Influence of Heat Stress on Arterial Baroreflex Control of Heart Rate in the Baboon

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SUMMARY. The influence of environmental heat stress on the arterial baroreflex control of heart rate (HR) was studied in eight conscious, chronically instrumented baboons. Inflations of balloon occluders around the inferior vena cava (IVC) and thoracic descending aorta (DA) were used to produce acute, graded changes in mean arterial blood pressure (MABP) in 5 mm Hg intervals ranging from ±5 to ±25 mm Hg. After determination of the HR responses to changes in MABP in the normothermic baboon (blood temperature ≤37.6°C), the animal was subjected to environmental heating to produce hyperthermia. When blood temperature reached approximately 39.5°C, HR responses to graded DA and IVC occlusions were again determined. During hyperthermia, the HR sensitivity (ΔHR/ΔMABP) to MABP changes was markedly diminished for reductions in MABP and significantly enhanced for increases in MABP. To determine whether these alterations in the HR response to changes in MABP were due to an alteration of the baroreflex control of HR, full, sigmoid-shaped HR-MABP curves for both the normothermic and hyperthermic states were constructed and characterized by total HR range, estimated slope of the steep portion of the curve, and MABP at the midpoint of the HR range (BPm). During hyperthermia (1) the whole HR-MABP curve shifted significantly upward by 35-40 beats/min, (2) total HR range, the estimated slope, and BPm did not change, and (3) the control point (pre-occlusion HR-MABP value) shifted upward along the steep portion of the HR-MABP curve. In six of the eight baboons, full HR-MABP curves were also constructed during either β-adrenergic blockade or cholinergic (Ch)-receptor blockade in the normothermic and hyperthermic state. Similar to that seen for the unblocked heart, the whole HR-MABP curves were also shifted upward during hyperthermia in this group of baboons with no alteration in the total HR range, the estimated slope, or BPm. The upward shift in the HR-MABP curve during Ch-receptor blockade, unlike during β-receptor blockade, was much greater than that which could be attributed only to the local effect of blood temperature. Although the control point was also shifted upward along the steep portion of the curve during β- or Ch-receptor blockade, the upward shift observed during β-adrenergic blockade was similar to that observed in the unblocked state. Thus, a heat-stress-induced hyperthermia produces a rise in HR without significantly altering the characteristics of the reflex control of HR by arterial baroreceptors. To rely solely on changes in HR sensitivity may lead to erroneous conclusions as to the effect of a particular stress on the baroreceptor reflex control of HR. Further, these results indicate that: (1) the upward shift in the HR-MABP curve is mediated by both the local effect of blood temperature on HR and cardiac sympathetic efferent neurons which are independent of the baroreceptor reflex, and (2) the upward shift in the control point is mediated predominantly by vagal withdrawal, probably as part of the compensatory response to a heat-induced hypotension. (Circ Res 51: 73-82, 1982)
the rise in internal temperature. Therefore, the objective of this study was to determine whether hyperthermia induced by environmental heat stress alters the characteristics of the reflex HR responses to acute ABP changes in the unanesthetized, chronically instrumented baboon. This was carried out by comparing the HR responses to graded occlusions of the descending aorta and inferior vena cava in normothermic vs. hyperthermic states.

Methods

Eight adolescent male baboons (9-13 kg) of the Papio anubis and Papio cynocephalus species were used in this study. They were utilized following quarantine clearance and adaptation to maintenance in a restraint chair.

Surgical Preparation

Each animal was subjected to two aseptic surgeries, which were performed under halothane anesthesia (0.5-5% in 100% O2). By means of a left thoracotomy, the inferior vena cava (IVC) and descending aorta (DA) were isolated 6-8 cm above the diaphragm, and balloon occluders (In Vivo Metrics) were positioned around these vessels. Also, the left atrium was cannulated via its appendage with a Tygon (Norton Plastics) catheter for measurement of left atrial pressure (LAP). Each baboon was allowed to recover fully from this thoracotomy (10-14 days) before the second surgery was performed. In the second surgery, the axillary arteries were exposed bilaterally. A Tygon catheter was inserted 10 cm into the left axillary artery so that its tip was in or near the aortic arch for measurement of ABP. Into the right axillary artery was inserted a closed-tip catheter which contained a copper-constantan thermocouple (Bailey Instruments) for the measurement of arterial blood temperature (Tm). Tm was used as an index of internal temperature, since it is the primary determinant of temperature of the thermosensitive preoptic anterior hypothalamic region of the brain in the subhuman primate (Hayward and Baker, 1968). The external jugular vein was also cannulated and used for drug infusion. All tubing from these two surgical procedures was passed subcutaneously to exit near the umbilicus.

