

Carotid baroreflex responsiveness in heat-stressed humans

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Crandall, C. G. Carotid baroreflex responsiveness in heat-stressed humans. *Am J Physiol Heart Circ Physiol* 279: H1955–H1962, 2000.— The effects of whole body heating on human baroreflex function are relatively unknown. The purpose of this project was to identify whether whole body heating reduces the maximal slope of the carotid baroreflex. In 12 subjects, carotid-vasomotor and carotid-cardiac baroreflex responsiveness were assessed in normothermia and during whole body heating. Whole body heating increased sublingual temperature (from 36.4 ± 0.1 to $37.4 \pm 0.1^\circ\text{C}$, $P < 0.01$) and increased heart rate (from 59 ± 3 to 83 ± 3 beats/min, $P < 0.01$), whereas mean arterial blood pressure (MAP) was slightly decreased (from 88 ± 2 to 83 ± 2 mmHg, $P < 0.01$). Carotid-vasomotor and carotid-cardiac responsiveness were assessed by identifying the maximal gain of MAP and heart rate to R wave-triggered changes in carotid sinus transmural pressure. Whole body heating significantly decreased the responsiveness of the carotid-vasomotor baroreflex (from -0.20 ± 0.02 to -0.13 ± 0.02 mmHg/mmHg, $P < 0.01$) without altering the responsiveness of the carotid-cardiac baroreflex (from -0.40 ± 0.05 to -0.36 ± 0.02 beats $\cdot\text{min}^{-1}\cdot\text{mmHg}^{-1}$, $P = 0.21$). Carotid-vasomotor and carotid-cardiac baroreflex curves were shifted downward and upward, respectively, to accommodate the decrease in blood pressure and increase in heart rate that accompanied the heat stress. Moreover, the operating point of the carotid-cardiac baroreflex was shifted closer to threshold ($P = 0.02$) by the heat stress. Reduced carotid-vasomotor baroreflex responsiveness, coupled with a reduction in the functional reserve for the carotid baroreflex to increase heart rate during a hypotensive challenge, may contribute to increased susceptibility to orthostatic intolerance during a heat stress.

hyperthermia; baroreceptor; orthostatic intolerance

IN HUMANS whole body heating increases heart rate (HR), cardiac output and contractility, splanchnic and renal vascular resistances, and muscle sympathetic nerve activity (4, 18, 21, 31). These responses, coupled with increases in cutaneous vascular conductance, result in skin blood flow increasing upward to 7 l/min during a heat stress (12, 18, 29). Each of the aforementioned variables contributes to the regulation of blood pressure. Thus, during a hypotensive challenge in an

individual exposed to heat, the functional reserve to further increase HR, cardiac output, and so forth, may be reduced, which could contribute to a predisposition for syncope. Alternatively, because baroreflexes can rapidly reset (3, 7, 8, 33), it is possible that during a heat stress, resetting occurs such that the capacity to regulate these variables is maintained.

Relatively few studies have been performed to investigate the effects of heat stress on baroreflex function. Investigators studying hyperthermic rats (35) and baboons (10) reported that baroreceptor modulation of HR is either increased or not changed, respectively, compared with normothermic conditions. Gorman and Proppe (10) clearly showed that in heat-stressed baboons, the baroreflex curve was shifted upward to accommodate the elevation in HR that accompanied the heat stress. It may be inappropriate to extend these findings to humans because physiological responses to heat stress are different, and in some cases opposing, among humans, rats, or baboons (12, 30). With respect to human-based studies, Yamazaki et al. (38) quantified the effects of carotid baroreceptor loading and/or unloading on vagally mediated changes in HR before and during whole body heating. They found that the maximal gain of this baroreflex was not altered, but the baroreflex curve was elevated, which was likely an adaptation to the increase in HR that occurred during the heat stress. Moreover, in a follow-up study, Yamazaki and Sone (39) calculated the slope of the relationship between spontaneous changes in blood pressure and corresponding baroreceptor-mediated changes in HR in normothermic and heat-stressed humans and found that the heat stress did not alter this method of assessing arterial baroreflex control of HR.

Little is known regarding the effects of heat stress on carotid baroreceptor control of arterial blood pressure in humans. On perturbing the carotid baroreceptors by increasing or decreasing pressure within a chamber placed on the subject's neck, the appropriate changes in blood pressure are observed (1, 2, 24, 26, 32). These changes in blood pressure have been attributed primarily to reflex alterations in peripheral vascular re-

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sistance (26). Assessment of the carotid-vascular baroreflex may provide insight into the effects of heat stress on baroreflex regulation of blood pressure. Thus the primary purpose of this study was to assess the effects of whole body heating on carotid baroreceptor control of arterial blood pressure in humans.

METHODS

Subjects. Twelve subjects (9 male and 3 female) participated in the study. The subjects' average age was 29 ± 2 yr, and all were of normal height (178 ± 2 cm), weight (73 ± 2 kg), and health. A written, informed consent from each subject was obtained before subject participated in this institutionally approved study.

Instrumentation. Each subject was instrumented for the measurement of sublingual temperature with a thermocouple placed under the tongue, and mean skin temperature was derived from the electrical average of six thermocouples attached to the skin. The subject was then dressed in a tube-lined suit that permitted the control of skin temperature by changing the temperature of the water perfusing the suit. Arterial blood pressure was continuously recorded, non-invasively, from a finger (Finapres) while beat-by-beat mean arterial pressure (MAP) was calculated by integrating individual blood pressure waveforms. Verification of Finapres-obtained blood pressure was confirmed in both normothermia and during the heat stress via auscultation. Beat-by-beat HR was obtained from the electrocardiogram (ECG).

