in this study. Each subject provided written consent that was approved by the Institutional Review Boards of the University of Texas Southwestern Medical Center and Texas Health Presbyterian Hospital Dallas before participation.

Protocol. Procedures were performed in a quiet temperature-controlled room (24°C). Testing was performed with each subject in the supine position to eliminate postural effects on the Valsalva maneuver responses (7, 22). Participants were instrumented for the measurement of internal temperature from a thermistor placed in the sublingual sulcus and mean skin temperature via the weighted average of six thermocouples attached to the skin (25). Participants were dressed in a tube-lined suit that permitted the control of skin temperature by changing the temperature of water perfusing the suit. The perfusion suit covered the entire body with the exception of the head, hands, and feet. Heart rate was obtained from electrocardiogram (SpaceLabs, Redmond, WA) with the signal interfaced with a cardiometer (CWE, Ardmore, PA). Beat-to-beat arterial blood pressure was continuously measured by noninvasive photoplethysmography (Finapres,

HEAT STRESS GENERALLY DOES NOT ALTER BAROREFLEX CONTROL OF MUSCLE SYMPATHETIC NERVE ACTIVITY (MSNA) OR HEART RATE (3, 5). HOWEVER, TOLERANCE TO AN ORTHOSTATIC CHALLENGE IS GREATLY ATTENUATED IN HEAT-STRESSED HUMANS (1, 11, 13). WHEN EXPOSED TO HEAT STRESS, SKIN BLOOD FLOW CAN INCREASE AS HIGH AS ~7 L/min, REQUIRING CARDIAC OUTPUT TO MORE THAN DOUBLE TO MAINTAIN BLOOD PRESSURE IN THE FACE OF SUBSTANTIAL ELEVATIONS IN CUTANEOUS VASCULAR CONDUCTANCE (18). UNDER SUCH HEAT STRESS CONDITIONS, NEURAL CONTROL OF SKIN BLOOD FLOW BECOMES CRITICAL FOR BLOOD PRESSURE REGULATION, ESPECIALLY DURING AN ORTHOSTATIC CHALLENGE (10, 17). A POSSIBLE MECHANISM FOR DECREASED ORTHOSTATIC TOLERANCE DURING HEAT STRESS CONDITIONS (1, 4, 9, 12, 13, 16, 28) MAY BE ATTENUATED SYMPATHETICALLY MEDIATED VASOCONSTRICTION. CONSISTENT WITH THIS HYPOTHESIS, CUTANEOUS VASOCONSTRICTION TO EXOGENOUS NOREPINEPHRINE IS REDUCED WHEN SUBJECTS ARE HEAT STRESSED RELATIVE TO NORMOTHERMIC CONDITIONS (27), WHEREAS THE ELEVATION IN ARTERIAL BLOOD PRESSURE TO SYSTEMIC INFUSIONS OF PHENYLEPHRINE IS ALSO REDUCED WHEN SUBJECTS ARE HEAT STRESSED (5). IN ADDITION, FACTORS ASSOCIATED WITH INCREASED CUTANEOUS BLOOD FLOW DURING A HEAT STRESS, SUCH AS NITRIC OXIDE, ARE CAPABLE OF ATTENUATING VASOCONSTRICTOR RESPONSES (20, 21). THESE FINDINGS, WHEN TOGETHER, SUGGEST THERE IS INADEQUATE SYMPATHETIC VASOCONSTRICTION IN HEAT-STRESSED SUBJECTS, DESPITE A NORMAL SYMPATHETIC NERVOUS SIGNAL.

Hemodynamic responses to a Valsalva maneuver could provide a noninvasive index of autonomic nervous system integrity, including sympathetic activation, during heat stress. Heart rate and blood pressure responses to the Valsalva maneuver are well documented and can be divided into four separate and distinct phases (see Fig. 1). Of these four phases, phase II is the most valuable in providing insight into sympathetic vasoconstriction during heat stress conditions (19). Therefore, the objective of the present investigation was to evaluate hemodynamic responses during a Valsalva maneuver, specifically phase IIb, to test the hypothesis that sympathetic mediated vasoconstriction is inhibited during moderate whole body heating in resting humans.

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Participants. Seven individuals (5 men, 2 women) participated in this study. The subject’s mean ± SD age, height, and weight were 31 ± 5 yr, 171 ± 7 cm, and 68 ± 12 kg, respectively. The phase of the menstrual cycle was not controlled in this study. Each subject provided written consent that was approved by the Institutional Review Boards of the University of Texas Southwestern Medical Center and Texas Health Presbyterian Hospital Dallas before participation.