After recovery from the second surgery, the baboon was placed in a restraint chair and maintained in a sound-attenuated chamber in which the ambient temperature (Ta) could be rapidly elevated and maintained at any level above 25°C. Patency of all catheters was maintained by the continuous infusion of heparinized saline (250 IU heparin in 50 ml saline per day).

Measured Variables

LAP and ABP were measured by Statham P231D strain gauge manometers. A cardiotachometer (Beckman Instruments), triggered by the ABP pulse, provided a continuous record of instantaneous HR. For the measurement of Tm, the implanted copper-constantan thermocouple was connected to a digital thermometer (Bat-8C, Bailey Instruments) which also had an analogue output. All measurements were continuously recorded on a Beckman RM recorder. Mean ABP (MABP) and mean LAP (MLAP) were also recorded by passing the pulsatile signals through low-pass filters in the Beckman recorder.

Experimental Protocol

Initial experiments were conducted 2-3 weeks after the thoracotomy. All experiments commenced early in the morning while the baboon was sitting quietly in a thermoneutral environment (25-27°C) and his Tm was near the lowest level in its diurnal cycle (Tm ≤ 37.6°C). The first procedure consisted of performing graded DA and IVC occlusions through manual manipulation of saline-filled syringes attached to the actuating tubing of the perivascular occluders. Elevations and reductions in MABP were produced in discrete intervals of ± 5-8, ± 9-12, ± 13-16, ± 17-21, ± 22-27 mm Hg and maintained for 1.0-1.5 minute. After release of an occlusion, no subsequent occlusion was performed until HR and MABP had returned to their pre-occlusion levels. This usually entailed a 3- to 5-minute period between occlusions. Preliminary experiments indicated that a series of consecutive DA occlusions tended to cause a gradual rise in the control (pre-occlusion) ABP level, while IVC occlusions had no effect on ABP. Therefore, DA and IVC occlusions were performed in a random sequence which was effective in maintaining a constant pre-occlusion ABP level throughout a series of occlusions.

After a satisfactory series of APB alterations had been achieved at normothermic Tm, Tm was elevated to 40-42°C which caused Tm to rise gradually. When Tm reached approximately 39.6°C, the elevations and reductions in ABP equivalent to the intervals produced in the normothermic state were again produced. Following satisfactory manipulation of ABP in the hyperthermic state, environmental heating was terminated.

In six of the eight baboons, in separate sessions on different days, the same general protocol described above was again performed but during either β-adrenergic or cholinergic (Ch)-receptor blockade.

To produce β-adrenergic blockade, propranolol HCl (In- delar; Ayerst, Inc.) was infused intravenously at a rate of 10 μg/kg per min following a bolus dose of 1 mg/kg. A prior test of the effectiveness of the β-adrenergic blocking dose involved the intravenous infusion of the β-adrenergic agonist isoproterenol (Isoprel; Vitarine Co., Inc.) at a maximum rate of 1.2 μg/kg per min. The lack of a tachycardia at this rate of isoproterenol infusion indicated that the above dose of propranolol was indeed an effective blocking dose. At the end of the experiment, the effectiveness of the β-adrenergic blockade was determined. While propranolol continued to be infused, atropine sulfate was injected (see below), followed by maximal positive and negative changes in ABP (± 35 mm Hg), inducing excessive excitement of the animal, or, in some cases, isoproterenol infusion (1.2 μg/kg per min). If there was a lack of significant changes in HR during each of the above interventions, it was inferred that an effective β-adrenergic receptor blockade was present during the entire experimental period.

To produce Ch-receptor blockade, atropine sulfate (Vitarine Co., Inc.) was injected at a bolus dose of 0.15 mg/kg and followed by a constant infusion of 2 μg/kg per min. Acute studies on two baboons indicated that the pronounced bradycardia in response to unilateral electrical stimulation of the right and left vagal nerve trunks was blocked by atropine at the above dosage throughout a 3- to 4-hour period. To determine the effectiveness of the Ch-receptor block at the end of an experiment in the conscious baboon, large negative and positive changes in ABP were produced following a bolus injection of 1 mg/kg of propranolol while atropine was continuing to be infused. No significant changes in HR during maximal increases or decreases in ABP (± 35 mm Hg) indicated that an effective block of the vagal influence on HR was present during the entire experimental period.

