Plasma hyperosmolality augments peripheral vascular response to baroreceptor unloading during heat stress

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IT IS KNOWN THAT HYPOCHLORHYDRATION inhibits thermoregulatory responses to heat stress and that both hypovolemia and plasma hyperosmolality inhibit thermoregulatory responses, such as cutaneous vasodilation and sweating, to heat stress (22, 30). The effect of hypovolemia on the thermally regulated peripheral vascular response is thought to be caused by baroreceptor unloading, because the modification of thermally regulated peripheral circulation by baroreceptor unloading or loading is similar to the modification induced by blood volume change (11, 12, 16, 20, 24, 25, 27, 29). Plasma hyperosmolality also inhibits thermoregulatory cutaneous vasodilation and sweating by elevating the body core temperature thresholds for these responses (34, 36). Thermal dehydration usually is a combined effect of hypovolemia and plasma hyperosmolality (22, 30).

Examining the interactive effects of hypovolemia or baroreceptor unloading and hyperosmolality on thermally induced peripheral vasodilation would enhance our understanding of the mechanism involved in the interaction between thermoregulation and body fluid regulation. However, the interactive effect of plasma hyperosmolality and central hypovolemia on peripheral vascular regulation during heat stress has not been studied.

In a previous study (26), investigators in our laboratory found that arterial pressure fell during progressive hyperthermia in rats under isotonic hypovolemia produced by diuretics, whereas arterial pressure remained constant with attenuated tail vasodilation under hyperosmotic hypovolemia. It was suggested in that study that blood pressure regulatory response to hypovolemia is augmented by plasma hyperosmolality during heat stress. From that study, we hypothesized that plasma hyperosmolality augments the inhibition of thermal peripheral vasodilation by baroreceptor unloading in humans. However, the effect of plasma hyperosmolality on baroreflex control of peripheral vascular response during heat stress is unknown.

To elucidate the interactive effects of plasma hyperosmolality and baroreceptor unloading on thermally induced peripheral vasodilation, we examined the effect of plasma hyperosmolality on peripheral vascular response to lower body negative pressure (LBNP) during heat stress. Our hypothesis was that plasma hyperosmolality enhances the inhibition of thermal vasodilation by baroreceptor unloading and, therefore, that the reduction of peripheral vascular conductance in response to LBNP is augmented by plasma hyperosmolality during heat stress. In the present study, we compared the response during heat stress with the response in normothermia. This comparison should provide us with useful information, because the mechanism of reduced cutaneous vascular conductance in response to LBNP during heat stress is likely to be different from that in normothermia (3, 11, 13, 16).

Previous studies reported the presence of interactive effect between baroreceptor unloading/unloading and plasma hyperosmolality on arginine vasopressin (AVP) secretion (8, 9, 19). Further, Takamata et al. (33) added that the increased body core temperature per se did not stimulate AVP secretion but, rather, enhanced osmotically induced AVP release, suggesting that the thermal stress interacts with plasma osmolality on AVP secretion. However, the interactive effect of plasma osmolality and baroreceptor unloading on AVP release has not been...
studied. Thus another aim of the present study was to examine the interaction between baroreceptor unloading and plasma osmolality on vasopressin release during heat stress.

METHODS

This study was approved by the Review Board on Human Experiments, Kyoto Prefectural University of Medicine, and all subjects gave their written, informed consent before participating in this study.

Subjects and experimental conditions. Seven healthy male subjects participated in this study. Their age was 21.7 ± 0.4 (20–23) yr (mean ± SE (range)); body weight, 64.9 ± 1.4 (57.2–78.6) kg; and height, 171.7 ± 1.4 (165–177) cm. They were relatively active but did not perform regular exercise training. We examined cardiovascular and hormonal responses to progressive LBNP in normothermia (NT) and during whole body heating (HT) under plasma hyperosmotic (HOSM) and normosmotic (NOSM) conditions. Thus the experimental conditions examined in the present study were NT-NOSM, NT-HOSM, HT-NOSM, and HT-HOSM. We conducted the experiments under the four different conditions in each subject on separate days. Each experiment was separated by at least 5 days, and the order of experiments was randomized.