Experimental protocol. After they were instrumented, each subject underwent a familiarization period where they were exposed to multiple neck pressure-suction ramps. The subject then rested in the supine position for 20–30 min before baseline hemodynamic and temperature data were obtained. Carotid baroreflex responsiveness was assessed via multiple neck pressure-suction ramps. Each ramp was separated by a minimum of 2 min. Skin temperature was then elevated by perfusing the tube-lined suit with warm water (46°C). Once sublingual temperature was substantially elevated, baseline hemodynamic and temperature data were once again recorded. Carotid baroreflex responsiveness was again obtained via multiple neck suction-pressure ramps. After the final carotid baroreflex ramp was completed, skin and sublingual temperatures were returned to preheat stress levels by perfusing the suit with cold water.

Carotid baroreflex assessment. Carotid-cardiac and carotid-vasomotor responses were assessed using stepped changes in neck suction and neck pressure (34). This was accomplished by placing a silicon-lined collar around the anterior two-thirds of the subject's neck. At end expiration, the subject held his/her breath, and a pressure of 40 mmHg was delivered to the chamber for four consecutive R waves of the subject's ECG. With each successive R wave, the pressure in the collar was then sequentially stepped to -65 mmHg in 15-mmHg steps. Each pressure-suction step was applied in a stair-step manner (i.e., without venting the collar to atmospheric pressure for each change in collar pressure). Each pressure step was triggered 50 ms after the R wave of the ECG. The ramp did not begin until the differences in R-R intervals between three consecutive beats were <30 ms. In both thermal conditions, six to eight neck pressure-suction ramps were performed. Beat-by-beat changes in the R-R interval, HR, and MAP that occurred in response to changes in neck pressure-suction were recorded and used to calculate carotid-cardiac and carotid-vasomotor reflex responsiveness. Because of the defined lag time in blood pressure in response to pulse changes in carotid sinus pressure (24, 32), MAP was

offset by two to four beats to align this response with the estimated carotid sinus pressure. Quantification of this blood pressure offset was identified for each ramp by counting the number of heartbeats before the maximal elevation in MAP during the initial carotid hypotensive stimulus (i.e., 40 mmHg neck pressure). This offset was typically larger (i.e., more beats) during the heat stress when HR was elevated. Estimated carotid sinus pressure (ECSP) was calculated from the difference between MAP and neck chamber pressure.

Data collection and statistics. HR and blood pressure data were sampled at 1,000 Hz, whereas temperature data were sampled at 20 Hz. A customized computer program controlled the neck collar device. This program also detected and recorded the R-R intervals, HR, and MAP on a beat-by-beat basis before, during, and after each ramp. Only those ramps with a linear correlation coefficient between neck chamber pressure and HR of >0.80 were accepted (24). A minimum of four acceptable ramps were obtained and averaged for each condition, although for most subjects five to six acceptable ramps were obtained.

Carotid-cardiac and carotid-vasomotor responses were evaluated by plotting the R-R intervals, HR, or MAP against ECSP (Fig. 1). For each subject and in each thermal condition, the stimulus-response curves were fit to a four-parameter logistic function model as described by Kent et al. (14), using the following equation

MAP, HR, or R-R interval

$$= A_1 \cdot \{1 + e^{[A_2(\text{ECSP} - A_3)]}\}^{-1} + A_4$$

where A_1 is the range of the response (maximum – minimum), A_2 is the gain coefficient, A_3 is the ECSP at maximum

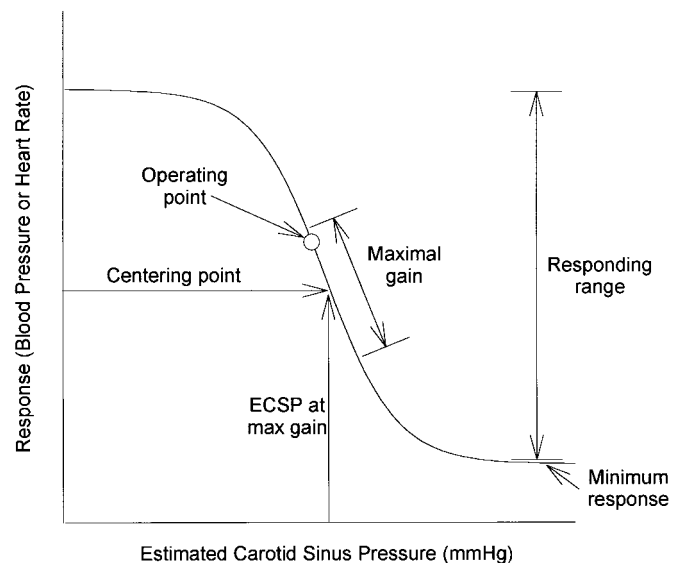


Fig. 1. Schematic illustrating the primary variables identified by the logistic function analysis. Maximal gain is the maximal slope of the relationship between estimated carotid sinus pressure (ECSP) and the response (i.e., heart rate or blood pressure) within the linear portion of the curve. This variable was used as an index of carotid baroreflex responsiveness. The responding range is the range of the response relative to changes in ECSP. The operating point is the response (i.e., heart rate or blood pressure) when pressure in the chamber is zero. The centering point is the response (i.e., heart rate or blood pressure) at the point of maximal gain of the reflex. Minimum response is the lowest heart rate or blood pressure during the hypertensive phase of the carotid sinus ramp. ECSP at maximum (max) gain is the ECSP at the point of maximal gain of the response.