A potential criticism of the above protocol involving Ch-receptor blockade is whether the reported central excitatory
effects of atropine sulfate (Donald et al., 1967) may have influenced the results obtained. In two of the six baboons undergoing autonomic blockade, therefore, the HR-MABP relationship in the normothermic and hyperthermic states, the change in control HR, and the change in HR observed during heat stress were compared for equivalent bolus doses (0.15 mg/kg) and infusion rates (2 μg/kg per min) of atropine sulfate and atropine methylnitrate, a cholinergic antagonist that does not readily cross the blood-brain barrier (Innes and Nickerson, 1975). The data reported for Ch-receptor blockade (see Results) were not different in any manner from those obtained during an infusion of atropine methylnitrate in the two baboons studied.

Data Analysis

Our initial step in data analysis was the calculation of HR sensitivity to changes in ABP. HR sensitivity is the ratio of the change in HR (ΔHR) to a change in MABP (ΔMABP). HR sensitivity was calculated for each ΔMABP induced by IVC and DA occlusions. For equivalent changes in MABP, HR sensitivity values from the normothermic state were compared with those obtained in the hyperthermic state.

To determine more fully the influence of hyperthermia on the baroreceptor control of HR, we constructed full HR-MABP curves for both normothermic and hyperthermic states. The average stimulus-response curve for a single baboon in a given state was constructed in the following manner: First, the average absolute MABP level achieved during each interval change in MABP was determined from a number of experiments performed on separate days. The average HR level elicited during a particular MABP change was then determined in the same manner for each interval change in MABP. Then, the average HR was plotted against the average MABP which produced the characteristic sigmoid-shaped HR-MABP relationship (see Fig. 4).

To describe the HR-MABP relationship for the entire group of baboons, we computed the interanimal average ΔHR for a given interval change in MABP by multiplying the interanimal average HR sensitivity value for each respective ΔMABP interval times the average value of each ΔMABP interval, i.e., ΔHR = (ΔHR/ΔMABP) × ΔMABP. The absolute mean HR and MABP values were then derived by adding the resulting ΔHR values and their corresponding ΔMABP to the mean absolute pre-occlusion HR and MABP levels for all eight baboons. The resulting plot of HR vs. MABP depicts the HR-MABP relationship for all the baboons as a group.

The individual and group HR-MABP curves in the normothermic and hyperthermic states were characterized by parameters similar to that introduced by Korner and colleagues (1973a, 1979). These parameters are (1) total HR range, (2) gain, i.e., slope of the steepest portion of the sigmoid curve, and (3) BF50. The total HR range for each animal was obtained from the maximum plateau HR level minus the minimum plateau HR level. The slope of the steep portion of the HR-MABP curve was the regression coefficient derived from linear regression analysis of the 3–5 data points lying on this portion of the curve which included the control (pre-occlusion) HR-MABP value and HR-MABP values that did not lie on the maximum and minimum plateau levels of the S-shaped curve. BF50 is the MABP level observed at one-half the HR range. Each curve parameter was determined for both the normothermic (control) and hyperthermic Ttherm states and compared.

Composite data from all animals are presented as mean ± SEM. Significant differences between values from normothermic and hyperthermic states were determined by utilizing the paired Student’s t-test (Snedecor and Cochran, 1967). Changes were considered significant when P values were ≤0.05.

Results

During environmental heating, Ttherm was allowed to rise from 36.9 ± 0.1°C to 39.5 ± 0.1°C before the ABP manipulations were done at a hyperthermic Ttherm. The time for Ttherm to rise to this level ranged from 70 to 110 minutes. During this rise in Ttherm, HR rose gradually from 93 ± 8 to 144 ± 7 bpm (P < 0.001). In some baboons, MABP changed very little during the whole period of heating. In others, MABP declined early in the heating period, sometimes by as much as 15 mm Hg, and then gradually returned to the control level as environmental heating was continued. For all eight baboons, MABP was 80.4 ± 4.3 mm Hg in the normothermic control state and 84.8 ± 1.7 mm Hg when ABP manipulations commenced at hyperthermic Ttherm. During heat-stress, the changes in systolic and diastolic pressures were similar to the MABP changes. Thus, the ABP manipulations in the hyperthermic state were performed around the same ABP levels as in the normothermic state, but the preocclusion HR levels were higher in the hyperthermic state. In four baboons in which MLAP measurements were obtained, MLAP had declined by −1.6 ± 0.9 mm Hg by the end of heating, which was not statistically different from the normothermic MLAP level. Ttherm changed less than 0.3°C during any series of IVC and DA occlusions in both normothermic and hyperthermic states.