Study protocol. Subjects were provided a meal (800 kcal; Calorie Mate; Otsuka Pharmaceutical, Tokushima, Japan) and 500 ml of mineral water 1 h before (around 8:00 AM) reporting to the laboratory. After reporting to the laboratory, the subjects sat on a chair and remained in a seated position for 60 min in a climatic chamber at 25°C (relative humidity 40%). A 21-gauge catheter was inserted into the antecubital vein during this period (at least 30 min before the first measurement). The blood pressure and heart rate were measured from the aorta by pressure tonometry (Jentow; Colin, Komaki, Japan). A tonometry transducer was fixed on the radial artery and was calibrated with an upper arm cuff. Mean arterial pressure (MAP) was calculated from the area under the curve of the arterial pressure trace, and pulse pressure (PP) was calculated from systolic and diastolic pressure. Systemic vascular conductance (SVC) was calculated from Q˙ and PP.

LBNP was applied in a graded stepwise fashion by increasing the negative pressure from 0 to ~40 mmHg in 10-mmHg steps. Each step was maintained for 3 min, and blood samples were collected before and after LBNP application (~65 min after the end of infusion) during the last 1 min of each LBNP level. To avoid arousal responses, we increased LBNP slowly over ~30 s before reaching the final level.

Measurements and data analyses. Heart rate (HR) was continuously monitored with electrocardiographic recording. Thoracic impedance (Z0) and stroke volume (SV) were measured using impedance cardiography (NEC Medical Systems, Tokyo, Japan), and SV was calculated using the equation of Kubicek et al. (18). Cardiac output (Q˙) was calculated as the product of HR and SV. Arterial blood pressure was measured in the left arm beat-by-beat via noninvasive tonometry (Jentow; Colin, Komaki, Japan). A tonometry transducer was fixed on the radial artery and was calibrated with an upper arm cuff. Mean arterial pressure (MAP) was calculated from the area under the curve of the arterial pressure trace, and pulse pressure (PP) was calculated from systolic and diastolic pressure. Systemic vascular conductance (SVC) was calculated from Q˙ and MAP.

Table 1. Baseline Tes, Tsk, P_{osmol} and ΔPV values and those values before application of LBNP

<table>
<thead>
<tr>
<th></th>
<th>NT-NOSM</th>
<th>NT-HOSM</th>
<th>HT-NOSM</th>
<th>HT-HOSM</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tes, °C</td>
<td>36.74 ± 0.12</td>
<td>36.73 ± 0.10</td>
<td>36.63 ± 0.06</td>
<td>36.73 ± 0.06</td>
</tr>
<tr>
<td>Before LBNP</td>
<td>36.73 ± 0.08</td>
<td>36.77 ± 0.08</td>
<td>36.94 ± 0.12*</td>
<td>37.63 ± 0.07†</td>
</tr>
<tr>
<td>Tsk, °C</td>
<td>33.12 ± 0.15</td>
<td>33.34 ± 0.12</td>
<td>33.59 ± 0.24</td>
<td>33.81 ± 0.08</td>
</tr>
<tr>
<td>Before LBNP</td>
<td>33.59 ± 0.09*</td>
<td>33.69 ± 0.12*</td>
<td>36.94 ± 0.06*</td>
<td>37.12 ± 0.13†</td>
</tr>
<tr>
<td>P_{osmol}, mosmol/kgH2O</td>
<td>286.4 ± 1.1</td>
<td>286.2 ± 1.0</td>
<td>283.8 ± 1.3</td>
<td>284.6 ± 1.1</td>
</tr>
<tr>
<td>Before LBNP</td>
<td>284.5 ± 1.4</td>
<td>296.2 ± 1.4†</td>
<td>285.3 ± 0.9</td>
<td>296.5 ± 1.0†</td>
</tr>
<tr>
<td>ΔPV, %</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Baseline</td>
<td>+10.8 ± 1.7*</td>
<td>+16.5 ± 1.6†</td>
<td>+9.0 ± 1.1*</td>
<td>+14.4 ± 1.4†</td>
</tr>
<tr>
<td>Before LBNP</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>