gain, and A_4 is the minimum response. From this model, the operating point (defined as the response when neck chamber pressure is zero) and centering point (defined as the response at maximal gain of the reflex) were calculated. The centering point and ECSP at maximum gain were used to identify the horizontal and vertical shifts, respectively, of the baroreflex curve (see Fig. 1). The gain of the response was identified from the first derivative of the logistic function and was used as the index of carotid baroreflex responsiveness. The location of the operating point relative to the responding range was also calculated as follows

$$(\text{operating point} - \text{minimum response}) \cdot \text{responding range}^{-1} \cdot 100$$

A paired *t*-test was used to compare differences in responses between normothermic and whole body heating trials. Data are expressed as means \pm SE. The level of significance was set at $P = 0.05$.

RESULTS

Whole body heating significantly increased sublingual temperature (36.4 ± 0.1 to $37.4 \pm 0.1^\circ\text{C}$, $P < 0.01$) and HR (59 ± 3 to 85 ± 3 beats/min, $P \leq 0.01$), whereas MAP decreased slightly (88 ± 2 to 83 ± 2 mmHg, $P < 0.01$).

The heat stress significantly attenuated the maximum gain of the carotid-vasomotor baroreflex (Fig. 2 and Table 1). Whole body heating shifted this baroreflex curve to a lower MAP (i.e., downward shift) to accommodate the slight reduction in MAP due to the heat stress. This shift was evidenced by a significant decrease in the centering point from 86 ± 2 to 81 ± 2 mmHg ($P < 0.01$). However, ECSP at maximal gain of the response was not significantly altered by the heat stress (98 ± 4 to 101 ± 4 mmHg, $P = 0.28$). Thus the heat stress did not shift the carotid-vasomotor reflex curve to a lower ECSP, as would be expected when blood pressure is reduced. The location of the operating point relative to the range of the response tended to increase by the heat stress ($P = 0.08$). A shift in the operating point in this direction would reduce the functional reserve to buffer decreases in carotid-sinus pressure through increasing blood pressure.

When the dependent variable was expressed as HR, the maximal gain of the carotid-cardiac baroreflex was unaffected by the heat stress (see Table 2); however, the curve shifted to a higher HR (i.e., upward shift) to accommodate the elevation in HR observed during the heat stress (Fig. 3). This shift was statistically verified by a significant increase in the centering point from 58 ± 3 to 82 ± 3 beats/min ($P < 0.01$). This baroreflex curve did not shift to lower ECSP (i.e., leftward shift) during the heat stress, as evidenced by a lack of change in ECSP at maximal gain (91 ± 4 to 95 ± 2 mmHg, $P = 0.15$), despite a significant decrease in blood pressure during the heat stress. The location of the operating point relative to the range of the response was significantly elevated during the heat stress ($P = 0.02$). A shift in the operating point in this direction reduces the functional reserve to buffer decreases in carotid sinus pressure via increasing HR.

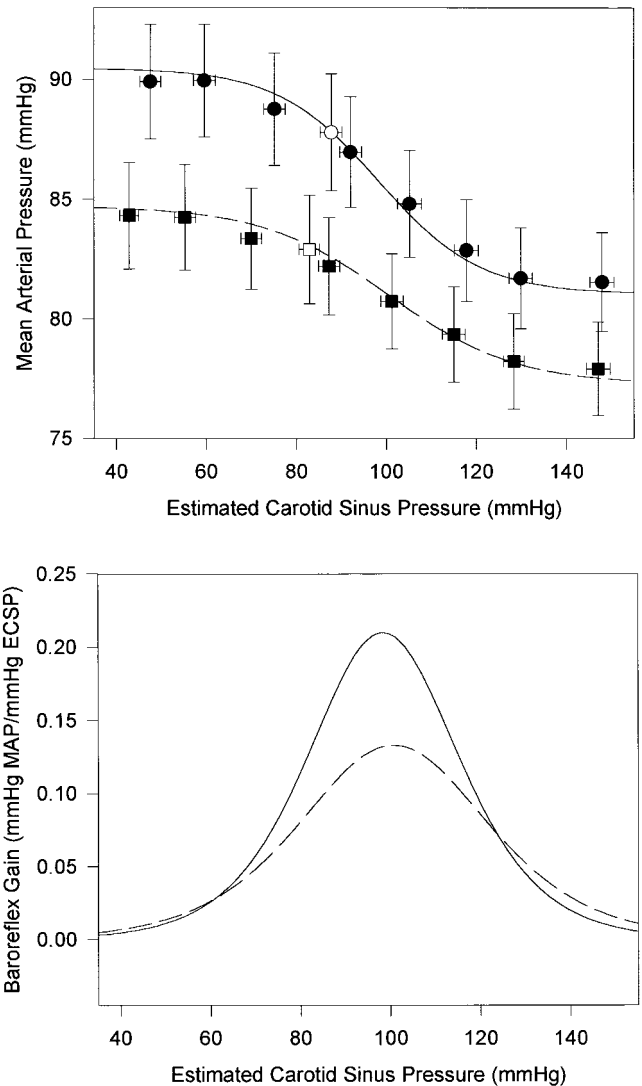


Fig. 2. Carotid-vasomotor baroreflex responses in normothermic (solid lines and circles) and heat-stressed (dashed lines and squares) humans. *Top*: baroreflex curve in both thermal conditions. *Bottom*: gain of the baroreflex in normothermia and during the heat stress. Whole body heating significantly reduced the gain of this baroreflex, shifted the baroreflex curve downward to lower blood pressures, and tended to move the operating points (open symbols) closer to threshold ($P = 0.08$; see Table 1). MAP, mean arterial blood pressure.