HR Response to Changes in ABP—General Description

Representative original records obtained during DA and IVC occlusions in normothermic and hyperthermic states are shown in Figures 1 and 2. In both normothermic and hyperthermic states, DA occlusion produced a rapid rise in systolic and diastolic pressures, pulse pressure, and MABP (Fig. 1). MLAP was
also elevated slightly. In response to the elevation in ABP, HR fell instantaneously and then either remained at that low level in the steady state or rose to a level in between the lowest and control level in the steady state. The two-component HR response to DA occlusion was a common occurrence.

IVC occlusions resulted in a reduction in systolic and diastolic pressures, pulse pressure, MABP and MLAP (Fig. 2). The reflex tachycardia during an IVC occlusion was most often a two-component response also. HR rose gradually to reach its peak level in approximately 15–25 seconds. Then, while the hypertensive stimulus was maintained, HR diminished to a steady state level which was about 10–20 beats/min less than the peak HR level.

In the following sections, HR levels designated as “peak HR” correspond to the maximum and minimum HR achieved during an IVC or DA occlusion, respectively, while “steady state HR” corresponds to that steady level achieved 30–45 seconds after the onset of a given occlusion. Because one baboon would not tolerate prolonged IVC and DA occlusions for more than 15–20 seconds, “steady state HR” data are from seven animals instead of eight.

HR Response to Changes in ABP in Normothermic vs. Hyperthermic States

For equivalent increases in MABP, a significantly greater reduction in peak and steady state HR was produced in the hyperthermic than in the normothermic state (Fig. 1). This enhancement of the reflex bradycardia was elicited in spite of the same elevation in MABP being accompanied by a smaller or equal increase in pulse pressures and MLAP in the hyperthermic state. On the other hand, the peak and steady state reflex tachycardia in response to equivalent reductions in MABP was reduced in most baboons (Fig. 2). For equivalent reductions in MABP, the reductions in systolic and pulse pressures were not different from the levels during normothermia. However, MLAP was reduced to a lesser degree during hyperthermia.

The average changes in peak HR sensitivity for given MABP changes are shown in Figure 3. HR sensitivity to DA occlusions was significantly enhanced for each equivalent MABP change at the elevated Tbi. The greatest enhancement in sensitivity occurred for increases in MABP that were less than 10 mm Hg. On the other hand, the HR sensitivity to reductions in MABP was significantly reduced in the hyperthermic state. The greatest reduction in HR sensitivity also occurred within 10 mm Hg of the initial MABP. These same trends in HR sensitivity were also observed for the steady state HR responses.

These changes in HR sensitivity to ABP changes can imply that the HR-MABP relationship is altered at the hyperthermic Tbi. To determine whether this was true, the characteristic HR-MABP curves for each animal in normothermic and hyperthermic states were constructed. Figures 4 and 5 illustrate the peak and steady state HR-MABP curves for one baboon and all the baboons, respectively. The most pronounced result is that the HR-MABP curve shifts upward in the hyperthermic state, while there appears to be very little, if any, change in the shape of the HR-MABP curve.

The average changes in peak HR sensitivity for each interval change in MABP (&MABP) in normothermic and hyperthermic states. Values are mean ± SE of the individual average HR sensitivities from eight baboons. * P < 0.05; † P < 0.01.
The data from analysis of the HR-MABP curves are shown in Table 1. Two things demonstrate that the shape of the HR-MABP curve did not change during hyperthermia. First, the total HR range over the same MABP range of ±25 mm Hg was not altered by hyperthermia. Second, the estimated slope of the steep portion of the HR-MABP curve showed no consistent difference between the normothermic and hyperthermic states. Also, $BP_{90}$ was unaltered by hyperthermia. On the other hand, both the maximum and minimum reflex HR levels increased markedly during hyperthermia. Thus, a major influence of hyperthermia is to shift the HR-MABP curve upward without significantly changing the characteristics of the curve or shifting it horizontally.

