special communication

Chronic isolation of carotid sinus baroreceptor region in conscious normotensive and hypertensive rats

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McKeown, Kelly P., and Artin A. Shoukas. Chronic isolation of carotid sinus baroreceptor region in conscious normotensive and hypertensive rats. Am. J. Physiol. 275 (Heart Circ. Physiol. 44): H322–H329, 1998.—We have developed a chronic technique to isolate the carotid sinus baroreceptor region in the conscious rat model. Our technique, when used in conjunction with other methods, allows for the study of the control of arterial pressure, heart rate, and cardiac output by the carotid sinus baroreceptor reflex in conscious, unrestrained rats. The performance of our technique was evaluated in two strains: normotensive Sprague-Dawley (SD) rats and spontaneously hypertensive rats (SHR). Each rat was instrumented with an aortic flow probe and a catheter placed in the right femoral artery to monitor cardiac output and arterial pressure, respectively. The cervical sympathetic trunk and aortic depressor nerve were ligated and cut bilaterally, leaving vagus nerves intact. The right and left carotid sinuses were isolated using our new technique. We tested the open-loop function of the carotid sinus baroreceptor reflex system in the conscious rat after recovery from the isolation surgery. We found that changes in nonpulsatile carotid sinus pressure caused significant changes in arterial pressure, heart rate, and total peripheral resistance in both rat strains. However, the cardiac output responses differed dramatically between strains. Significant changes were seen in the cardiac output response of SHR, whereas no significant changes were observed in normotensive SD rats. We have found this technique to be a highly reliable tool for the study of the carotid sinus baroreceptor reflex system in the conscious rat.

carotid sinus baroreceptor reflex; hypertension; arterial compliance; cardiac output; stroke volume

ALL OF THE MECHANISMS by which the carotid sinus baroreceptor reflex participates in the regulation of cardiac output are not yet understood. However, we know that reflex-mediated excitation or inhibition of the vasomotor center directly alters heart rate and contractility, which, in turn, affect stroke volume and cardiac output. In addition, vasomotor control of the systemic vascular bed can also contribute to variations in stroke volume. Particularly, changes in vascular capacitance and total peripheral resistance affect the return of blood to the heart, thereby modifying end-diastolic filling pressure and cardiac output via the Frank-Starling mechanism.

Clearly, the study of the carotid sinus baroreceptor reflex system provides us with a powerful method to investigate interactions between the heart and systemic circulation in the regulation of cardiac output under normal and pathophysiological conditions. As a result, several investigators have developed techniques, primarily in the dog model, to study the carotid sinus baroreceptor reflex system. Moissejeff (6) was the first to report a technique to completely isolate the carotid sinus baroreceptor regions from the systemic circulation in the anesthetized dog. This method created a blind sac in the carotid sinus region in which the pressure to the baroreceptors was controlled at any desired level. Some 50 years later, continued interest in the carotid sinus baroreceptor reflex system prompted Stephenson and Donald (14) to develop a technique for the reversible isolation of the carotid sinuses in the conscious dog. Both techniques are highly effective in the dog model, but their extensive surgical methods become more difficult and potentially detrimental when performed in smaller animals such as the rat.

Various factors have compelled many investigators to select the rat model for studies involving neural control of the circulation. Although advantageous in terms of costs and management, the size of the rat poses severe limitations to the surgical methods that can be applied to this model and to the instrumentation available for the measurement of hemodynamic variables. These limitations have been prevalent, and often prohibitive, in the study of the carotid sinus baroreceptor reflex system in the rat. Early efforts to isolate the carotid sinus regions of the rat (7, 15) were met with varying degrees of success. In 1991, our laboratory (13) developed a highly effective technique to completely isolate the carotid sinus baroreceptor region of the rat without extensive surgery. Nonetheless, one major problem persists with this method: experimental studies using our technique must be carried out while the rat is under anesthesia. This is problematic because the type and the level of anesthesia are thought to alter the function of the carotid sinus baroreceptor reflex system in the rat (4).

Our interest in cardiac output regulation by the carotid reflex system under pathophysiological conditions, such as hypertension, necessitated the evolution of our acute isolation technique into a chronic one. We now describe a new, chronic technique to isolate the carotid sinus baroreceptor region in the conscious rat model. This method allows for the study of reflex...
regulation of the circulation and, combined with other techniques, permits us to study the regulation of cardiac output in the rat without anesthetic effects. To test the efficacy of this technique and our ability to discriminate differences in circulatory control and regulation, we have performed these procedures in two rat strains, normotensive Sprague-Dawley (SD) rats and spontaneously hypertensive rats (SHR). We purposely selected these two strains in light of reports that they have markedly different arterial compliances (11), one major factor that has been shown to alter cardiac output regulation by the carotid sinus baroreceptor reflex system (10). Thus our purpose is to describe the technique for the bilateral isolation of the carotid sinus regions in the rat and to compare the reflex-induced changes in cardiac output in conscious normotensive and hypertensive strains of rat.