When the dependent variable of the carotid-cardiac baroreflex was expressed as the R-R interval, the maximal gain of this response and operational range were significantly attenuated by the heat stress (see Fig. 4 and Table 3). Moreover, the heat stress shifted the baroreflex curve to a lower R-R interval (decrease in the centering point from $1,030 \pm 55$ to 716 ± 26 ms, $P < 0.01$), whereas the location of the operating point relative to the responding range was unaffected by the heat stress ($P = 0.14$).

DISCUSSION

The primary finding of this study was that whole body heating significantly attenuated carotid baroreceptor control of blood pressure. This conclusion was

Table 1. Carotid-vasomotor responses

	Normothermia	Heat Stress	P Value
Maximal gain, mmHg/mmHg	-0.20 ± 0.02	-0.13 ± 0.02	<0.01
Responding range, mmHg	9.4 ± 1.0	7.4 ± 1.0	<0.01
ECSP at maximum gain, mmHg	98 ± 4	101 ± 4	0.28
Operating point, mmHg	88 ± 2	83 ± 2	<0.01
Centering point, mmHg	86 ± 2	81 ± 2	<0.01
Minimum response, mmHg	81 ± 2	77 ± 2	0.03
Operating point relative to responding range, %	71 ± 3	76 ± 4	0.08

Data are expressed as means \pm SE. ECSP, estimated carotid sinus pressure; responding range, range of the response to changes in ECSP; operating point, blood pressure when pressure in the chamber is zero; centering point, blood pressure at maximal gain of the reflex; minimum response, lowest blood pressure during the hypertensive phase of the carotid sinus ramp. The operating point relative to responding range identifies the location of the operating point relative to the entire baroreflex curve, calculated as (operating point - minimum response) \cdot responding range⁻¹ \cdot 100.

based on the observation that the maximal gain of the carotid-vasomotor baroreflex was reduced \sim 35% by the heat stress. In contrast, the maximal gain of the carotid-cardiac baroreflex was unaffected by the heat stress when the dependent variable was expressed as HR. Expressing these same data as R-R intervals revealed a \sim 50% reduction in the maximal gain of the response. Finally, the carotid-vasomotor response was shifted to a lower MAP (i.e., downward shift), whereas the carotid-cardiac baroreflex curve was shifted to a higher HR (i.e., upward shift) to accommodate the hemodynamic changes that occur during the heat stress.

Interpretation of the effects of heat stress on the carotid-cardiac baroreflex is conflicting depending on whether the dependent variable is expressed as HR or

Table 2. Carotid-cardiac responses when dependent variable is expressed as heart rate

	Normothermia	Heat Stress	P Value
Maximal gain, beats \cdot min ⁻¹ \cdot mmHg ⁻¹	-0.40 ± 0.05	-0.36 ± 0.02	0.21
Responding range, beats/min	12 ± 1	13 ± 1	0.13
ECSP at maximum gain, mmHg	91 ± 4	95 ± 2	0.15
Operating point, beats/min	60 ± 3	85 ± 3	<0.01
Centering point, beats/min	58 ± 3	82 ± 3	<0.01
Minimum response, beats/min	52 ± 2	75 ± 3	<0.01
Operating point relative to responding range, %	61 ± 7	78 ± 4	0.02

Data are expressed as means \pm SE. Operating point, heart rate when pressure in the chamber is zero; centering point, heart rate at maximal gain of the reflex; minimum response, lowest heart rate during the hypertensive phase of the carotid sinus ramp. The operating point relative to responding range identifies the location of the operating point relative to the entire baroreflex curve, calculated as (operating point - minimum response) \cdot responding range⁻¹ \cdot 100.