Hyperthermia was accompanied also by a significant upward shift of the control point (i.e., the HR-MABP level prior to occlusions) along the steep portion of the curve (Figs. 4 and 5; Table 1). The peak and steady state reflex bradycardia portion of the curve significantly increased from 24 ± 2% to 40% ± 3% in the hyperthermic state and the reflex tachycardia portion decreased by the same amount.

**Normothermic and Hyperthermic HR-MABP Relationship during Cholinergic and $\beta$-Adrenergic Receptor Blockade**

In six of the eight baboons, separate experiments were performed on different days to determine the influence of heat stress on the HR-MABP relationship with only the cardiac vagal influence on HR intact ($\beta$-receptor blockade) or with only the sympathetic efferent influence on HR intact (Ch-receptor blockade). Before DA and IVC occlusions were performed in the hyperthermic state, $T_{bi}$ was elevated by 2.2 ± 0.1°C during environmental heating.

From a normothermic level of 92 ± 6 beats/min, $\beta$-receptor blockade decreased HR by 11 ± 2 beats/min ($P < 0.05$) while Ch-receptor blockade increased HR by 44 ± 4 beats/min ($P < 0.05$). MABP was not significantly altered from its control level of 83 ± 3 mm Hg during either receptor block.
TABLE 1

Peak (n = 8) and Steady State (n = 7) HR-MABP Curve Analysis in Normothermic and Hyperthermic States

<table>
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<tr>
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<th>Peak HR response</th>
<th>Steady state HR response</th>
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<tr>
<td></td>
<td>N</td>
<td>H</td>
</tr>
<tr>
<td>Maximum HR (beats/min)</td>
<td>177 ± 10</td>
<td>168 ± 10</td>
</tr>
<tr>
<td>Minimum HR (beats/min)</td>
<td>62 ± 5</td>
<td>70 ± 8</td>
</tr>
<tr>
<td>Total HR range (beats/min)</td>
<td>112 ± 7</td>
<td>97 ± 10</td>
</tr>
<tr>
<td>Maximum reflex bradycardia</td>
<td>−27 ± 2</td>
<td>−19 ± 2</td>
</tr>
<tr>
<td>(beats/min)</td>
<td>−45 ± 2*</td>
<td>−53 ± 2†</td>
</tr>
<tr>
<td>Maximum reflex tachycardia</td>
<td>86 ± 8</td>
<td>71 ± 8</td>
</tr>
<tr>
<td>(beats/min)</td>
<td>73 ± 9</td>
<td>55 ± 6†</td>
</tr>
<tr>
<td>Estimated slope (beats/min per mm Hg)</td>
<td>8.1 ± 1.0</td>
<td>5.2 ± 0.7</td>
</tr>
<tr>
<td>BP50 (mm Hg)</td>
<td>80 ± 3</td>
<td>84 ± 4</td>
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</table>

Values are mean ± se. N = normothermic state; H = hyperthermic state.

* 0.05 > P > 0.01; † P < 0.01.

In the normothermic state, the maximum peak and steady state reflex bradycardia (−27 ± 3 and −21 ± 2 beats/min, respectively) were not significantly altered during β-receptor blockade. In contrast, Ch-receptor blockade completely abolished the initial, peak reflex bradycardia and significantly reduced the magnitude of the steady state bradycardia by 59 ± 4%. In addition, the rate of reduction of HR in response to an elevation in ABP was noticeably attenuated during Ch-receptor blockade. Whereas the unblocked, peak bradycardia occurred within the first 2–5 seconds of the ABP elevation, the Ch-blocked heart required approximately 20–30 seconds before it achieved its lowest HR level, which is equivalent to the time when the steady state HR level was analyzed. Therefore, in order to make quantitative comparisons of the HR-MABP relationship during β- or Ch-receptor blockade, only the steady state HR-MABP curves are presented.

At the normothermic Tm, the maximum peak and steady state reflex tachycardia in response to decreases in ABP (+86 ± 7 and +72 ± 8 beats/min, respectively) were consistently attenuated during either β- or Ch-receptor blockade. The magnitude of the steady state reflex tachycardia was reduced by an average of 57 ± 4% (P < 0.01) during β-receptor and 48 ± 9% (P < 0.01) during Ch-receptor blockade.