METHODS

Male SD rats and SHR (350–450 g) were housed in a virus-free central holding facility before use in these experiments. All procedures were approved by the Institutional Animal Care and Use Committee. On different days, each rat underwent two distinct surgeries, an aortic flow probe implantation followed by a bilateral carotid sinus isolation. A period of 1 wk between surgeries was ample time for the animal to recover from the flow probe implantation and for enough scar tissue to form around the aorta and flow probe, thus ensuring a highly reliable flow signal. After surgery, each animal was independently housed in the laboratory. In the daytime during normal working hours, 6:00 AM to 6:00 PM, the animals were exposed to normal daylight and artificial light. During the evening, in the absence of any personnel, the lights in the laboratory were shut off, thus exposing the rats to a normal nighttime atmosphere. Animals were not restrained within their cages, and each was provided with food and distilled water ad libitum.

Surgical Procedures

General methodology. Animals were anesthetized with a single intramuscular injection of ketamine and acepromazine (120 mg/kg and 50 mg/kg, respectively). Body temperature was maintained at −37°C throughout all surgical procedures via a servo-controlled heating pad. Sterile materials and aseptic technique were consistently used. Postoperatively, each rat received two injections, penicillin (100,000 U im) and fluid electrolyte (20 ml sc, 0.5% dextrose and 0.225% sodium chloride solution). We found the electrolyte injection to be an effective means of preventing postoperative dehydration. Wounds were treated with topical antibiotics immediately after surgery and, if necessary, during recovery. A daily record was kept of the animal’s body weight, cardiac output, level of activity, food and water intake, and general overall appearance.

Aortic flow probe implantation. After induction of anesthesia, the rat was intubated with a 14-gauge Teflon catheter. The chest was opened via a right lateral thoracotomy at the level of the fourth intercostal space. At this time, the rat was placed on a respirator (model SAR-830, CWE, Ardmore, PA) and ventilated with room air. A 2.5-mm flow probe (Transonic Systems, Ithaca, NY) was fitted around the ascending aorta. Motion of the probe was prevented by stabilizing its cable with one of three sutures (2-0) used for rib closure. The cable was then tunneled subcutaneously to a midline incision dorsal to the scapulas where the probe connector was anchored in place. After the rat was removed from mechanical ventilation, the tracheal tube was withdrawn and any fluid remaining in the mouth cavity was aspirated. The duration of this entire procedure was ~1 h.

Bilateral carotid sinus isolation. One week to ten days after the aortic flow probe implantation, we performed the bilateral carotid sinus isolation. Anesthesia [ketamine and acepromazine (120 mg/kg and 50 mg/kg, respectively)] was induced once again and supplemented hourly (0.1 ml im) throughout the course of this 3-h procedure. A special catheter was inserted into the right femoral artery and connected to a transducer (Statham P23 Db) to monitor arterial pressure. We constructed this catheter from ~20 cm of Tygon microbore tubing (0.040-in. ID, 0.070-in. OD; Norton Scientific, Akron, OH) bonded to 2.5 cm of Micro-Renathane tubing (0.025-in. ID, 0.040-in. OD; Braintree Scientific, Braintree, MA). Only the Renathane segment of the catheter was placed into the lumen of the vessel because it is flexible and highly blood compatible, thus minimizing clotting. The microbore tubing was then coiled in a single loop at the site of cannulation and sutured to the underlying muscle. The dead space of the catheter was carefully measured and filled with heparinized saline (200 U/ml).

The cervical neck region was exposed through a ventral midline incision. Superficial glands were separated, and the sternomastoid muscles were retracted bilaterally. We found it possible to complete this procedure without severing the omohyoid muscles. The sternohyoid muscles were looped and retracted over the trachea to reveal each carotid sinus region in turn. To eliminate buffering effects from the aortic arch and cardiopulmonary baroreceptors, the cervical sympathetic trunk, aortic depressor nerve, and contiguous blood vessels were completely ligated and cut bilaterally (3). The bilateral vagus nerves were left intact.