Data are means ± SE of 7 subjects. NT-NOSM, normosmotic condition in normothermia; NT-HOSM, hyperosmotic condition in normothermia; HT-NOSM, normosmotic condition with whole body heating; HT-HOSM, hyperosmotic condition with whole body heating; LBNP, lower body negative pressure; Tes, esophageal temperature; Tsk, mean skin temperature; P_{osmol}, plasma osmolality; ΔPV, percent change in plasma volume. *Significantly different compared with corresponding baseline value. †Significantly different compared with NOSM.
RESULTS

Variables before LBNP application. The baseline $T_{es}$, $T_a$, $P_{osmol}$, and $\Delta PV$ values and the corresponding values before LBNP application are shown in Table 1. Whole body heating with a water-perfused suit increased $T_{es}$ by $0.30 \pm 0.07^\circ$C in NT-HOSM and by $0.90 \pm 0.09^\circ$C from the corresponding baseline level in HT-HOSM before application of LBNP ($P < 0.01$). The increase in $T_{es}$ in HT-HOSM was significantly larger than in HT-NOSM. $T_a$ was not significantly different from the baseline value in NT conditions. $T_a$ before LBNP was higher in HT than in NT conditions. $P_{osmol}$ before LBNP application was higher in HOSM than in NOSM by $10.1 \pm 1.2$ mosmol/kgH$_2$O in the NT condition and by $12.2 \pm 0.8$ mosmol/kgH$_2$O in the HT condition. $PV$ increased by infusion in all conditions, and the increase was higher in HOSM than in NOSM in both thermal conditions.

Table 2 shows the cardiovascular variables before LBNP application. MAP was similar among all conditions. HR was higher in HT than in NT conditions, and HR in HT-HOSM tended to be higher than in NT-NOSM ($P = 0.10$). All SV, $Q\dot{}$, and SVC values were similar among the four conditions. $Z_0$ in HOSM conditions was higher than in NOSM conditions, and there was no thermal effect in NOSM or HOSM conditions. FVC was significantly higher in HT than in NT conditions, and FVC was similar between NOSM and HOSM within the thermal conditions.

Baseline plasma hormone levels before LBNP application are shown in Table 3. The plasma catecholamine concentrations did not differ among the four experimental conditions. $[AVP]^P$ was higher in HOSM than in NOSM in both thermal conditions, and $[AVP]^P$ in HT-HOSM was higher than in NT-HOSM ($P < 0.01$), but there was no thermal effect in NOSM conditions. Neither plasma hyperosmolality nor heat stress affected PRA.

Table 2. Cardiovascular variables before LBNP

<table>
<thead>
<tr>
<th></th>
<th>NT-NOSM</th>
<th>NT-HOSM</th>
<th>HT-NOSM</th>
<th>HT-HOSM</th>
</tr>
</thead>
<tbody>
<tr>
<td>MAP, mmHg</td>
<td>72.5±1.8</td>
<td>74.0±1.9</td>
<td>72.7±2.0</td>
<td>79.8±2.9</td>
</tr>
<tr>
<td>PP, mmHg</td>
<td>63.3±3.4</td>
<td>57.1±2.6</td>
<td>57.7±3.5</td>
<td>62.4±2.5</td>
</tr>
<tr>
<td>HR, beat/min</td>
<td>60.2±2.5</td>
<td>62.5±2.8</td>
<td>71.7±2.3</td>
<td>78.2±3.3†</td>
</tr>
<tr>
<td>SV, ml/beat</td>
<td>117.7±11.7</td>
<td>115.1±11.8</td>
<td>102.8±9.2</td>
<td>101.9±10.6</td>
</tr>
<tr>
<td>Q, l/min</td>
<td>7.00±0.67</td>
<td>7.27±0.73</td>
<td>7.47±0.82</td>
<td>7.86±0.70†</td>
</tr>
<tr>
<td>$Z_0$, Ω</td>
<td>22.2±0.4</td>
<td>21.0±0.4*</td>
<td>21.4±0.3</td>
<td>20.7±0.3*†</td>
</tr>
<tr>
<td>SVC, ml/min⁻¹·mmHg⁻¹</td>
<td>97.3±9.7</td>
<td>99.4±11.2</td>
<td>103.8±12.6</td>
<td>100.3±11.0</td>
</tr>
<tr>
<td>FVC, ml/100 ml⁻¹·100 mmHg⁻¹</td>
<td>8.16±0.86</td>
<td>8.96±1.20</td>
<td>15.17±2.89†</td>
<td>17.50±2.04†</td>
</tr>
</tbody>
</table>

