

Baroreceptor control of the cutaneous active vasodilator system

C. G. CRANDALL, J. M. JOHNSON, W. A. KOSIBA, AND D. L. KELLOGG, JR.
*Departments of Physiology and Medicine, University of Texas Health Science Center
at San Antonio, San Antonio, Texas 78284*

Crandall, C. G., J. M. Johnson, W. A. Kosiba, and D. L. Kellogg, Jr. Baroreceptor control of the cutaneous active vasodilator system. *J. Appl. Physiol.* 81(5): 2192–2198, 1996.—We sought to identify whether reductions in cutaneous active vasodilation during simulated orthostasis could be assigned solely to cardiopulmonary or to carotid baroreflexes by unloading cardiopulmonary baroreceptors with low levels of lower body negative pressure (LBNP) or unloading carotid baroreceptors with external pressure applied over the carotid sinus area [carotid pressure (CP)]. Skin blood flow was measured at a site at which adrenergic function was blocked via bretylium tosylate iontophoresis and at an unblocked site. During LBNP of -5 and -10 mmHg in hyperthermia, neither heart rate (HR) nor cutaneous vascular conductance (CVC) at either site changed ($P > 0.05$ for both), whereas forearm vascular conductance (FVC) was reduced (-5 mmHg: from 21.6 ± 4.8 to 19.8 ± 4.1 FVC units, $P = 0.05$; -10 mmHg: from 22.3 ± 4.0 to 19.3 ± 3.7 FVC units, $P = 0.002$). LBNP of -30 mmHg in hyperthermia reduced CVC at both sites (untreated: from 51.9 ± 5.7 to $43.2 \pm 5.1\%$ maximum, $P = 0.02$; bretylium tosylate: from 60.9 ± 5.4 to $53.2 \pm 4.4\%$ maximum, $P = 0.02$), reduced FVC (from 23.2 ± 3.6 to 18.1 ± 3.3 FVC units; $P = 0.002$), and increased HR (from 83 ± 4 to 101 ± 3 beats/min; $P = 0.003$). Pulsatile CP (45 mmHg) did not affect FVC or CVC during normothermia or hyperthermia ($P > 0.05$). However, HR and mean arterial pressure were elevated during CP in both thermal conditions (both $P < 0.05$). These results suggest that neither selective low levels of cardiopulmonary baroreceptor unloading nor selective carotid baroreceptor unloading can account for the inhibition of cutaneous active vasodilator activity seen with simulated orthostasis.

skin blood flow; baroreflex; human; cardiopulmonary baroreceptors; carotid; temperature regulation; peripheral circulation; bretylium

IN THERMALLY NEUTRAL ENVIRONMENTS, skin receives ~5–10% of cardiac output, whereas in conditions of heat stress, skin blood flow (SkBF) can reach 50–70% of cardiac output, approaching 8 l/min (12). This increase in SkBF is accomplished initially through withdrawal of sympathetic vasoconstrictor activity and, in nonglabrous areas, by increased sympathetic vasodilator activity. The active vasodilator component mediates the majority of the reflex thermoregulatory increase in SkBF (23). In addition to these thermoregulatory reflexes, SkBF is also controlled by nonthermoregulatory reflexes, including baroreflexes (12, 15, 25, 30). For example, Kellogg et al. (15) used bretylium iontophoresis to block adrenergic vasoconstrictor activity and measured cutaneous vascular conductance (CVC) at unblocked and bretylium-treated sites during -40 mmHg lower body negative pressure (LBNP) in normothermia and hyperthermia. They found reductions in

CVC induced by this level of LBNP in normothermia to be due to enhanced vasoconstrictor activity, whereas in hyperthermia, reductions in CVC were due primarily to withdrawal of cutaneous active vasodilator activity. Thus baroreceptor-mediated control of CVC can be important in the maintenance of blood pressure, particularly in hyperthermia, when the skin represents a significant fraction of the total vascular conductance.