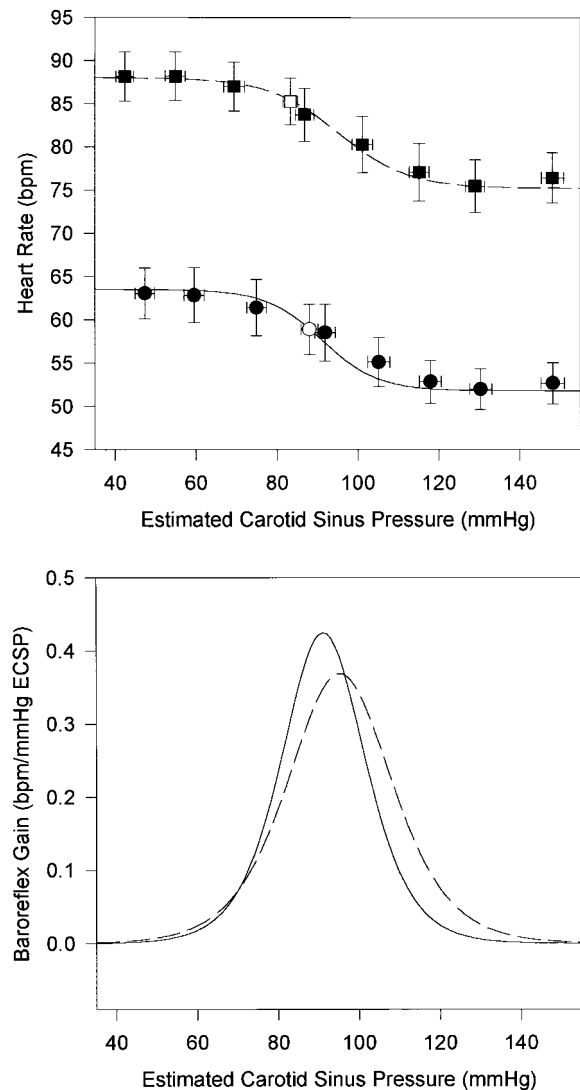


Fig. 3. Carotid-cardiac baroreflex responses in normothermic (solid lines and circles) and heat-stressed (dashed lines and squares) humans when the dependent variable is expressed as heart rate. *Top*: baroreflex curve in both thermal conditions. *Bottom*: gain of the reflex in normothermia and during the heat stress. Whole body heating did not alter the gain of this baroreflex; however, the curve was shifted upward to higher heart rates, and the operating points (open symbols) of the reflex were shifted closer to threshold during the heating protocol (see Table 2). bpm, Beats/min.

as R-R intervals. Given the hyperbolic relationship between the HR and R-R interval, coupled with a significant increase in HR during the heat stress, the appropriateness of expressing the carotid-cardiac reflex as a R-R interval may be questioned. However, the intent of this project was not to investigate which dependent variable should be used when assessing the effects of heat stress on carotid-cardiac baroreflex responsiveness. For this reason, data were included that express the carotid-cardiac baroreflex as both HR and R-R intervals.

It is interesting to note that the carotid baroreflex adjusts to the prevailing HR and blood pressure during the heat stress. This is evident on observing the hori-

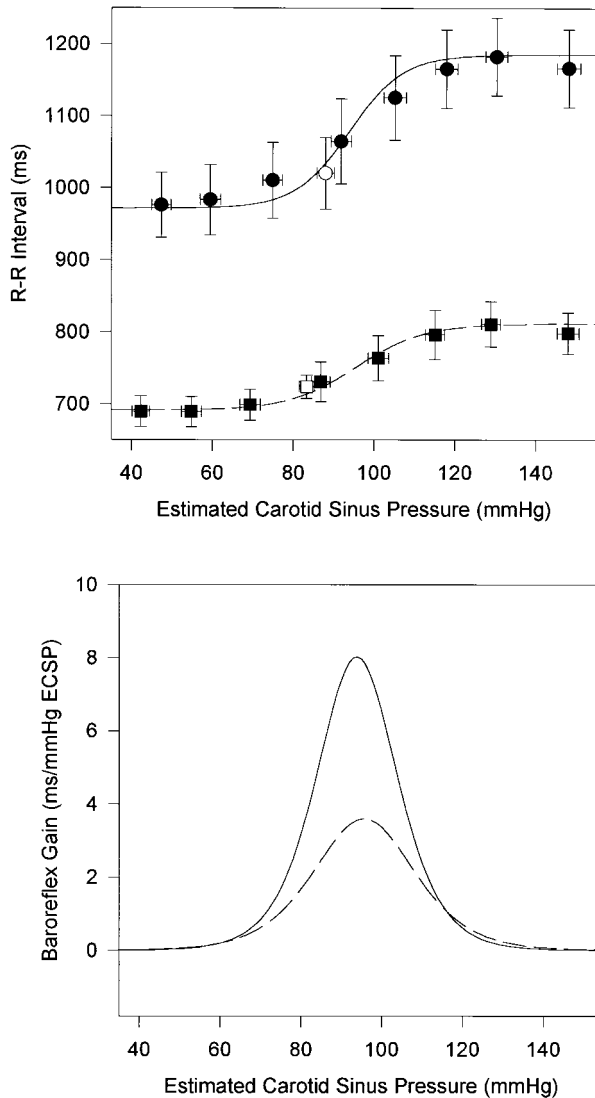


Fig. 4. Carotid-cardiac baroreflex responses in normothermia (solid lines and circles) and during whole body heating (dashed lined and squares) when the dependent variable was expressed as R-R intervals. *Top*: baroreflex curve in both thermal conditions. *Bottom*: gain of this reflex in normothermia and during whole body heating. Heat stress significantly attenuated the gain of this baroreflex and shifted the baroreflex curve downward to lower R-R intervals. The location of the operating points (open symbols) relative to the entire baroreflex curve were not significantly altered by the heat stress.

zontal shift (i.e., change in the centering point) of the baroreflex curves (see Figs. 2–4). Such a shift of the baroreflex curve is necessary to appropriately buffer changes in tension at the carotid baroreceptor when the operating point of the baroreflex curve is changed. Similar shifts of the carotid baroreflex curve to the prevailing HR and/or blood pressure have been observed during exercise (26), pharmacological interventions (8, 33), and circadian rhythm-induced changes in blood pressure and HR (13).

Relatively few studies have been conducted to specifically investigate the effects of heat stress on baroreflex function. With respect to nonhuman studies, depending on the technique used to assess the baroreflex

and/or the animal model, heat stress increases or does not change cardiac (10, 35) or vasomotor (23) baroreflex responsiveness. To the author's knowledge, only a few studies have assessed the effects of heat stress on baroreflex function in humans. Consistent with the present study, Yamazaki et al. (38) reported that the sensitivity of the carotid-cardiac baroreflex (expressed as HR) was not altered during the heat stress. Moreover, in a follow-up study, Yamazaki and Sone (39) assessed arterial baroreflex control of HR in heated humans by quantifying the slope of the relationship between spontaneously occurring sequences of three or more consecutive heartbeats in which both arterial blood pressure and interbeat intervals were simultaneously increasing or decreasing. On the basis of this technique, they concluded that whole body heating did not alter arterial baroreflex control of HR.