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Fig. 1. Blood pressure (BP), heart rate (HR), and mouth pressure responses to a Valsalva maneuver in the normothermic and heat stress conditions from a representative subject.

Phases of the Valsalva maneuver are indicated on the BP tracings (6, 8, 19, 23, 24). Phase I is a brief rise in BP with a reduction in HR mechanically induced by increased intrathoracic and intra-abdominal pressure. Phase II can be divided into two distinct phases. Early phase II (phase IIa) is a fall in BP due to impeded venous return and partial blunting of vagal withdrawal. Late phase II (phase IIb) is a recovery of BP due primarily to increased sympathetic activity. Phase III is a sudden, brief reduction in BP and increase in HR from the mechanical release of the Valsalva maneuver. Phase IV is a BP elevation coupled with a decrease in HR due to increased stroke volume being ejected into constricted systemic vascular beds.

Ohmeda, Louisville, CO) from a finger kept at heart level. Verification of mean arterial pressure (MAP) was confirmed in normothermia and during the heat stress via brachial artery auscultation (SunTech, Raleigh, NC). Before the Valsalva, for both normothermic and heat stress trials, any differences in Finapres-obtained MAP were corrected based on the MAP values obtained from brachial artery auscultation. Thermoneutral water (34°C) was perfused through the suit during normothermic data collection. Subjects performed three Valsalva maneuvers under normothermic conditions. A mouthpiece was placed into the subject’s mouth, which was connected to an analog manometer to monitor intrathoracic pressure. A small leak in the apparatus ensured the subject was not closing his or her glottis during the maneuver. After 1 min of spontaneous breathing, at the end of a normal inspiration, subjects blew into the apparatus for 15 s, while maintaining a pressure of 30 mmHg throughout this duration. Each Valsalva maneuver was separated by 5 min to allow adequate recovery.

Whole body heating was performed by perfusing 46°C water through the tube-lined suit (Med-Eng, Ottawa, Canada). This method of heating typically increases skin temperature to ~38°C and sublingual temperature by ~0.6–1.0°C, following 30–60 min of heating. Once sublingual temperature increased ~0.8°C, the temperature of the water was reduced to attenuate the rate of rise of internal temperature throughout the ensuing data collection period. Three Valsalva maneuvers were repeated with the subjects in this heat stress condition, each separated by 5 min.

Data collection and analysis. Data were continuously acquired throughout normothermic and heat stress conditions at a sampling rate of 50 Hz using a data collection system (Biopac System, Santa Barbara, CA). Beat-by-beat MAP was calculated by integrating individual blood pressure wave forms. Baseline MAP was determined from a 30-s interval before initiation of the Valsalva maneuver. MAP was calculated from a single cardiac cycle that corresponded to the following phases of the Valsalva maneuver: phase I as the maximum MAP following initiation of the Valsalva maneuver, phase II, as the minimum MAP during straining, phase IIb as the maximum MAP before release of the Valsalva maneuver, phase III as the lowest MAP following the release of the Valsalva maneuver, and phase IV as the highest MAP following the release of the Valsalva maneuver. Changes in MAP (ΔMAP) from pre-Valsalva values were calculated for each phase of the Valsalva maneuver in both thermal conditions. Moreover, the ΔMAP from phase IIa to IIb was calculated. ΔMAP for each phase were averaged across the three Valsalva maneuvers performed during each thermal condition.

Data were statistically analyzed using paired t-tests to determine differences between normothermic and heat stress conditions for the indicated phases. Statistical significance was accepted at P < 0.05. Data are expressed as means ± SD.

RESULTS

Heart rate, MAP, and mean skin and internal temperatures are presented in Table 1. Typical cardiovascular and thermal responses associated with whole body heating were observed.

Representative tracings of blood pressure, heart rate, and mouth pressure responses to a Valsalva maneuver are presented in Fig. 1, while ΔMAP from pre-Valsalva baseline for each phase of the Valsalva maneuver are presented in Table 2.