A fine needle threader was used to place a length of 7-0 prolene at the root of the bifurcation of the common carotid artery. The suture was then tied about the external carotid artery just caudal to the origin of the occipital carotid artery. Once tied, this suture prevented any retrograde blood flow from the occipital and external carotid arteries into the carotid sinus region. This procedure also excluded the carotid body chemoreceptors from the isolated carotid sinus region. Therefore, the chemoreceptors were not exposed to changes in carotid sinus pressure (CSP) and did not participate in an induced reflex response. This effect of the surgical isolation was confirmed by Brunner et al. (1), using intracarotid injections of sodium cyanide in the dog. The common carotid artery was ligated near the posterior border of the sternomastoid muscle and clamped (Acland microvascular clamp, ASSI, Westbury, NY), ~5 mm distal to that site. An incision was made in the isolated segment of the carotid. Two stainless steel ball bearings (1/32-in. OD, Salem Specialty Ball, West Simsbury, CT) were deposited in the lumen with a Teflon catheter (25 gauge) used in conjunction with a gated vacuum source. Next, a saline-filled catheter, identical to the one placed in the femoral artery, was inserted directly behind the beads and loosely tied within the vessel. After the microvascular clamp was removed, we advanced the catheter ~5 mm into the artery, making sure that its tip remained proximal to the sinus. A 1-ml glass syringe was then used to inject the beads through the sinus and into both branches of the internal carotid artery, thus completing the isolation. The catheter was temporarily connected to a transducer in series with a column of saline adjusted to provide a hydrostatic pressure ~5 mmHg greater than the mean arterial pressure (MAP) of the rat. This procedure was then repeated on the
contralateral side (see Fig. 1 for a diagram of the instrumentation).

A coil made in the Renathane tubing allowed for natural positioning of the carotid catheter within its vessel; this orientation was stabilized by suturing the microbore segment to a superficial muscle in the region. The left and right carotid catheters were united to form a single line via a stainless steel three-way connector (Small Parts, Miami Lakes, FL) placed at the level of the manubrium. The dead space of the femoral line was then filled with heparin (1,000 U/ml). Finally, the femoral and carotid catheters were externalized at the back and linked in a “closed-loop” configuration (see Fig. 1). This configuration provided a simple means of sealing off the femoral line while, most importantly, allowing for closed-loop functioning of the baroreceptors during recovery. The catheters were protected by fitting the rat with a custom-made vest that slipped over the rat’s forelimbs and fastened at its back.

Experimental Procedure

We evaluated the performance of the technique in the conscious rat model on the 2 days immediately after chronic isolation of the baroreceptors. In preliminary trials, we observed that the open-loop baroreflex responses obtained in a single animal varied considerably with the time of day. Therefore, the protocol we now describe was consistently conducted in the early morning (7:00–8:00 AM) while the rat remained in its cage in a quiet, darkened room separate from where the animals were normally housed. Thus all experiments were conducted under the same lighting condition (dark) at the same time of day.

Initial preparations. First, the femoral catheter was detached from the carotid line. Its contents were withdrawn and replaced with heparinized saline (200 U/ml). Two lengths of Tygon tubing were passed through a spring; one segment was attached to the femoral artery catheter and the other to the carotid line. Each Tygon segment was connected to a four-way stopcock and then to its appropriate transducer (femoral or carotid). A shunt was inserted between both four-way stopcocks to permit closed-loop communication between the femoral and carotid lines (see Fig. 1). When desired, the shunt valve was closed off, allowing for experimentation in the open-loop condition. The open-loop isolated sinus pressure was varied at will by adjusting the height of a column of saline in series with the carotid transducer. Finally, the aortic flow probe was connected to a flowmeter via an extension cable to monitor aortic blood flow.

Protocol. To allow the rat to become acclimated to peripheral instrumentation and ambient conditions in the laboratory, a period of 20 min preceded experimentation. Arterial pressure and aortic blood flow were monitored continuously while the baroreceptors remained in the closed-loop state. During this period and throughout the entire protocol, the rat was undisturbed and unrestrained within its cage.

After this period, the rat was placed on an open-loop CSP equal to its MAP for a 2-min stabilization period. CSP was then switched at regular 2-min intervals from a low level (50 mmHg) to a high level (200 mmHg). We chose these CSP values because they are inclusive of the range of the reflex system in anesthetized normotensive and hypertensive rats (7, 15). This alternation sequence was repeated three times. Measurements of each variable were made during the last 10 s of the 2-min period following a change in CSP, a time at which the variables had reached a steady state. An average was taken over this 10-s portion of the observation period.