Data are means±SE of 7 subjects. MAP, mean arterial pressure; PP, pulse pressure; HR, heart rate; SV, stroke volume; Q, cardiac output; $Z_0$, thoracic impedance; SVC, systemic vascular conductance; and FVC, forearm vascular conductance. *Significantly different compared with NOSM. †Significantly different compared with NT conditions.

Table 3. Plasma hormone levels baseline, after infusion but before application of LBNP

<table>
<thead>
<tr>
<th></th>
<th>NT-NOSM</th>
<th>NT-HOSM</th>
<th>HT-NOSM</th>
<th>HT-HOSM</th>
</tr>
</thead>
<tbody>
<tr>
<td>$[E]^P$, pg/ml</td>
<td>22.9±4.2</td>
<td>34.3±6.5</td>
<td>37.1±11.1</td>
<td>42.9±9.2</td>
</tr>
<tr>
<td>$[NE]^P$, pg/ml</td>
<td>104.3±9.0</td>
<td>91.4±15.8</td>
<td>121.4±12.2</td>
<td>100.0±7.9</td>
</tr>
<tr>
<td>PRA, ng ANG 1·min⁻¹·l⁻¹</td>
<td>1.0±0.2</td>
<td>0.9±0.3</td>
<td>1.4±0.3</td>
<td>0.9±0.2</td>
</tr>
<tr>
<td>$[AVP]^P$, pg/ml</td>
<td>0.62±0.10</td>
<td>3.47±0.65*</td>
<td>1.25±0.21</td>
<td>5.28±0.68†</td>
</tr>
</tbody>
</table>

Data are means±SE of 7 subjects. $[E]^P$, plasma epinephrine concentration; $[NE]^P$, plasma norepinephrine concentration; PRA, plasma renin activity; $[AVP]^P$, plasma arginine vasopressin. *Significantly different compared with NOSM. †Significantly different compared with NT conditions.
Hemodynamic and hormonal responses to LBNP. Figure 1 shows the changes in MAP, PP, SV, and Z₀ in response to LBNP application in the four conditions. MAP was well maintained during LBNP in all conditions. PP decreased only at 40 mmHg in NT-NOSM (P < 0.01) but did not change in other conditions. There was a graded reduction in SV in response to changes in LBNP level. The decrease in SV tended to be larger in NT than in HT conditions, but the response was not significantly different among the conditions. The Z₀ response in NT-NOSM was larger than that in NT-HOSM at 30 mmHg. The change in Z₀ was similar between HT-NOSM and HT-HOSM.

The HR response to LBNP tended to be larger in HT-NOSM than HT-HOSM, but there was no significant difference among the conditions (Fig. 2, top). The response of SVC was similar among the four conditions (Fig. 2, middle). The reduction of FVC at 40 mmHg LBNP in HT-HOSM was significantly larger than the reduction in HT-NOSM and in NT conditions (P < 0.05) (Fig. 2, bottom). In contrast, the reduction of FVC in response to LBNP was not influenced by plasma hyperosmolality in normothermia (Fig. 2, bottom left).
T_{es} increased and  \overline{T}_{sk} decreased progressively during LBNP application, and the responses to a graded LBNP were not affected by plasma hyperosmolality in both NT and HT conditions (Fig. 3).