The mechanism resulting in impaired carotid-vasomotor responsiveness during the heat stress remains unknown. One possibility is central inhibition of the baroreflex secondary to whole body heating. The primary neural structures governing thermoregulation are located in the hypothalamus (36), and electrical stimulation of the hypothalamus modifies the baroreceptor reflex (9, 28). Thus it is possible that whole body heating alters baroreceptor control of blood pressure through hypothalamic modification of the baroreflex. Such a response would likely alter efferent neural responses associated with a change in carotid baroreceptor tension. However, arguing against this hypothesis is the observation that the heat stress did not change carotid-cardiac baroreflex responsiveness (when expressed as HR). If the aforementioned hypothesis is valid, it is conceivable that the heat stress would alter efferent neural responses to both the periphery and the heart.

An integral component of the baroreflex is the response of a neurotransmitter at a neuroeffector junc-

Table 3. Carotid-cardiac responses when dependent variable is expressed as R-R intervals

	Normothermia	Heat Stress	P Value
Maximal gain, ms/mmHg	7.5 ± 1	3.7 ± 0.7	<0.01
Responding range, ms	214 ± 21	120 ± 13	<0.01
ECSP at maximum gain, mmHg	94 ± 5	96 ± 2	0.34
Operating point, ms	1,030 ± 55	716 ± 26	<0.01
Centering point, ms	1,078 ± 49	752 ± 26	<0.01
Minimum response, ms	1,185 ± 54	812 ± 30	<0.01
Operating point relative to responding range, %	71 ± 7	80 ± 4	0.14

Data are expressed as means ± SE. Operating point, R-R interval when pressure in the chamber is zero; centering point, R-R interval at maximal gain of the reflex; minimum response, highest R-R interval (lowest heart rate) during the hypertensive phase of the carotid sinus ramp. The operating point relative to responding range identifies the location of the operating point relative to the entire baroreflex curve, calculated as (operating point - minimum response) · responding range⁻¹ · 100.

tion. Kregel and Gisolfi (15) as well as Massett et al. (17) showed that vasoconstrictor responses to α -adrenergic agents were significantly attenuated in heated rats. Thus it is possible that the reduced carotid-vasomotor baroreflex responsiveness observed in the present study was due to altered α -adrenergic-mediated peripheral vasoconstriction. However, in the aforementioned studies, altered α -adrenergic vasoconstriction was not observed until the rats were heated to core temperatures $>39^{\circ}\text{C}$. This is in contrast to the present study in which internal temperature did not exceed 38°C for any subject. Moreover, it is unclear whether the aforementioned responses observed in heated rats also occur in heated humans. Nevertheless, the possibility remains that the reduction in carotid-vasomotor baroreflex function was due to impaired peripheral vasoconstriction associated with whole body heating.

Potts et al. (25) revealed that increasing arterial compliance decreases the sensitivity of the carotid-vasomotor baroreflex independently of baroreflex-mediated changes in HR, left ventricular contractility, or vascular resistance. This was accomplished by increasing arterial compliance approximately fourfold via inclusion of a hydraulic compliant chamber to the arterial circulation. The effects of heat stress specifically on arterial vascular compliance in humans are unknown. Studies in anesthetized dogs and conscious rats suggest that whole body heating either does not change or decreases vascular compliance (6, 11, 19, 20). However, in these animal studies, the degree of heating was significantly more pronounced than that imposed in the present experiment; moreover, physiological responses to a heat stress in rats and dogs relative to humans can vary greatly (12, 30). Thus, although it is unlikely that reduced carotid-vasomotor baroreflex responsiveness was due to an increase in arterial vascular compliance associated with the heat stress, the present data do not permit the exclusion of this hypothesis.

An alternate hypothesis leading to impaired carotid-vasomotor baroreflex responsiveness during the heat stress could be related to observations that the carotid baroreflex may not have an efferent limb governing skin blood flow (5, 37). For example, electrical stimulation of the carotid sinus nerve does not consistently decrease skin sympathetic nerve activity but decreases muscle sympathetic nerve activity (37). This finding suggests that the carotid baroreflex may not have an efferent limb governing cutaneous vascular conductance. In support of this hypothesis, we were unable to show changes in cutaneous vascular conductance in either thermal condition during 3 min of carotid baroreceptor unloading via 45-mmHg pulsatile neck pressure (5). If, as these data suggest, the carotid baroreflex does not have an efferent limb governing cutaneous vascular conductance, then during a heat stress, a large fraction of cardiac output is being distributed to a region (i.e., the skin) that is not under the control of carotid baroreceptors. Therefore, when the carotid baroreceptors are perturbed, the vasculature of

the skin cannot be recruited to assist with the regulation of blood pressure and may ultimately cause a reduction in the responsiveness of the reflex.

Independently of changes in carotid baroreflex responsiveness, whole body heating significantly shifted the operating point of the carotid-cardiac baroreflex away from the centering point and closer to threshold, whereas a tendency for this shift was revealed for the carotid-vascular baroreflex ($P = 0.08$). A shift of the operating point in this direction effectively decreases the functional reserve of the carotid baroreceptors to buffer decreases in blood pressure via elevating HR and vascular resistance.