The mechanisms controlling SkBF in response to a challenge to blood pressure may depend on the degree of unloading of the individual baroreceptor populations (i.e., cardiopulmonary and sinoaortic baroreceptors). Moreover, the control by individual baroreceptor populations of the cutaneous vasoconstrictor and active vasodilator systems may differ. Cardiopulmonary baroreceptor unloading via low levels of LBNP (13, 19) in normothermia yielded results suggesting cutaneous vasoconstriction in some (30), but not all (2, 32), studies. When greater levels of LBNP are applied, unloading a combination of cardiopulmonary and sinoaortic baroreceptors, substantial reductions in SkBF are more consistently observed (12, 15, 25, 30). On the other hand, muscle blood flow shows a much more consistent vasoconstriction in response to low levels of LBNP. A question that naturally arises from these observations is which baroreceptor population is mediating these changes in SkBF and whether this is accomplished through modulation of the cutaneous vasoconstrictor and/or active vasodilator systems. The purpose of the present study was to identify whether selective unloading of cardiopulmonary or of carotid baroreceptors is capable of reducing cutaneous active vasodilator activity.

METHODS

Subjects

Six subjects (5 men, 1 woman) participated in each of two protocols. The subjects' ages were between 27 and 33 yr, and all were of normal weight (72 ± 4 kg), height (175 ± 2 cm), and health as identified by physical examination. Written informed consent was obtained from all subjects before participation in this institutionally approved study.

Experimental Procedures

Mean arterial pressure (MAP) was continuously recorded from the electrical integration of the pulsatile blood pressure signal obtained from a finger (Finapres) by the Penaz method and referenced at heart level. Heart rate (HR) was obtained from the electrocardiogram (ECG). Forearm SkBF was monitored by laser-Doppler flowmetry and indexed as laser-Doppler flow (LDF; Moor and Vasamedics) at a control site and an adjacent site (area = 0.6 cm²) treated with bretylium via iontophoresis (14). Bretylium blocks the release of trans-

mitter from adrenergic nerve endings, thereby presynaptically blocking vasoconstrictor nerve function at that location. Thus reflex changes in SkBF from this area of skin are attributed to changes in active vasodilator control (14, 15). Studies in our laboratory demonstrated the efficacy of bretylium blockade to last at least 5 h after its administration by iontophoresis (14, 15, 21). An index of CVC was calculated from the ratio of LDF to MAP. On completion of each protocol, heaters surrounding the LDF probes were used to raise local skin temperature (T_{sk}) to 42°C. Local temperature was held at this level for 30 min to elicit maximal cutaneous vasodilation (29). Values for CVC were then converted to percentages of maximum for that site. Forearm blood flow (FBF) was measured on the contralateral arm three times per minute by using venous occlusion plethysmography. Forearm vascular conductance (FVC) was calculated as the ratio of FBF to MAP.

Internal temperature was monitored with a thermocouple placed sublingually (T_{sl}). T_{sk} was monitored from the electrical average of six thermocouples placed at representative sites on the body surface (28). The subject wore a two-piece tube-lined suit that permitted alterations in T_{sk} of both the upper and lower body by changing the temperature of the water perfusing the suit. The suit covered the entire body surface with the exception of the head, feet, and arms.

Protocol 1: cardiopulmonary baroreflex assessment. Sixty to 90 min after the iontophoretic administration of bretylium, the subject entered the LBNP device. The box was attached to a vacuum source capable of rapidly reducing pressure within the box. The two-piece water-perfused suit permitted the waist seal of the LBNP device to be sealed directly to the skin, thereby effectively eliminating air leakage at this seal and associated cooling (32). For ~30–45 min, the subject lay supine while being instrumented for measurements of LDF, MAP, HR, and FBF. The subject then rested quietly for ~10 min, after which the effectiveness of the bretylium treatment was assessed with a 3-min period of whole body cooling (14) accomplished by perfusing the suit with 10–15°C water. Water temperature was subsequently raised to return T_{sk} to a normothermic level. Approximately 8–10 min after the cold stress, the subject was exposed to –30 mmHg of LBNP for 3 min. After a recovery period, heat stress was initiated by increasing T_{sk} to ~38°C with the water-perfused suit. The resultant increase in internal temperature activates the cutaneous active vasodilator system, thus enabling the investigation of the effects of LBNP on this system. Once internal temperature and SkBF at both sites were elevated and stable, bouts of LBNP at –5, –10, and –30 mmHg were applied for 3 min each (order randomly chosen). The beginning of each bout was separated from the end of the preceding bout by ~10 min. The two lower levels of LBNP were chosen to unload selectively cardiopulmonary baroreceptors while the higher level was chosen to unload both cardiopulmonary and sinoaortic baroreceptors. Preliminary data revealed that in hyperthermia intermediate levels of LBNP (i.e., –15 and –20 mmHg) were often accompanied with elevations in HR, suggesting significant unloading of sinoaortic baroreceptors (13, 19). After the three bouts of LBNP, T_{sk} was then returned to normothermia, and local temperature surrounding the laser-Doppler probes was elevated to 42°C as described in *Experimental Procedures*.