We consistently observed that the changes in cardiac output, MAP, heart rate, aortic flow, and cardiac output. Stroke volume was calculated as the ratio of cardiac output to heart rate. The total peripheral resistance was calculated as the ratio of MAP to cardiac output normalized to body weight. Comparisons were drawn between the dependent variables of MAP, heart rate, and cardiac output by a paired t-test at low and high CSP. Differences in the measured variables between rat strains were assessed at either CSP by a Student's t-test of the means. For all analyses, differences were considered significant if P < 0.05.

RESULTS

Mean baseline values of each hemodynamic variable are shown in Table 1 for SD rats and SHR under closed-loop conditions (CSP varying with arterial pressure) and open-loop conditions (CSP fixed at the control, or closed loop, level of MAP).

We consistently observed that the changes in cardiac output and stroke volume elicited by the carotid sinus baroreceptor reflex system were different between the two strains of rat. We therefore divided the strains into two groups, normotensive and hypertensive, for the purpose of statistical analysis.

Fig. 1. Rat completely instrumented with aortic flow probe, femoral artery cannula, and bilateral carotid sinus isolation. See METHODS for description of surgical procedures. Under open-loop conditions, femoral and carotid lines are separated and connected to a transducer and a variable pressure source, respectively. Under closed-loop conditions, femoral and carotid lines are conjoined to allow for communication of systemic arterial pressure to bilateral carotid sinus regions.
Shown in Fig. 2 is an actual experimental recording from an SD rat in the conscious state. Measured variables are presented for the rat under closed-loop conditions (Fig. 2, left, bilateral CSP after arterial pressure) and open-loop conditions (Fig. 2, right, CSP controlled at a fixed level). Note the decrease in heart rate variability as CSP is held at any static level under open-loop conditions. All rats, regardless of strain, exhibited this suppression of heart rate variability on switching from the closed-loop to the open-loop state.

As seen in Fig. 2, right, an increase in CSP from 50 to 200 mmHg causes an immediate decrease in arterial pressure, heart rate, and cardiac output. At steady state, the arterial pressure remains at a level below control, whereas cardiac output and heart rate return to their control values. Figure 3 shows a similar experimental recording of a conscious SHR rat under open-loop conditions. As CSP is increased from 50 to 200 mmHg, there is a concomitant decrease in arterial pressure, heart rate, and cardiac output. However, in the hypertensive rat, the decreases in arterial pressure and cardiac output are sustained throughout. Both experimental recordings (Figs. 2 and 3) are indicative of the responses seen in each group of rats.

As seen in Fig. 4, MAP was significantly affected by the level of CSP in both rat strains. Figure 4 also indicates that SHR rats did have a significantly greater MAP than SD rats at each CSP (P < 0.02 and P < 0.03 for CSP of 50 and 200 mmHg, respectively). Despite these large fluctuations in MAP, the zero aortic flow signals remained stable in all rats. We attribute the constancy of zero aortic flow to stable acoustic coupling of the probe and vessel. Proper coupling was guaranteed by allowing sufficient time (at least 1 wk) for scar tissue to form about the probe and aorta after the implantation.

The heart rate response to changes in CSP (Fig. 5) was significant in SD rats (P < 0.03) and was considered marginally significant in SHR rats (P < 0.06). Normotensive rats had higher heart rates than hypertensive rats regardless of CSP, although this difference was significant at only a low CSP (P < 0.04). Variations in CSP did not effect significant changes in the cardiac output of SD rats (see Fig. 6). On the contrary, signifi-
significant differences ($P < 0.002$) in the cardiac output response of SHR rats were observed as a result of changing CSP between 50 and 200 mmHg.

Absolute stroke volume and stroke volume normalized to body weight are shown as functions of CSP in Fig. 7, A and B, respectively. There were significant decreases in stroke volume and stroke volume normalized to body weight in SHR rats ($P < 0.003$) when CSP was changed between 50 and 200 mmHg. However, no significant changes in stroke volume were observed in response to raising and lowering CSP in SD rats.

Shown in Fig. 8 are the calculated total peripheral resistances of SHR and SD rats at CSP of 50 and 200 mmHg. In both rat strains, total peripheral resistance decreased significantly in response to an increase in CSP. At either CSP, the total peripheral resistance of SHR was higher than that of SD rats, although this difference was significant at only the high CSP ($P < 0.04$). In SHR there was a 27% increase in total peripheral resistance when CSP was changed from 200 to 50 mmHg, whereas in SD rats the increase in total peripheral resistance nearly doubled that of SHR, amounting to an increase of 45%.