Table 1. Cardiovascular and thermal responses to whole body heating

<table>
<thead>
<tr>
<th></th>
<th>Normothermia</th>
<th>Heat Stress</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Heart rate, beats/min</td>
<td>55 ± 9</td>
<td>89 ± 12</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Mean arterial pressure, mmHg</td>
<td>88 ± 11</td>
<td>84 ± 9</td>
<td>0.11</td>
</tr>
<tr>
<td>Mean skin temperature, °C</td>
<td>34.5 ± 0.3</td>
<td>38.7 ± 0.2</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Sublingual temperature, °C</td>
<td>36.4 ± 0.3</td>
<td>37.3 ± 0.5</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

Values are means ± SD.
In phase IIa, the reduction in MAP was larger during heat stress (−20 ± 8 mmHg) compared with normothermia (−1 ± 15 mmHg; \( P = 0.01 \)). Likewise, in phase IIb, the ∆MAP was larger during heat stress (−13 ± 7 mmHg) compared with normothermia (3 ± 13 mmHg; \( P = 0.01 \)). The ∆MAP from the end of phase IIa to the end of phase IIb, indicative of α-adrenergic vasoconstrictor responsiveness (19), tended to be greater during heat stress (7 ± 5 mmHg) compared with normothermia (4 ± 5 mmHg; \( P = 0.06 \)). Finally, the MAP overshoot during phase IV was significantly greater during heat stress (25 ± 10 mmHg) compared with normothermia (8 ± 9 mmHg; \( P = 0.02 \)).

### DISCUSSION

The primary finding of this study is that hemodynamic responses during a Valsalva maneuver are altered by heat stress. The difference in the reduction in MAP at the end of phase IIa and IIb, both relative to pre-Valsalva MAP, between thermal conditions was quite pronounced, with the reduction being significantly greater when subjects were heat stressed. Contrary to the proposed hypothesis, the increase in MAP from the end of phase IIa to the end of phase IIb, while subjects were heat stressed approached significance (\( P = 0.06 \)), suggesting that sympathetic activation to the vasculature during this phase of the Valsalva maneuver tended be greater, not attenuated, during the heat stress. Despite this tendency for an enhanced vasoconstrictor response, absolute MAP remained below pre-Valsalva baseline at phase IIb when subjects were heat stressed, whereas it returned to baseline during normothermia (see Table 1), likely due to the greater reduction in MAP at the end of phase IIb when subjects were heat stressed. Finally, the ∆MAP observed during phase IV was significantly higher during heat stress relative to normothermia.

The large drop in MAP observed in phase IIa of the Valsalva maneuver during heat stress is consistent with previous findings (29). This reduction in MAP is due to mechanical impedance of venous return, leading to decreased thoracic filling. Thoracic filling is not only influenced by changes in venous resistance, but is also dependent on other factors, including blood volume, pressure in regional circulations, and right atrial pressure (24). Stewart and colleagues (24) demonstrated that decreased thoracic blood volume during upright tilt leads to a larger decrease in blood pressure during phase IIa of the Valsalva maneuver in normothermic individuals compared with the supine position. Heat stress is known to reduce thoracic blood volume (2), likely due to a displacement of blood to the cutaneous vascular bed to aid in heat dissipation. Furthermore, Fritsch-Yelle and colleagues (8) suggested that large phase IIa reductions in blood pressure during the Valsalva maneuver were attributed to reduced plasma volume. When considered together, although the heat stress of the intensity and duration imposed on the present subjects was unlikely to appreciably reduce blood volume, perhaps reductions in central blood volume accompanying the heat stress (2) are a primary mechanism, resulting in similar hemodynamic responses to the Valsalva maneuver relative upright standing and reductions in systemic blood volume (8, 24). In addition, the highly compliant nature of the skin during a heat stress may also reduce the pressure gradient for venous return during phase IIb. With less blood being returned to the central circulation during the Valsalva maneuver when subjects are heat stressed, the reduction in MAP during phase II would be expected to be greater.

Vogel and colleagues (26) used blood pressure recovery time (PRT; time interval from the bottom of phase III to the return of systolic blood pressure to pre-Valsalva baseline) during the Valsalva maneuver as a quantitative index of autonomic failure. Patients with autonomic failure (i.e., multiple system atrophy, neurogenic orthostatic hypotension, autonomic neuropathy) have significantly longer PRT compared with healthy controls (26). When calculated from the present data set, no differences in PRT were identified, suggesting that the differences in the observed MAP responses when subjects were heat stressed may be more related to changes in vascular volumes and compliance that accompany whole body heating, rather than due to changes in autonomic control of the vasculature.