Protocol 2: carotid baroreflex assessment. On a separate day from *protocol 1*, the effects of carotid sinus baroreceptor unloading on SkBF were assessed. First, the effectiveness of the bretylium blockade on vasoconstrictor function was assessed by a cold stress as described in *Protocol 1*. Shortly after the cold stress and return of T_{sk} to normothermia, 45 mmHg pulsatile pressure was applied for 3-min over the area of the

carotid sinus [carotid pressure (CP)] with a lead collar connected to a pressure source (7). Pulsatile pressure was accomplished by opening a solenoid between the pressure source and the neck collar 50 ms after the R wave of the ECG for a duration of 500 ms. CP was used to induce carotid baroreceptor unloading, which, directionally, is the same perturbation at the carotid sinus that occurs with high levels of LBNP. After the CP bout in normothermia, heat stress was induced to activate the vasodilator system. Once CVC at both sites was elevated and stable, the subject underwent another 3-min bout of 45 mmHg CP. After this procedure, T_{sk} was returned to normothermic levels, after which local temperatures around the LDF probes were elevated to 42°C to maximally vasodilate the cutaneous vasculature (29).

Data Collection and Statistics

All data except FBF were sampled once per second via a personal computer and averaged over 20-s intervals. FBF was measured three times per minute for 2 min before baroreceptor unloading and throughout the period of baroreceptor unloading. Values for CVC were normalized with respect to the maximal value from each site obtained by local heating to 42°C (29). Paired *t*-tests were performed to compare the averaged data from the 2-min period before the perturbation (i.e., cold stress, LBNP, or CP) with data from the final minute of the perturbation. Comparison of the reduction in CVC at the untreated sites with the reduction in CVC at the bretylium-treated sites during the LBNP trials in hyperthermia was also accomplished by using a paired *t*-test. All data are given as means \pm SE.