**DISCUSSION**

To our knowledge, this is the first time that data have been obtained concerning the control of arterial pressure, cardiac output, heart rate, and stroke volume by the carotid sinus baroreceptor reflex system in the conscious rat. A total of 16 rats were prepared using our new technique. We successfully obtained data in 9 of the 16 rats, 5 SD and 4 SHR. The predominant difficul-

![Fig. 3. Experimental recording of conscious spontaneously hypertensive rat (SHR). Hemodynamic variables are shown for a conscious, unrestrained SHR rat under open-loop conditions. Note dramatic decrease in arterial pressure, cardiac output, and heart rate as bilateral CSP is raised from 50 to 200 mmHg. In SHR rat, cardiac output and arterial pressure responses are sustained throughout steady state.](http://ajpheart.physiology.org/)

![Fig. 4. Changes in mean arterial pressure of SHR and SD rats induced by switching CSP. $P$ values between variable at low and high CSP within a single strain are indicated in figure. Respective $P$ values between strains at a CSP of 50 or 200 mmHg are $P < 0.03$ and $P < 0.02$.](http://ajpheart.physiology.org/)

![Fig. 5. Changes in heart rate of SHR and SD rats induced by switching CSP. $P$ values between variable at low and high CSP within a single strain are indicated in figure. Respective $P$ values between strains at a CSP of 50 or 200 mmHg are $P < 0.04$ and $P < 0.06$.](http://ajpheart.physiology.org/)
ties we encountered in the seven unsuccessful rats were 1) loss of the carotid sinus isolation because of a rupture of the external carotid artery at the site of the prolene tie, 2) irremediable clotting of the femoral artery catheter (usually a consequence of the carotid sinus rupture during closed-loop conditions), and 3) aortic rupture at the site of the flow probe (twice in the SHR). Despite these technical problems, we have found the method to be highly reliable in the study of the carotid sinus reflex system in the conscious rat model.

Stephenson and Donald (14) developed the first technique to reversibly isolate the carotid sinus regions in the conscious dog. Their method required the ligation of all branches of the internal carotid artery. Vascular occluders were then placed both distal and proximal to the sinus about the external and common carotid arteries. Between the two occluders, a catheter was implanted in the arterial wall. The indwelling catheter enabled them to selectively control CSP once the occluders were inflated. Clearly, it is not possible for such a technique to be applied in the rat model because of size limitations in the rat. We therefore developed a blind sac isolation technique, similar to the one reported by our group in anesthetized Long-Evans rats (13), for application in the conscious rat model. Our new method differs from that of Stephenson and Donald (14) in that it does not allow for blood perfusion of the carotid sinus region. However, it does permit the exposure of the carotid sinuses to systemic arterial pressure during nonexperimental periods.

In a previous study (13), we were able to demonstrate that the carotid sinus baroreceptor reflex system does have a significant effect on the control of arterial pressure in the rat. One deficit of that study was its inability to partition the relative contributions of systemic factors, i.e., total peripheral resistance and vascular capacitance, from those of the heart, i.e., heart rate and stroke volume, in the overall regulation of arterial pressure by the carotid sinus reflex. An earlier study by
Schmidt et al. (12) in the dog emphasized the importance of this partitioning in our understanding of the homeostatic mechanisms involved in reflex regulation of arterial pressure. The method that we have developed is the first to provide this essential information in the rat model. In addition, we know of no other study that has reported these data in conscious SD rats and SHR.

The data shown in Figs. 4–8 indicate the effect that the carotid sinus reflex system has on the control of arterial pressure through changes in heart rate, stroke volume, and total peripheral resistance. Figure 4 shows that the arterial pressure of SHR is significantly higher than that of SD rats at either CSP in the conscious state and that the reflex system has the ability to significantly change MAP. This is consistent with the findings of Nosaka and Wang (7), who studied the baroreceptor reflex in anesthetized SHR and SD rats. Using α-chloralose as the anesthetic agent, these investigators found the maximum changes in arterial pressure to be 43 mmHg in normotensive rats and 53 mmHg in SHR. Our data are comparable to theirs; we find the maximum changes in arterial pressure to be 33 and 42 mmHg in normotensive rats and SHR, respectively. An increase in the arterial pressure of SHR is caused by an elevation in both total peripheral resistance and cardiac output, whereas in SD rats the elevation in arterial pressure is caused solely by the increase in total peripheral resistance. This is evident from Figs. 6 and 8. Before our study, no conclusions could be reached as to the contribution of cardiac output to the arterial pressure changes. One strength of the technique lies in its ability to provide a complete description of the reflex system with measured cardiac output responses.