Figure 6 shows the interanimal average steady state HR-MABP curves during Ch-receptor blockade in both the normothermic and hyperthermic states. The HR-MABP curve shifted upward during hyperthermia in a manner similar to what was observed in the unblocked, hyperthermic state. Figure 7 shows the interanimal average steady state HR-MABP curves during β-receptor blockade in both the normothermic and hyperthermic states. Again, the HR-MABP curve shifted upward during hyperthermia in a manner similar to what was observed in the unblocked, hyperthermic state.
the control point compared to the unblocked or Ch-receptor blocked, hyperthermic state.

**Discussion**

The results of this investigation demonstrate that: (1) the reflex bradycardia in response to acute arterial hypertension is enhanced and the reflex tachycardia in response to arterial hypotension is attenuated during hyperthermia induced by environmental heat stress, and (2) the HR-MABP relationship is shifted upward during heat stress without pronounced changes in the characteristics of the baroreflex control of HR. This investigation provides the first detailed study of the influence of environmental heat stress on the baroreflex control of HR. It should be emphasized that the data was obtained only at Tbi levels that were the lowest of the diurnal cycle (<37.6°C) and the highest that could be comfortably tolerated by the baboons (39.6°C). What alterations, if any, occur within this range of Tbi is unknown since HR-MABP reflex data were not obtained during the development of hyperthermia.

In this study, a given series of DA and IVC occlusions producing elevations and reductions in ABP were accompanied by similar directional changes in systolic pressure, pulse pressure, and MABP. Previous investigations have shown that pulse pressure and pulse frequency may influence discharge patterns from arterial baroreceptors and the magnitude of the reflex vasomotor responses (Ead et al., 1952; Angell-James and Daly, 1970). However, we chose to consider MABP as the predominant baroreceptor stimulus for the following two reasons. First, Korner et al. (1972) have shown that the stimulus-response curves derived from single (MABP only) and multiple (MABP, PP, and RAP) regression functions during IVC and DA occlusions were very similar, which indicates that the single regression function based only on MABP changes is a reasonable index of the complex pressure function generated during balloon inflation. Second, in the technical sense, a given change in MABP was consistently and easily established during each occlusion, which permitted the analysis of the HR-ABP relationship to be performed with greater accuracy. Therefore, the analysis of the baroreflex control of HR and the conclusions presented were based solely upon the relationship of HR to MABP.

Since blood gases and ventilatory rates were not measured in the present study, it is difficult to assess their potential influence on the results observed during hyperthermia in the conscious baboon. However, Hales et al. (1979) have reported that, in the conscious baboon, arterial PO2, PCO2, and pH are unchanged from control (normothermic) periods during mild, moderate, or severe hyperthermia. As in humans, essentially all heat loss in the baboon is through the skin (i.e., thermoregulatory sweating) and not through panting (Hales et al., 1977). However, hyperventilation has been shown to occur frequently in baboons (Funkhouser et al., 1967) and humans (Baltrip, 1954; Gaudio and Abramson, 1968; Rowell et al., 1969) during whole body heating with increases in minute volume of 1-2 liters/min. Evidence from the conscious dog indicates that lung inflation receptors have a substantial influence in modulating the reflex responses to carotid chemoreceptor stimulation (Vatner and Rutherford, 1981). Results of a study on the conscious rabbit by Korner et al. (1973b) suggest that hyperventilation may slow the heart rate without exerting a significant influence on the shape of the

TABLE 2
Steady State HR-MABP Curve Analysis in the Normothermic and Hyperthermic States during Cholinergic and β-Adrenergic Receptor Blockade (n = 6)

<table>
<thead>
<tr>
<th></th>
<th>Cholinergic blockade</th>
<th>β-Blockade</th>
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<tr>
<td></td>
<td>N</td>
<td>H</td>
</tr>
<tr>
<td>Maximum HR (beats/min)</td>
<td>172 ± 12</td>
<td>197 ± 8*</td>
</tr>
<tr>
<td>Minimum HR (beats/min)</td>
<td>125 ± 4</td>
<td>144 ± 5*</td>
</tr>
<tr>
<td>Total HR range (beats/min)</td>
<td>47 ± 9</td>
<td>52 ± 6</td>
</tr>
<tr>
<td>Estimated slope (beats/min per mm Hg)</td>
<td>3.1 ± 0.4</td>
<td>3.9 ± 0.5</td>
</tr>
<tr>
<td>BPm (mm Hg)</td>
<td>86 ± 2</td>
<td>88 ± 2</td>
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</table>

Values are mean ± se. N = normothermic state; H = hyperthermic state.