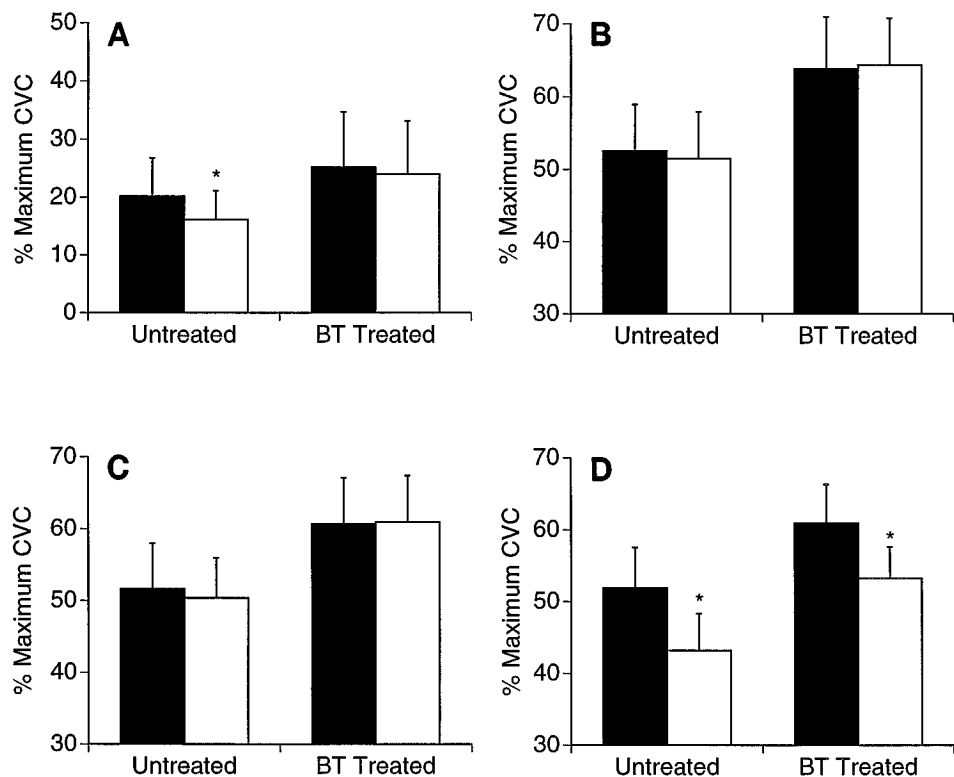
RESULTS

Protocol 1

Cold stress reduced CVC at untreated sites from 21.9 ± 6.8 to $14.5 \pm 4.8\%$ of maximum ($P = 0.02$). At bretylium-treated sites CVC was not significantly altered (from 25.6 ± 9.8 to $24.6 \pm 8.5\%$ maximum CVC; $P = 0.10$), verifying that bretylium treatment was effective in blocking adrenergically mediated cutaneous vasoconstriction. Exposure to –30 mmHg LBNP in normothermia (Fig 1) showed significant reductions in CVC at untreated sites (from 20.2 ± 6.6 to $16.1 \pm 5.0\%$ maximum CVC; $P = 0.03$) but not at bretylium-treated sites (from 25.2 ± 9.6 to $24.0 \pm 9.1\%$ maximum CVC; $P = 0.07$). HR during this bout of LBNP was significantly elevated, whereas FVC was significantly reduced (Table 1).

Increasing T_{sk} from 34.6 ± 0.1 to $38.1 \pm 0.2^\circ\text{C}$ led to an increase in T_{sl} from 36.59 ± 0.06 to $37.12 \pm 0.14^\circ\text{C}$ and engaged the cutaneous active vasodilator system because CVC at bretylium-treated sites was significantly increased. During hyperthermia, LBNP at –5 mmHg did not significantly change CVC at the untreated site (from 52.6 ± 6.4 to $51.5 \pm 6.4\%$ maximum CVC; $P = 0.15$) or at the bretylium-treated site (from 63.8 ± 7.1 to $64.4 \pm 6.5\%$ maximum CVC; $P = 0.58$; see Fig. 1). Similarly, LBNP at –10 mmHg did not change CVC at either site (untreated: from 51.6 ± 6.3 to $50.4 \pm 5.6\%$ maximum CVC, $P = 0.38$; bretylium-treated: from 60.7 ± 6.4 to $60.9 \pm 6.4\%$ maximum CVC, $P = 0.79$). LBNP at –30 mmHg significantly reduced CVC both at

Fig. 1. Average cutaneous vascular conductance (CVC) before and during lower body negative pressure (LBNP) at -30 mmHg in normothermia (A) and -5 (B), -10 (C), and -30 mmHg (D) LBNP in hyperthermia at both untreated and bretteylium-treated (BT) sites. Order of LBNP stages in hyperthermia was randomly applied. Filled bars, control; open bars, LBNP. LBNP of -30 mmHg in normothermia significantly reduced CVC at untreated site only ($*P < 0.05$). In hyperthermia, LBNP at -5 and -10 mmHg did not affect CVC, whereas -30 mmHg LBNP significantly reduced CVC at both untreated and BT-treated sites ($*P < 0.05$).



untreated sites (from 51.9 ± 5.7 to $43.2 \pm 5.1\%$ maximum CVC; $P = 0.02$) and at bretteylium-treated sites (from 60.9 ± 5.4 to $53.2 \pm 4.4\%$ maximum CVC; $P = 0.02$). These reductions were not different between sites ($P = 0.63$), suggesting that the reduction in CVC at the untreated site was primarily due to a reduction in active vasodilator activity. There were no significant changes in HR (Table 1) during LBNP trials at -5 or -10 mmHg. HR significantly increased during LBNP at -30 mmHg in hyperthermia. FVC (Table 1) was significantly reduced by all levels of LBNP. No significant change in T_{sk} occurred during LBNP in either thermal condition ($P \geq 0.12$; see Table 1).

Protocol 2

Consistent with the blockade of the vasoconstrictor system by bretteylium treatment, CVC at untreated sites significantly decreased during the cold stress (from 13.5 ± 1.6 to $8.6 \pm 0.9\%$ maximum CVC; $P = 0.02$) but did not significantly change at the bretteylium-treated sites (from 21.6 ± 3.5 to $19.5 \pm 3.0\%$ maximum CVC; $P = 0.07$). In normothermia, 45 mmHg CP significantly elevated HR (from 65.6 ± 5.5 to 69.6 ± 5.4 beats/min; $P = 0.002$) and MAP (from 89.8 ± 3.3 to 99.0 ± 3.8 mmHg; $P = 0.004$), showing that this perturbation evoked a carotid baroreflex (Fig 2). Nevertheless, CVC