Potential limitations of the interpretation of the results. Transmission of pressure and suction from the neck collar to the carotid sinus is incomplete (16, 27). In the present experiment, ECSP was not adjusted to account for this phenomenon. The intent of this study was to assess differences in carotid baroreflex responsiveness between normothermic and heat stress conditions. It was presumed that the neck collar pressure-suction transmission characteristics were unaffected by the heat stress, and thus it became unnecessary to correct for incomplete pressure-suction transmission. In support of this hypothesis, Querry et al. (27) recently reported that neck collar pressure-suction transmission characteristics during dynamic exercise were similar to those measured during resting conditions. Although unreported, it is reasonable to conclude that exercise in the aforementioned study was sufficient to increase neck skin blood flow to a level similar to that achieved during passive heating. Thus it is doubtful that the heat stress changed the characteristics of the tissue of the neck sufficiently to alter the transmission of pressure and suction from the collar to the carotid baroreceptors. Therefore, it is unlikely that the changes observed in carotid-vasomotor baroreflex responsiveness in the present study would have been altered by correcting for incomplete transmission of pressure-suction across the tissue of the neck, because identical adjustments would have been performed on the data collected in both thermal conditions.

In the present study, after a period of sustained carotid sinus hypotension, carotid sinus pressure was changed on a beat-by-beat basis by rapidly applying pressure or suction to a collar placed on the subject's neck. Recently, studies (22, 26) have been performed in which neck collar pressure and suction were held for a duration of 5 s at each of seven neck chamber pressures while the subsequent maximal response was obtained, usually within the next 5 s. One may argue that a more-complete baroreflex response could be obtained using the latter method, being that this method has a longer time window in which to identify a maximal response to a change in ECSP. Such an argument may be valid, particularly because others (1, 2, 26) have shown that the time required to elicit a maximal blood pressure response to carotid sinus perturbations is between 5 and 10 s after the perturbation. In the present method to assess carotid-vasomotor baroreflex sensitivity, the blood pressure responses were offset by

only 2–4 heartbeats relative to the chamber pressure and thus may underestimate the maximal response to a given neck chamber pressure or suction. However, to the author's knowledge, no direct comparison has been performed between the beat-by-beat and sustained techniques to assess carotid-vasomotor baroreflex function. Furthermore, the range of the blood pressure response in normothermia with the present technique was quantitatively similar to that reported in resting subjects by Potts et al. (26), where the carotid-vascular response was assessed using the aforementioned 5-s sustained neck suction/pressure technique. Nevertheless, the possibility cannot be excluded that differing responses could have been obtained had the sustained neck suction-pressure technique been used to assess carotid baroreflex function.

In summary, whole body heating decreased the responsiveness of the carotid-vasomotor baroreflex without altering the responsiveness of the carotid-cardiac baroreflex when this reflex was expressed as HR. However, these curves were shifted to a lower blood pressure (i.e., downward shift) and to a higher HR (i.e., upward shift), respectively, to accommodate the decrease in blood pressure and increase in HR that accompanied the heat stress. Reduced carotid-vasomotor baroreflex responsiveness, as well as a reduction in the functional reserve for the carotid baroreflex to increase HR during a hypotensive challenge, may contribute to increased susceptibility to orthostatic intolerance during a heat stress.