* P < 0.01.
A major effect of elevated Tbi on the baroreflex control of HR was a reduction in HR sensitivity (ΔHR/ΔMABP) in the tachycardia response and an increase in HR sensitivity in the bradycardia response for equivalent reductions and elevations in MABP. Changes in HR sensitivity have been utilized in other investigations as an index of the influence of stress, such as exercise and hypoxia, on the baroreflex control of HR (Bevegard and Shepherd, 1966; Robinson et al., 1966; Guazzi et al., 1970). In this approach, it is generally believed that changes in sensitivity, as defined above, indicate an interaction between the stress being imposed and the baroreceptor reflex, whereas, no changes in sensitivity indicate that the stress and the baroreceptor reflex influence a cardiovascular variable in a noninteractive or additive manner. Application of this reasoning to the present study would indicate that heat stress does alter the baroreflex control of HR because HR sensitivity to ABP changes is altered during heat stress.

However, caution is required when inferring interaction between a stress and baroreceptor control of HR based solely on changes in HR “sensitivity.” It is theoretically possible that during a stress the HR-MABP control point may merely shift to a different position on the curve describing the baroreceptor-mediated HR-MABP relationship. For example, if the stress was accompanied by an upward shift in the HR-MABP control point on the HR-MABP curve without changing the characteristics of the HR-MABP relationship, it would be expected that HR sensitivity to hypotensive stimuli would diminish and the HR sensitivity to hypertensive stimuli would increase. In this case, it would be incorrect to conclude that the characteristics of the baroreflex control of HR was altered by the stress just because HR sensitivities to ABP changes were altered.

Therefore, to determine more fully the effects of hyperthermia on the baroreceptor-mediated HR response in unanesthetized baboons, full HR-MABP curves were constructed for the normothermic and hyperthermic states and analyzed similar to the method of Korner et al. (1973a, 1973b, 1979). Their rationale is that if the inputs characteristic of a particular disturbance (e.g., heat stress) influence the baroreflex control of HR, the parameters which characterize the baroreceptor-mediated HR-MABP curve will be altered from the values observed during control conditions. On the other hand, if only the mean level of HR is altered by the disturbance, causing an upward or downward shift, then the disturbance does not exert a significant direct influence on the baroreceptor control of HR.

Thus, the most notable finding of this present study was that the HR-MABP curves shifted upward in response to an elevation in Tbi without significant changes in the HR range, estimated slope, and BP50 of the HR-MABP relationship. These results imply that external heat stress elicits a rise in HR independent of the mechanisms of control by the arterial baroreceptors with no alteration in the characteristics of the baroreflex control of HR. This conclusion is similar to that of Korner et al. (1973b) with regard to the influence of artificial hyperventilation on the baroreflex control of HR in the conscious rabbit. They hypothesized that the fibers from lung inflation receptors project to part of the cardiac motoneuron pool which does not receive projections from any circulatory baroreceptors. Perhaps the neuronal pool activated by environmental heat stress also does not project to cardiac motoneurons that are connected to baroreceptors.

A major cause of the upward elevation in the HR-MABP relationship during heat stress must be the direct, local influence of temperature on the sinoatrial node. Jose et al. (1970) have shown that the local temperature effect elevates HR about 7—9 beats/min per °C rise in Tbi. In this study, the maximum and minimum HR levels of the HR-MABP relationship were displaced by 35—40 beats/min following an average 2.6°C rise in Tbi. Thus, with the local effect being 7—9 beats/min per °C, about 18—23 beats/min of the upward shift of the HR-MABP curve can be attributed to the local effect of Tbi on the sinoatrial node. However, since the upward shift in the HR-MABP curve is larger than predicted from the local influence of Tbi on HR, other mechanisms, presumably neural, must also be involved. The HR-MABP relationship during either β- or Ch-receptor blockade was also shifted upward during hyperthermia with no significant alterations in total HR range, BP50, or slope. The magnitudes of the upward shift in the maximum and minimum plateau levels were as large or larger than that predicted for the local effect of Tbi. During β-receptor blockade, the plateau levels of the HR-MABP curve were elevated by 22 beats/min for a 2.2°C rise in Tbi. During Ch-receptor blockade, the upward displacement was approxiamtely a 28 beats/min increase for a 2.2°C rise in Tbi. The local effect of Tbi (+9 beats/min per °C) in these two instances would be predicted to cause a 20 beats/min increase in the plateau levels, which is similar to the upward displacement observed during β-receptor blockade. Therefore, these data would indicate that, in addition to the local effect of Tbi, cardiac efferent sympathetic neurons, independent of the arterial baroreflex, may be involved in producing the upward shift in the baroreceptor-mediated HR-MABP relationship during hyperthermia.