Table 1. Hemodynamic and skin temperatures before and during LBNP

	LBNP Stage							
	-30 mmHg	PValue	-5 mmHg (HS)	PValue	-10 mmHg (HS)	PValue	-30 mmHg (HS)	PValue
MAP, mmHg								
Pre-LBNP	79 ± 2		71 ± 2		74 ± 3		74 ± 3	
LBNP	77 ± 2	0.12	73 ± 2	0.31	74 ± 3	0.52	71 ± 5	0.39
HR, beats/min								
Pre-LBNP	59 ± 3		81 ± 6		82 ± 5		83 ± 4	
LBNP	68 ± 2	<0.01	83 ± 6	0.13	85 ± 6	0.26	101 ± 3	<0.01
FVC, units								
Pre-LBNP	6.1 ± 1.1		21.6 ± 4.8		22.3 ± 4.0		23.2 ± 3.6	
LBNP	3.6 ± 0.8	<0.01	19.8 ± 4.1	0.05	19.3 ± 3.7	<0.01	18.1 ± 3.3	<0.01
T_{sk} , °C								
Pre-LBNP	34.67 ± 0.20		38.10 ± 0.17		38.11 ± 0.19		38.05 ± 0.18	
LBNP	34.61 ± 0.19	0.12	38.03 ± 0.17	0.15	38.10 ± 0.19	0.6	37.97 ± 0.21	0.3

Values are means \pm SE. LBNP, lower-body negative pressure; HS, heat stress; MAP, mean arterial pressure; HR, heart rate; FVC, forearm vascular conductance; T_{sk} , skin temperature. P values are for comparison between pre-LBNP and LBNP periods.

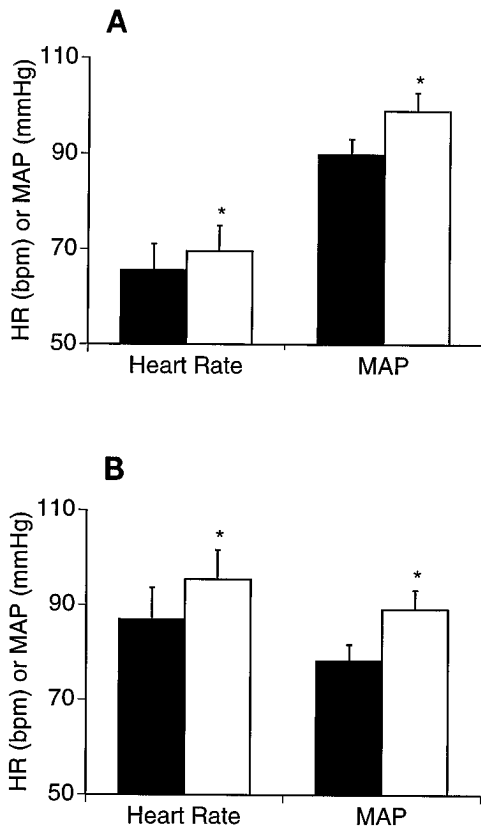


Fig. 2. Responses in heart rate (HR) and mean arterial pressure (MAP) to unloading carotid baroreceptors with 45 mmHg pulsatile pressure applied over carotid sinus area (carotid pressure) in both normothermia (A) and hyperthermia (B). Filled bars, control; open bars, 45 mmHg carotid pressure. bpm, Beats/min. Carotid pressure significantly elevated both HR and MAP in both thermal conditions (* $P < 0.05$), suggesting a carotid baroreflex was initiated by application of carotid pressure.

at neither the untreated sites (from 19.8 ± 6.0 to $22.3 \pm 4.8\%$ maximum CVC; $P = 0.2$) nor the bretylium-treated sites (from 23.8 ± 3.8 to $24.4 \pm 4.2\%$ maximum CVC; $P = 0.5$) significantly changed during CP (Fig 3). Moreover, 45 mmHg CP did not change FVC (4.3 ± 0.8 to 4.4 ± 0.7 FVC units; $P = 0.7$).

Application of CP during hyperthermia raised both HR (from 86.9 ± 6.7 to 95.4 ± 6.2 beats/min; $P = 0.002$) and MAP (from 78.2 ± 3.5 to 89.1 ± 4.1 mmHg; $P = 0.005$), whereas CVC at untreated sites (from 77.0 ± 6.1 to $75.4 \pm 5.9\%$ maximum CVC; $P = 0.6$) and at bretylium-treated sites (from 62.8 ± 5.2 to $65.2 \pm 5.6\%$ maximum CVC; $P = 0.5$) as well as FVC (from 19.7 ± 4.7 to 19.2 ± 4.2 FVC units; $P = 0.6$) were unaffected (Figs. 2 and 3).