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REFERENCES

- Baskerville AL, Eckberg DL, and Thompson MA. Arterial pressure and pulse interval responses to repetitive carotid baroreceptor stimuli in man. *J Physiol (Lond)* 297: 61–71, 1979.
- Båth E, Lindblad LE, and Wallin BG. Effects of dynamic and static neck suction on muscle sympathetic activity, heart rate and blood pressure in man. *J Physiol (Lond)* 311: 551–564, 1981.
- Chapleau MW, Hajduczuk G, and Abboud FM. Peripheral and central mechanisms of baroreflex resetting. *Clin Exp Pharmacol Physiol* 15, Suppl: 31–43, 1989.
- Crandall CG, Farr D, and Etzel RA. Cardiopulmonary baroreceptor control of muscle sympathetic nerve activity in heat-stressed humans. *Am J Physiol Heart Circ Physiol* 277: H2348–H2352, 1999.
- Crandall CG, Johnson JM, Kosiba WA, and Kellogg DL Jr. Baroreceptor control of the cutaneous active vasodilator system. *J Appl Physiol* 81: 2192–2198, 1996.
- Deschamps A and Magder S. Effects of heat stress on vascular capacitance. *Am J Physiol Heart Circ Physiol* 266: H2122–H2129, 1994.
- Drummond HA and Seagard JL. Acute baroreflex resetting: differential control of pressure and nerve activity. *Hypertension* 27: 442–448, 1996.
- Fritsch JM, Rea RF, and Eckberg DL. Carotid baroreflex resetting during drug-induced arterial pressure changes in humans. *Am J Physiol Regulatory Integrative Comp Physiol* 256: R549–R553, 1989.
- Gebber GL and Snyder DW. Hypothalamic control of baroreceptor reflexes. *Am J Physiol* 218: 124–131, 1970.
- Gorman AJ and Proppe DW. Influence of heat stress on arterial baroreflex control of heart rate in the baboon. *Circ Res* 51: 73–82, 1982.
- Horowitz M, Sugimoto E, Okuno T, and Morimoto T. Changes in blood volume and vascular compliance during body heating in rats. *Pflügers Arch* 412: 354–358, 1988.
- Johnson JM and Proppe DW. Cardiovascular adjustments to heat stress. In: *Handbook of Physiology. Environmental Physiology*. Bethesda, MD: American Physiological Society, 1996, sect. 4, vol. I, chapt. 11, p. 215–243.
- Kasting GA, Eckberg DL, Fritsch JM, and Birkett CL. Continuous resetting of the human carotid baroreceptor-cardiac reflex. *Am J Physiol Regulatory Integrative Comp Physiol* 253: R732–R736, 1987.
- Kent BB, Drane JW, Blumenstein B, and Manning JW. A mathematical model to assess changes in the baroreceptor reflex. *Cardiology* 57: 295–310, 1972.
- Kregel KC and Gisolfi CV. Circulatory responses to vasoconstrictor agents during passive heating in the rat. *J Appl Physiol* 68: 1220–1227, 1990.
- Ludbrook J, Mancina G, Ferrari A, and Zanchetti A. Factors influencing the carotid baroreceptor response to pressure changes in a neck chamber. *Clin Sci Mol Med* 51: 347S–349S, 1977.
- Masset MP, Lewis SJ, and Kregel KC. Effect of heating on the hemodynamic responses to vasoactive agents. *Am J Physiol Regulatory Integrative Comp Physiol* 275: R844–R853, 1998.
- Minson CT, Wladkowski SL, Cardell AF, Pawelczyk JA, and Kenney WL. Age alters cardiovascular response to direct passive heating. *J Appl Physiol* 84: 1323–1332, 1998.
- Morimoto T. Thermoregulation and body fluids: role of blood volume and central venous pressure. *Jpn J Physiol* 40: 165–179, 1990.
- Morimoto T, Miki K, Nose H, Itoh T, and Yamada S. Changes in vascular compliance during hyperthermia. *J Therm Biol* 9: 149–151, 1984.
- Niimi Y, Matsukawa T, Sugiyama Y, Shamsuzzaman ASM, Ito H, Sobue G, and Mano T. Effect of heat stress on muscle sympathetic nerve activity in humans. *J Auton Nerv Syst* 63: 61–67, 1997.
- Norton KH, Boushel R, Strange S, Saltin B, and Raven PB. Resetting of the carotid arterial baroreflex during dynamic exercise in humans. *J Appl Physiol* 87: 332–338, 1999.
- O'Leary D and Johnson JM. Baroreflex control of the rat tail circulation in normothermia and hyperthermia. *J Appl Physiol* 66: 1234–1241, 1989.
- Pawelczyk JA and Raven PB. Reductions in central venous pressure improve carotid baroreflex responses in conscious men. *Am J Physiol Heart Circ Physiol* 257: H1389–H1395, 1989.
- Potts JT, Hatanaka T, and Shoukas AA. Effect of arterial compliance on carotid sinus baroreceptor reflex control of the circulation. *Am J Physiol Heart Circ Physiol* 270: H988–H1000, 1996.
- Potts JT, Shi XR, and Raven PB. Carotid baroreflex responsiveness during dynamic exercise in humans. *Am J Physiol Heart Circ Physiol* 265: H1928–H1938, 1993.
- Querry RG, Smith SA, Stromstad M, Ide K, Raven PB, and Secher NH. Anatomical and transmission characteristics of carotid sinus stimulation during exercise in man (Abstract). *FASEB J* 13: A1048, 1999.
- Reis DJ and Cuénod M. Central neural regulation of carotid baroreceptor reflexes in the cat. *Am J Physiol* 209: 1267–1279, 1965.
- Rowell LB. Human cardiovascular adjustments to exercise and thermal stress. *Physiol Rev* 54: 75–159, 1974.
- Rowell LB. Hyperthermia: a hyperadrenergic state. *Hypertension* 15: 505–507, 1990.
- Rowell LB, Brengelmann GL, and Murray JA. Cardiovascular responses to sustained high skin temperature in resting man. *J Appl Physiol* 27: 673–680, 1969.
- Shi X, Potts JT, Foresman BH, and Raven PB. Carotid baroreflex responsiveness to lower body positive pressure-in-

- duced increases in central venous pressure. *Am J Physiol Heart Circ Physiol* 265: H918–H922, 1993.
33. **Smith ML, Fritsch JM, and Eckberg DL.** Rapid adaptation of vagal baroreflexes in humans. *J Auton Nerv Syst* 47: 75–82, 1994.
34. **Sprenkle JM, Eckberg DL, Goble RL, Schelhorn JJ, and Halliday HC.** Device for rapid quantification of human carotid baroreceptor-cardiac reflex responses. *J Appl Physiol* 60: 727–732, 1986.
35. **Stauss HM, Morgan DA, Anderson KE, Massett MP, and Kregel KC.** Modulation of baroreflex sensitivity and spectral power of blood pressure by heat stress and aging. *Am J Physiol Heart Circ Physiol* 272: H776–H784, 1997.
36. **Ström G.** Central nervous regulation of body temperature. In: *Handbook of Physiology. Neurophysiology*. Washington, DC: Am. Physiol. Soc., 1960, sect. 1, vol. II, chapt. XLVI, p. 1173–1196.
37. **Wallin BG, Sundlof G, and Delius W.** The effect of carotid sinus nerve stimulation on muscle and skin nerve sympathetic activity in man. *Pflügers Arch* 358: 101–110, 1975.
38. **Yamazaki F, Sagawa S, Torii R, Endo Y, and Shiraki K.** Effects of acute hyperthermia on the carotid baroreflex control of heart rate in humans. *Int J Biometeorol* 40: 200–205, 1997.
39. **Yamazaki F and Sone R.** Modulation of arterial baroreflex control of heart rate by skin cooling and heating in humans. *J Appl Physiol* 88: 393–400, 2000.