Figure 4 shows the hormonal responses to LBNP. The response of [E]_{p} to LBNP was similar among the conditions. The response of [NE]_{p} to −40 mmHg LBNP was significantly augmented during heat stress, but plasma hyperosmolality did not affect the response to LBNP. The response of PRA to LBNP was similar among the conditions. [AVP]_{p} was significantly higher in HOSM in both thermal conditions (Table 3) and increased during a graded LBNP (P < 0.01), but neither hyperosmolality nor heat stress influenced the response of [AVP]_{p} to LBNP.

**DISCUSSION**

The present study demonstrates that plasma hyperosmolality enhanced the reduction of FVC in response to baroreceptor unloading during thermally vasodilated conditions. The reduction of FVC at −40 mmHg LBNP in HT-HOSM was significantly larger than the reduction in HT-NOSM (P < 0.05). In contrast, the reduction of FVC in response to LBNP was not influenced by plasma hyperosmolality in normothermia (Fig. 1). In the present study, we could not measure central venous pressure (CVP) for ethical reasons. Thus we could not determine the functional relationship between peripheral vascular response and the level of baroreceptor unloading. However, the increase in Z_{0} and the decrease in SV during LBNP were similar between HT-NOSM and HT-HOSM. Cai et al. (1) showed that the change in Z_{0} could be used to estimate central blood volume, and Peters et al. (28) reported that the linear relationship between SV and CVP was not influenced by heat stress, suggesting that SV can be used as an index of CVP even during heat stress. Assuming that changes in Z_{0} (1) and also SV (28) can represent the change in central blood volume, or CVP, our results suggest that the enhanced FVC response during LBNP in HT-HOSM is not due to a larger degree of baroreceptor unloading as a result of increased blood pooling in the lower extremities in this condition. Therefore, there exists an interactive effect of baroreceptor unloading and plasma hyperosmolality on the peripheral vascular response during heat stress, but not in normothermia. However, the
possibility that the augmented reduction in HT-HOSM is due
to the larger degree of baroreceptor unloading compared with
HT-NOSM cannot be completely excluded, because the reli-
ability of the Z0 during heat stress has not been examined, and
SV is controlled by several factors other than cardiac filling
pressure.

The increase in Tes in HT-HOSM (0.90 ± 0.09°C) was
larger than that in HT-NOSM (0.30 ± 0.07°C) before LBNP
exposure. This large difference is caused by osmotic inhibition
of thermoregulatory responses (34, 36). FVC was similar
between HT-NOSM and HT-HOSM, although Tes was much
higher in HT-HOSM, suggesting that a larger thermal drive is
required to elicit similar vasodilation level in this condition. In
addition, the decrease in body weight throughout the heating
protocol was significantly smaller in HT-HOSM (0.31 ± 0.05
kg) than in HT-NOSM (0.43 ± 0.07 kg), suggesting that
thermoregulatory sweating is also inhibited by plasma hyper-
osmolality. Thus, although the heating protocol, or thermal
environment to which the subjects were exposed, was exactly
the same in both HT-NOSM and HT-HOSM conditions, sub-
jects received much larger thermal stress in HT-HOSM than in
HT-NOSM. The larger thermal stress, or the greater increase in
tes induced by inhibition of thermoregulation, could be the
underlying mechanism of the augmented FVC response in-
duced by plasma hyperosmolality during heat stress. The ΔFVC
response to LBNP in HT-NOSM would be significantly
higher if the increase in Tes was similar to that in HT-HOSM.
However, Peters et al. (28) suggested that the capacity, but not
the sensitivity, of FVC response to LBNP is affected by
increased body core temperature. This suggestion is supported
by the finding from the earlier studies that the percent decrease
in FVC in response to moderate LBNP (−30 to −40 mmHg)
during heat stress (ΔTes 0.3–0.9°C) is similar to, or even
smaller than, that in normothermia, although the decrease in
FVC is enhanced during heat stress (3, 10, 28, 31). These
results suggest that heat stress or hyperthermia increases the
capacity for, but not sensitivity to, the reduction of peripheral
vascular conductance and that the level of vasodilation before
LBNP application influences the reduction of FVC during
LBNP. In the present study, therefore, we employed a 60-min
heating protocol before LBNP to produce a similar level of
FVC between HT-NOSM and HT-HOSM (Table 2) to elimi-
nate the effect of vasodilation level before LBNP. Indeed, the
FVC level was not different between HT-NOSM and HT-
HOSM (Table 2). Thus the augmented reduction of FVC
during LBNP in HT-HOSM compared with HT-NOSM is not
due to a higher level of peripheral vasodilation before LBNP
application. Furthermore, the percent reduction of FVC at −40
mmHg LBNP was significantly larger in HT-HOSM (∼58.8 ± 4.1%) than in HT-NOSM (∼44.7 ± 8.1%) (P < 0.05, Fig. 5).
These results suggest that the sensitivity, not the capacity,
of FVC response to LBNP is augmented in HT-HOSM compared
with HT-NOSM, i.e., plasma hyperosmolality possibly modi-
fies the sensitivity of the peripheral vascular response to
baroreceptor unloading during thermally vasodilated condi-
tions. The contribution of plasma hyperosmolality and higher
body core temperature as a result of hyperosmolality during
heat stress to the augmented peripheral vascular response to
baroreceptor unloading is difficult to estimate, because the
reported results of the effect of hyperthermia on baroreflex
responses are inconsistent (4, 15, 32, 35). Nevertheless, our
results suggest that the inhibition of thermal peripheral vaso-
dilation by baroreceptor unloading is enhanced by plasma
hyperosmolality when the thermal vasodilation level is similar
to the normosmotic condition.