DISCUSSION

A number of studies have shown that the cutaneous circulation participates in the baroreflex-mediated responses to actual or simulated orthostasis (e.g., Refs. 12, 15, 25, 30). In normothermia, vasoconstrictor activity is increased, whereas in hyperthermia cutaneous active vasodilation is withdrawn during simulated orthostasis (15). However, the baroreceptor population(s) initiating these responses is not known. The

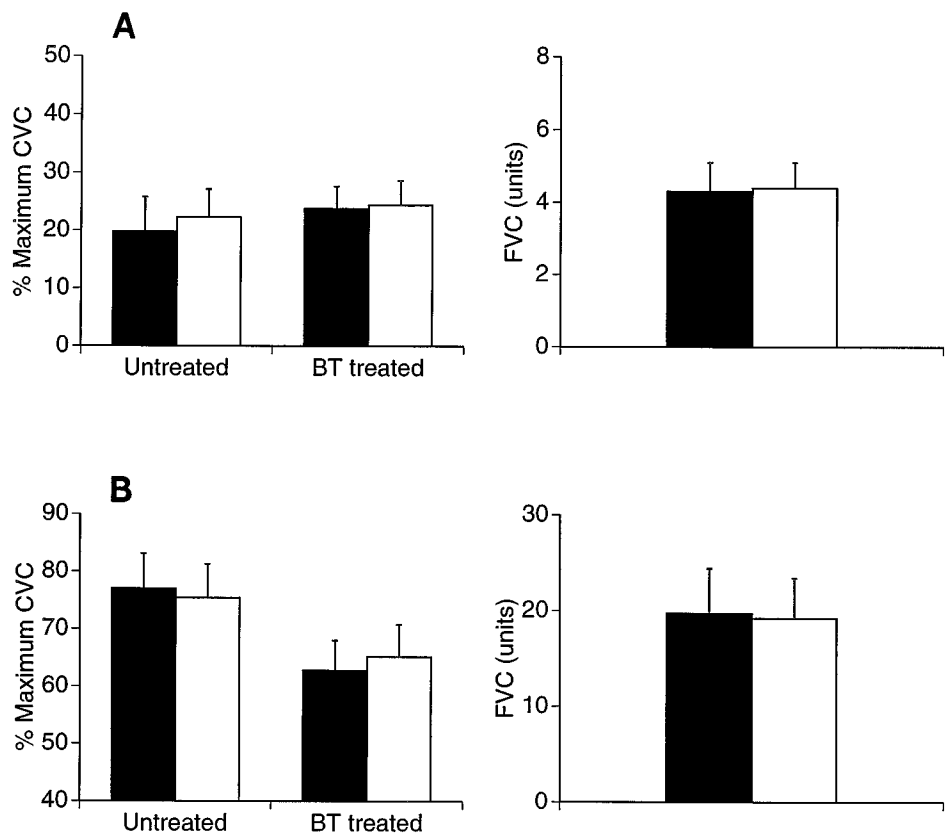
primary purpose of this study was to test whether the mechanism for the withdrawal of active vasodilator activity is mediated solely by cardiopulmonary or carotid baroreflexes. Our findings do not support these singular mechanisms. Cardiopulmonary baroreceptor unloading in hyperthermia with -5 and -10 mmHg LBNP did not evoke reductions in CVC. Similarly, selectively decreasing carotid sinus transmural pressure in either normothermia or hyperthermia did not elicit responses in CVC despite increases in HR and MAP, reflective of a carotid baroreflex. When lower extremity pooling of blood was further increased with -30 mmHg LBNP, significant and equal reductions in CVC were observed at both the untreated and bretylium-treated sites.

Application of low levels of LBNP was selected to unload specifically the cardiopulmonary baroreceptors, whereas -30 mmHg LBNP was chosen to unload both the cardiopulmonary and sinoaortic baroreceptors. In normothermia, graded levels of LBNP up to about -20 mmHg cause limb and splanchnic vasoconstriction, but they do so in the absence of measurable changes in aortic mean pressure, pulse pressure, or rate of pressure change, signals important to arterial baroreceptors (13, 19). There is also no increase in HR with these levels of LBNP (13, 19). At more severe levels (beyond -20 LBNP), aortic pulse pressure narrows and HR increases (13). For this reason, it is generally accepted that increases in HR indicate a change in the signal to the arterial baroreceptors (19), an assumption adopted in this study. However, the possibility that the aortic and carotid baroreceptors were affected by -5 and -10 mmHg LBNP cannot be ruled out because these perturbations have been shown to change aortic pulse area (27) and carotid arterial diameter (16). Whether such changes are sufficient to evoke sinoaortic baroreflexes is unknown. Nevertheless, neither reductions in CVC nor increases in HR with these low levels of LBNP were observed.