As seen in Fig. 6, the cardiac output of SHR decreases significantly (P < 0.002) in response to raising CSP, whereas no significant change is measured in the cardiac output of SD rats (P < 0.15). The strains do, however, show similar significant heart rate responses to increases in CSP (see Fig. 5). Heart rate decreased an average of 3.3% in SHR and 4.0% in SD rats. Thus the primary cause of dissimilar cardiac output responses in the two strains is a difference in their stroke volume responses to changing CSP. The absolute stroke volume and stroke volume normalized to body weight are shown as functions of CSP in Fig. 7. Stroke volume significantly decreases with increasing CSP in the SHR, whereas the stroke volume of the SD rats is invariant with regard to changes in CSP.

As seen from Table 1, changing from closed-loop conditions to open-loop conditions, the baseline hemodynamic variables did not change significantly. We purposefully switched the conditions such that the mean open-loop carotid pressure was equal to MAP under closed-loop conditions. Schmidt et al. (12) have shown in the dog model that changing from nonpulsatile to pulsatile pressure (2 Hz and 50 mmHg pulse pressure) at the same mean level with the vagus intact caused arterial pressure, cardiac output, and total peripheral resistance to fall ~10%. They found that the response depended on the absolute level of the CSP, the frequency of pulsation, and pulse amplitude. Despite these obvious changes, these investigators (12) concluded that “the sensitivity of the overall carotid sinus reflex system to physiologically probable changes in the pulse pressure or pulse rate of intrasinus pressure is not quantitatively important compared with the reflex sensitivity to alteration of mean intrasinus pressure.” Although our data, in the conscious rat model, are in agreement with their conclusion we are currently unable to conclusively explain the reason for the differences in experimental results at this time, the obvious reason being that our experiments were performed in the conscious chronic rat model and those of Schmidt et al. (12) in the dog under pentobarbital anesthesia.

The data we present in Figs. 4–8 are qualitatively similar to those reported in a recent study by Potts et al. (10). With the use of the dog model, these investigators found that the gain of the baroreceptor reflex system in its control of arterial pressure, cardiac output, and stroke volume was attenuated when the arterial compliance was artificially increased. The increase in arterial compliance was achieved by adding an external compliance chamber to the arterial circulation of the dog. This technique ultimately enabled the investigators to alter the ratio of arterial to venous compliance experimentally within the same animal. Under these conditions, no significant changes were observed in heart rate or left ventricular contractility. Potts et al. (10) therefore concluded that an increase in the arterial-to-venous compliance ratio alters carotid sinus reflex control of the circulation. The reflex changes in cardiac output and stroke volume are diminished in the presence of a larger arterial compliance. They attribute this attenuation to passive blood volume shift between the arterial and venous segments of the circulation.

A similar mechanism could conceivably account for the differences we observed in the cardiac output and stroke volume responses of SHR and SD rats. This, of course, would require that the two strains have markedly different arterial-to-venous compliance ratios. Existing data confirm that this is indeed the case. Samar and Coleman (11) reported that, despite having similar venous compliances, SHR have significantly smaller arterial compliances (~50%) than normotensive rats. This is in agreement with studies by Caputo et al. (2) for isolated carotid arteries in vitro and by Levy et al. (5) for the entire systemic vascular bed of the rat.

We cannot deny the possibility that differences in the cardiac output and stroke volume responses of normotensive and hypertensive rats might be caused by differences in reflex control of cardiac contractility between the strains. However, in rats of the same age group as those used in our study, Pfeffer and Frohlich (9) found no differences in the maximum acceleration of flow, peak flow velocity, or stroke work of SHR and normotensive strains. Although this particular study (9) was carried out in ether-anesthetized rats, a prior study (8) by the same group of investigators determined that the cardiac index (cardiac output per kilo-
gram body weight) under ether anesthesia most closely approximated that of the unanesthetized rat. This study confirms that it is now possible to obtain necessary hemodynamic data for the study of the carotid sinus baroreceptor reflex system in the conscious rat. In addition, we have been able to show marked differences in the cardiac output response to carotid sinus activation in normotensive and hypertensive rats. Further studies are needed to compare normotensive and hypertensive strains to fully account for the differences we observed in cardiac output regulation by the carotid sinus baroreceptor reflex system.

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