The effect of plasma hyperosmolality was specific during
heat stress, or the vasodilated condition, and this effect was not
observed in normothermia. It has been reported that the reduc-
tion of forearm cutaneous vascular conductance induced by LBNP during heat stress is due to the withdrawal of the thermal active vasodilator system, and the reduction of cutaneous vascular conductance during normothermia is due to the increased activity of sympathetic vasoconstrictor tone (3, 16). In the present study, the increase in $T_{es}$ in HT-NOSM was relatively small (0.30 ± 0.07°C). One may suspect that the increased FVC in HT-NOSM before LBNP application is merely due to the withdrawal of vasoconstrictor tone, because heat stress was mild. However, the recent study by Kamiyo et al. (14) indicated that the active vasodilator system is activated by even a mild degree of heat stress. Taking these findings together, we speculate that the augmented reduction of FVC during LBNP in HT-HOSM condition compared with HT-NOSM is due to the augmented withdrawal of the active vasodilator system if the difference in the change in FVC is due to the reduction of cutaneous vascular conductance. However, the changes in plasma epinephrine ($\Delta [E_p]$) and norepinephrine concentration ($\Delta [NE_p]$), plasma renin activity ($\Delta [PRA]$), and plasma arginine vasopressin concentration ($\Delta [AVP_p]$) in response to LBNP in normothermia (left) and during heat stress (right). Data are means ± SE of 7 subjects. *$P < 0.05$ compared with before LBNP. †$P < 0.05$, normothermia vs. heat stress.

Fig. 5. Percent changes in FVC at −40 mmHg LBNP. Data are means ± SE of 7 subjects. §$P < 0.05$, NOSM vs. HOSM.
further study is needed to examine this hypothesis, because we did not directly evaluate the contribution of vasoconstrictor activity or cutaneous vascular response (17).

A higher [AVP]p in HT-HOSM may be involved in the augmented reduction of ΔFVC in response to LBNP. However, the [AVP]p in NT-HOSM was higher than in NT-NOSM, but the higher [AVP]p did not enhance ΔFVC response to LBNP in NT. Nakajima et al. (26) reported that intravenous administration of a V1 antagonist in hyperosmotic and hypovolemic rats did not alter arterial pressure regulation or the response of tail vascular conductance during progressive hyperthermia, suggesting that increased [AVP]p does not modify osmotic inhibition of the peripheral vasodilatory response to heat stress. In addition, Goldsmith (7) reported that the baroreflex function was not enhanced with a physiological increase of plasma AVP levels. Taken together, the data in the present study do not support the hypothesis that increased AVP contributes to enhanced reductions in FVC during LBNP.