Despite the lack of changes in CVC or HR at -5 and -10 mmHg LBNP in hyperthermia, significant reductions in FVC occurred. Therefore, we are confident that cardiopulmonary baroreceptors were sufficiently unloaded to evoke efferent responses, presumably mediating vasoconstriction of noncutaneous vasculature in the forearm. Such an observation of a preferential efferent response during cardiopulmonary baroreceptor unloading is not new because Tripathi and Nadel (30) made similar observations during graded LBNP in normothermia.

In contrast to results from -5 and -10 mmHg LBNP in hyperthermia, CVC decreased and HR increased during -30 mmHg LBNP in both normothermia and hyperthermia. In normothermia, decreases in CVC during LBNP were solely attributable to increased sympathetic adrenergic activity because there were no significant changes in CVC at the site lacking a functional sympathetic adrenergic vasoconstrictor system (i.e., the bretylium-treated site). This lack of change in CVC at the bretylium-treated site during LBNP sug-

Fig. 3. CVC and forearm vascular conductance (FVC) during carotid baroreceptor unloading with 45 mmHg pulsatile pressure delivered over carotid sinus area (carotid pressure). *A*: normothermia. *B*: hyperthermia. Filled bars, control; open bars, 45 mmHg carotid pressure. Despite hemodynamic responses to carotid pressure (see Fig. 2), CVC was not significantly altered, supporting the conclusion that carotid baroreflex did not affect cutaneous vasoconstriction or active vasodilation at this level of carotid baroreceptor unloading. Moreover, lack of change in FVC suggests this level of carotid pressure did not evoke forearm muscle vasoconstriction.



gests that changes in the control of SkBF occur within the area of blockade. Therefore, reductions in SkBF at the untreated site are not due to vasoconstriction of larger vessels upstream. In hyperthermia, LBNP at -30 mmHg caused equal reductions in CVC at the untreated and bretylium-treated sites, suggesting this reduction in CVC in both cases was mediated largely or entirely by withdrawal of cutaneous active vasodilator activity, in keeping with earlier findings by Kellogg et al. (15).

Vissing et al. (32) suggested the reductions in SkBF during LBNP in hyperthermia were due to LBNP-induced reductions in T_{sk} and not to baroreceptor reflexes because in their studies when T_{sk} was held constant, no changes in SkBF were observed during LBNP. In the present study, however, T_{sk} was maintained constant throughout all LBNP procedures (see Table 1) and significant decreases in CVC were observed during the LBNP trials at -30 mmHg. However, in agreement with Vissing et al., our findings suggest that low levels of LBNP in hyperthermia do not affect CVC.

Previously, it was not known whether the carotid baroreflex contributed to the reduction in CVC during general baroreceptor unloading in hyperthermia. To address this question, we applied CP to the subjects in both normothermia and hyperthermia to identify whether the carotid baroreflex has an efferent limb governing SkBF because this stimulus has been shown to selectively unload the carotid baroreceptor and evoke appropriate baroreflex-mediated HR and MAP responses (7). We did not observe changes in CVC during

the CP trials. Because unloading of carotid baroreceptors during LBNP at -30 mmHg should be far more subtle than during the CP procedure, the reduction in CVC observed during higher levels of LBNP was not, independently, the result of carotid baroreceptor unloading.

Our data suggesting a lack of significant control of SkBF by the carotid baroreflex are consistent with the results of others. For example, unlike muscle sympathetic nerve activity, skin sympathetic nerve activity often does not have the detectable cardiac rhythm suggestive of modulation by the arterial baroreceptors (11). Furthermore, carotid sinus nerve stimulation did not measurably change skin sympathetic nerve activity (34), suggesting that neural control of SkBF is not under significant carotid baroreflex control. In contrast, Beiser et al. (3) evoked reductions in estimated skin vascular resistance with increased carotid baroreceptor transmural pressure. Beiser et al. estimated forearm SkBF via its elimination by epinephrine iontophoresis in one arm. We are unsure how to explain the differences in results between the present study (or those involving measurements of skin sympathetic nerve activity) and those reported by Beiser et al. They may relate to the direction of application of the stimulus (i.e., carotid distention rather than compression) or the method of assessing SkBF. Nevertheless, we are confident that we evoked a carotid baroreflex, as evidenced by changes in HR and MAP. We do not rule out the possibility that more prolonged or more marked carotid unloading might have measurable effects on the skin circulation and the active vasodilator system.