Counter to the proposed hypothesis, the increase in MAP between phases IIa to IIb tended to be greater when subjects were heat stressed (heat stress: 7 ± 5 mmHg; normothermia: 4 ± 5 mmHg). It may be that the tendency for a greater increase in MAP between phase IIa to IIb was related to the larger reduction in MAP during phase IIa of the Valsalva maneuver while heat stressed (−20 ± 8 mmHg), with that greater hypotensive stimulus evoking a more potent sympathetic vasoconstrictor response. As mentioned above, this larger reduction in MAP during phase IIa is likely related to a greater volume of blood being diverted away from the central circulation to the cutaneous circulation (i.e., a greater capacitor). When this stored blood is released during phase IV of the Valsalva maneuver, a larger increase in MAP would occur due to a larger absolute volume returning to the central circulation relative to when subjects were normothermic. Furthermore, the release of this stored blood occurs at a point of heightened sympathetic activity and vascular tone of noncutaneous beds, secondary to greater reductions in blood pressure in phase II when subjects are heat stressed, which likely also contributes to the larger phase IV overshoot.

Counter to previous observations that heat stress does not alter baroreflex control of MSNA (3, 5), Yamasaki et al. (29) reported a reduced baroreflex gain of MSNA during a Valsalva maneuver when subjects were in this thermal condition. However, these findings are limited for two reasons. First, baroreflex gain was derived from linear regression analyses of relatively few MSNA bursts (−6–8) during phase II of the Valsalva maneuver. Second, like that observed in the present study, a narrower range of ∆MAP was observed in the normothermic condition (−19 mmHg) compared with a wider range in ∆MAP (−31 mmHg) during heat stress. Analyzing relatively few MSNA bursts when subjects were normothermic,

### Table 2. Average change in mean arterial pressure from pre-Valsalva baseline during the indicated phase of the Valsalva maneuver while subjects were normothermic and heat stressed

<table>
<thead>
<tr>
<th>Valsalva Maneuver Phase</th>
<th>Normothermia, mmHg</th>
<th>Heat Stress, mmHg</th>
<th>( P ) Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>13 ± 7</td>
<td>10 ± 3</td>
<td>0.21</td>
</tr>
<tr>
<td>IIa</td>
<td>−1 ± 15</td>
<td>−20 ± 8</td>
<td>0.01</td>
</tr>
<tr>
<td>IIb</td>
<td>3 ± 13</td>
<td>−13 ± 7</td>
<td>0.01</td>
</tr>
<tr>
<td>IV</td>
<td>8 ± 9</td>
<td>25 ± 10</td>
<td>0.02</td>
</tr>
</tbody>
</table>

Values are means ± SD.

Counter to the proposed hypothesis, the increase in MAP from the end of phase IIa to IIb was attributed to reduced plasma volume. When considered together, although the heat stress of the intensity and duration imposed on the present subjects was unlikely to appreciably reduce blood volume, perhaps reductions in central blood volume accompanying the heat stress (2) are a primary mechanism, resulting in similar hemodynamic responses to the Valsalva maneuver relative upright standing and reductions in systemic blood volume (8, 24). In addition, the highly compliant nature of the skin during a heat stress may also reduce the pressure gradient for venous return during phase IIb. With less blood being returned to the central circulation during the Valsalva maneuver when subjects are heat stressed, the reduction in MAP during phase II would be expected to be greater.

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coupled with a larger range of the arterial blood pressure response when subjects were heat stressed, may result in inaccurate assessment of baroreflex gain, given the sigmoidal relationship of baroreflex responses, because, during heat stress, there is a greater potential to include data points that occur at threshold or saturation of the baroreflex function curve, potentially reducing the calculated gain.

Limitations. Arterial blood pressure was not directly measured via arterial cannulation, but rather was estimated non-invasively by photoplethysmography via the Finapres. However, this method has been shown to accurately track changes in blood pressure during Valsalva straining (14, 15), and thus we are confident in the values of the changes in blood pressure obtained in the present study. While the observed differences in phases IIa and IV following a heat stress are presumed to be related to changes in central blood volume (2), no measure of central blood volume was performed in this study. Finally, the interpretation of the data is limited to moderate increases in internal temperature. We cannot exclude the possibility that differing responses would be observed should a less or more severe heat stress be imposed.

Conclusion. In conclusion, hemodynamic responses during a Valsalva maneuver are affected by whole body heating. These differences are likely a consequence of larger reductions in venous return during the Valsalva maneuver while subjects are heat stressed. Counter to the proposed hypothesis, there was no evidence that heat stress attenuates vasoconstrictor responsiveness based on the magnitude of the increase in MAP between phase IIa and IIb of the Valsalva maneuver.

GRANTS
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DISCLOSURES
No conflicts of interest, financial or otherwise, are declared by the author(s).

REFERENCES