At a normothermic Tbi, the HR-MABP control point on the HR-MABP curve is located at the lower portion of the HR-MABP curve. At the hyperthermic Tbi level, the HR-MABP control point was shifted upward on the HR-MABP curve. In the context of no changes in HR range or slope during hyperthermia, this upward shift in the HR-MABP control point would explain why the maximum reflex bradycardia
and tachycardia were significantly increased and reduced, respectively, during hyperthermia. It was observed in this study, as well as by others studying humans (Rowell et al., 1971), that ABP tends to fall during the early phase of heating. Perhaps, the arterial baroreceptor reflex is attempting to compensate for this fall in ABP, with part of the compensation being a reflex tachycardia accompanied by an upward shift of the control point on the stimulus-response curve. The efferent mechanisms mediating the heat-induced “compensatory” reflex tachycardia and thus the upward shift of the control point on the HR-MABP curve may be determined by analyzing the relative changes in the control point for the unblocked heart and during either β- or Ch-receptor blockade during hyperthermia. Heart rate was elevated 52 beats/min for a +2.6°C change in Tbi which is 12–17 beats/min greater than the increase in the plateau levels. Since no significant change in the total HR range occurred in the unblocked heart and the controlled hyperthermic MABP level was not altered from its normothermic level, the result was an average 14 beats/min increase in the control point along the steep portion of the unblocked, hyperthermic HR-MABP curve. During Ch- or β-receptor blockade, MABP and the total HR range of the HR-MABP curves also were not significantly altered during hyperthermia. Thus, the control point increased by 9 beats/min during Ch-receptor blockade and 15 beats/min during β-receptor blockade. This indicates that both the cardiac efferent sympathetics and vagus, respectively, may be involved in mediating a “compensatory” elevation in HR during hyperthermia in response to the heat stress-induced hypotension sometimes observed in baboons (Proppe, 1980; this study) and man (Rowell et al., 1969; Rowell et al., 1971). However, the magnitude of the elevation of the control point observed during β-receptor blockade (i.e., with only the vagal influence on HR intact) is equivalent to the 14 beats/min increase seen for the unblocked-hyperthermic state. The fact that the compensatory reflex rise in HR due to sympathetic activation or vagal withdrawal are not additive in nature may reflect the dominant influence of vagal tone in determining the control, resting HR level in the conscious animal (Levy and Zieske, 1969).

Although in the present study the baroreflex control of HR was unaltered with hyperthermia, it should be emphasized that a similar preservation of the baroreflex control of vascular resistance is not implied by the authors. In humans, Heistad et al. (1973) reported that heating one hand abolished the cutaneous vasoconstrictor response of the opposite hand to lower body negative pressure (LBNP) but did not significantly affect the reflex tachycardia. In contrast, Crossley et al. (1966) and Johnson et al. (1973) demonstrated in humans exposed to whole body heating that the cutaneous bed still retained the ability to vasoconstrict in response to LBNP but was not capable of overriding the heat-induced vasodilation (Johnson et al., 1973). Whether the present findings would be observed for cold stress is uncertain although the reflex tachycardia during LBNP has been shown in humans to be significantly attenuated with cold thermal stimuli of one hand (Heistad et al., 1973). It is difficult, however, to project whether the above results do indeed indicate an influence of thermal stimuli on the baroreflex control of vascular resistance or HR, since full stimulus-response curves were not constructed. As demonstrated in the present study, to rely solely on alterations in reflex responses, i.e., HR sensitivity or changes in vascular resistance, without the construction of full stimulus-response curves may lead to erroneous conclusions as to the influence of a physiological stress on a baroreceptor reflex.

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