Unloading the carotid sinus with 45 mmHg CP in normothermia and hyperthermia also did not significantly reduce FVC. These results are surprising in light of data suggesting muscle sympathetic nerve activity to increase during this procedure (10, 22, 33). Previous findings regarding the effects of carotid sinus baroreceptor perturbations on reflex control of the forearm vasculature are mixed, with some studies reporting responses in forearm vasculature (3, 6, 17, 31) but others finding no change (1, 4, 8, 24). These differences in results may relate to the time during the carotid stimulation in which the data were obtained because some studies show evanescent efferent responses to neck pressure and/or suction (6, 17, 33). Differences may also be attributed to neck collar design, neck pressures applied, and mode of pressure delivery. Regardless, in the present study a carotid baroreflex was evoked, as evidenced by the changes in MAP and HR, but this same stimulus did not cause a change in CVC.

It is possible that the relative contribution of the aortic baroreflex in modulating CVC is greater than that of the carotid baroreflex and that the aortic baroreceptors are the primary baroreceptor population governing CVC during conditions such as orthostasis. Disproportionate control of an efferent response by the carotid and aortic baroreceptors has previously been identified. For example, in humans it has been shown that the aortic baroreceptors have a greater role than the carotid baroreceptors in controlling HR (9, 18) and muscle sympathetic nerve activity (26). Unfortunately, procedures used to selectively activate and/or deactivate the aortic baroreflex in humans (5, 9, 26) cannot address the questions asked in this study because vasoactive drugs are administered, which would confound our SkBF measurements. Although this problem might be addressed by using skin sympathetic nerve activity as the dependent variable, it could prove difficult to distinguish active vasodilator activity from the recording of mixed nerve activity.

Although we did not see active vasodilator withdrawal at lower levels of LBNP, we did confirm that response at a more severe level. In humans it is difficult to unload the cardiopulmonary baroreceptors to a comparable level to that observed with -30 mmHg LBNP in hyperthermia without also unloading the sinoaortic baroreceptors. Nevertheless, if substantial cardiopulmonary baroreceptor unloading was required to evoke a cutaneous vascular response, then this threshold might not be reached until sinoaortic baroreceptors were also unloaded. This hypothesis suggests the cardiopulmonary baroreceptors mediate the change in CVC during high levels of LBNP, whereas concomitant unloading of sinoaortic baroreceptors has no effect on the cutaneous vasculature. Such a hypothesis would be difficult if not impossible to test in healthy humans.

Alternatively, it might be that a combination of cardiopulmonary and sinoaortic baroreceptor unloading is required to evoke a withdrawal of cutaneous active vasodilator activity. Previous studies suggest that unloading the cardiopulmonary baroreceptors increases the sensitivity of the sinoaortic baroreceptor

reflex (20, 31). Thus the sinoaortic baroreceptors may contribute to the reduction in CVC during higher levels of LBNP, but the sensitivity of these baroreceptors must first be increased through reduced cardiopulmonary afferent firing.

In conclusion, data from the present study suggest that low levels of LBNP in hyperthermia, which primarily unload the cardiopulmonary baroreceptors, do not affect cutaneous vasoconstrictor or active vasodilator activities. Despite the absence of a cutaneous vascular response, these levels of LBNP significantly reduced FVC, suggesting that cardiopulmonary baroreflexes were engaged. Similarly, carotid baroreflex unloading initiated a carotid sinus baroreflex but did not evoke changes in CVC in normothermia or hyperthermia. Reductions in CVC during LBNP at -30 mmHg in both normothermia and hyperthermia must therefore be due to greater cardiopulmonary baroreceptor unloading, aortic baroreceptor unloading, or an interaction between cardiopulmonary and sinoaortic baroreceptor unloading.

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Address for reprint requests: J. M. Johnson, Dept. of Physiology, Univ. of Texas Health Science Center at San Antonio, San Antonio, TX 78284-7756.

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