In the present study, PV increased significantly more, and Z0 was lower, in the HOSM conditions than in the NOSM conditions, whereas in a previous study in our laboratory (34), the increase in PV was similar to the infusion rate employed in the present experiment. Because hypervolemia or increased central blood volume might attenuate the cardiovascular responses to LBNP (21), we might underestimate the reduction of FVC during LBNP in HOSM conditions. Thus, although the greater increase in PV in HOSM than in NOSM should not interfere with our conclusion; the higher PV in HOSM than in NOSM could modify the FVC response to LBNP.

In the present study, the [AVP]p before application of LBNP was higher in the HOSM than in the NOSM conditions, and [AVP]p in HT-HOSM was significantly higher than in NT-HOSM. In contrast, heat stress did not increase [AVP]p in the normosmotic condition, i.e., [AVP]p in HT-NOSM was similar to that in NT-NOSM. This result is consistent with another previous report from our group (33), which showed that increased body temperature per se does not stimulate AVP secretion but augments AVP release when Pmonal was higher than 295 mosmol/kgH2O. In the present study, we examined the interactive effect of Pmonal and baroreceptor unloading during heat stress and in normothermia. We found a significant increase in [AVP]p during LBNP at −30 and −40 mmHg in all conditions, and the increase was similar among the conditions (Table 3 and Fig. 3), suggesting that the baroreceptor unloading and hyperosmotic effects on plasma AVP secretion are additive. Leimbach et al. (19) found that a subgroup of normal subjects in whom osmolality was >295 mosmol/kgH2O showed increases in AVP only during high-level LBNP producing tachycardia and narrowed PP, suggesting that plasma hyperosmolality modifies AVP secretion induced by baroreceptor unloading. In contrast, Goldsmith et al. (8) reported that acute baroreceptor unloading with LBNP, at either low or high level, after osmotic stimulation did not result in further enhancement of AVP secretion in humans, and they concluded that the effect of baroreceptor unloading on AVP secretion is very small in humans. The reason for these inconsistent results from earlier studies is unclear, but [AVP]p before LBNP application was lower in the present study compared with Goldsmith’s study. This lower [AVP]p in our study might be the result of a larger amount of isotonic or hypertonic saline infusion before LBNP, the longer supine resting period after infusion, and/or the sensitivity of hormone assay. The duration of LBNP application also may be involved (8, 9, 19). In any case, at least under the conditions employed in the present study, there is apparently no interactive effect of plasma hyperosmolality and central hypovolemia on AVP release.

Escourrou et al. (6) reported that body heating increased NE and PRA. In contrast, in our present study, neither NE nor PRA was higher in HT than in NT conditions (Table 3). HR in heat-stressed conditions was also far greater in that study than in the present study. One possible reason is that the thermal stress in that study seems to have been greater than in the present study. Another possible reason for the different results between the two studies is that the level of PV before the heating protocol is different. Saline infusion before body heating substantially increased PV in the present study (Table 1), but Escourrou et al. did not infuse saline before the heating protocol. Furthermore, subjects fasted overnight in the study by Escourrou et al., but in our study, subjects ate breakfast and drank water before reporting to the chamber. We speculate that the increased PV is a major factor, but further studies are required to identify the exact reason for the different findings between the two studies.

In summary, we found that the reduction of peripheral vascular conductance in response to LBNP was enhanced by plasma hyperosmolality during heat stress, or peripheral vasodilated conditions, but not in normothermia. Thus the interactive effect could contribute effectively to the maintenance of arterial pressure during heat stress in hyperosmotic hypovolemia, e.g., thermal dehydration (27). In addition, we found that baroreceptor unloading stimulates AVP release, but we could not find any interaction between plasma hyperosmolality and baroreceptor unloading in normothermia or during heat stress.

GRANTS

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