Normalization of arterial pressure after barodenervation: role of pressure natriuresis

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OSBORN, JOHN W., AND SARAH K. ENGLAND. Normalization of arterial pressure after barodenervation: role of pressure natriuresis. Am. J. Physiol. 259 (Regulatory Integrative Comp. Physiol. 28): R1172-R1180, 1990.—Studies in several species have demonstrated that mean arterial pressure (MAP) is normal or only slightly elevated after chronic arterial baroreceptor denervation. We hypothesized that the absence of sustained hypertension after barodenervation was the result of a pressure natriuresis response, secondary to sympathetic vasoconstriction of nonrenal vasculature. To test this hypothesis, MAP, sodium balance (Na\textsubscript{b}), and water balance were measured before and after aortic baroreceptor denervation (ABD), sinoaortic denervation (SAD), or sham surgery in conscious rats. MAP was increased 20.0 ± 3.7 mmHg 1 day after ABD but returned to control by day 3. ABD had no significant effect on daily Na\textsubscript{b} or water balance. The responses to SAD were similar to those after ABD, with the exception that a significant natriuresis was observed the first day after SAD. However, this was followed by a significant antinatriuresis on day 2, when MAP was still elevated. By day 3 after SAD, MAP, Na\textsubscript{b}, and water balance were not significantly different from control. These results suggest that the normalization of MAP after ABD or SAD is not the result of pressure natriuresis but rather failure to maintain a chronic elevation of sympathetic activity after barodenervation.

arterial baroreceptors; hypertension; renal function

DENERVATION OF the afferent projections of the carotid sinus and aortic arch baroreceptors (sinoaortic denervation; SAD) results in a rapid, sympathetically mediated vasoconstriction and acute hypertension in anesthetized animals. However, the issue of whether SAD leads to permanent elevations of arterial pressure in unanesthetized animals has been the subject of considerable controversy. Initial studies in the rat showed that arterial pressure remained elevated for as long as 10 wk after SAD (16). However, in that study, arterial pressure was monitored indirectly in restrained rats, and the hypertension may have been an acute response to the stress of restraint rather than a chronic response to SAD. This idea was suggested by a later study employing 24-h computerized measurements of arterial pressure in unrestrained dogs (7). That study and recent other studies in rats (17, 23), rabbits (20), and monkeys (6) have concluded that SAD does not chronically elevate arterial pressure. However, there are also recent contradictory reports of chronic hypertension after SAD in dogs (14), baboons (4), and rats (5, 22).

Although the issue of whether SAD results in sustained hypertension remains controversial, it is clear that the initial level of hypertension observed after SAD is not maintained over time (4, 14, 20). There are two general hypotheses to explain why arterial pressure returns to normal or near-normal levels after SAD. The first hypothesis is that the “effective” sympathetic hyperactivity induced by SAD is not maintained chronically. This includes the level of sympathetic nerve discharge, release of neurotransmitters, and/or the sensitivity of vascular and cardiac effectors to these transmitters. The second hypothesis is that, despite a sustained increase in sympathetic nerve discharge to the peripheral vasculature, SAD does not chronically elevate renal sympathetic nerve activity. According to the systems model of Guyton and colleagues (12), if it is assumed that SAD does not chronically shift the “renal function curve” to a higher operating pressure (via increased renal nerve activity), hypertension after SAD will lead to a secondary increase of renal sodium and water excretion (pressure natriuresis and diuresis). This will lead to blood volume contraction and decreased cardiac output, resulting in a normalization of arterial pressure. This arterial pressure control system is unique in that, although the response time is relatively slow, it is an integral control system (rather than proportional) with “infinite gain” (12). Therefore, given enough time, and if the set point of the renal function curve is not changed, arterial pressure will always return to normal levels, despite chronic alterations in peripheral vascular resistance. Based on this hypothesis, it is therefore conceivable that arterial pressure returns to control after SAD despite chronic elevations of sympathetic nerve discharge to the peripheral vasculature.

The purpose of the present study was to determine whether the absence of sustained hypertension in arterial baroreceptor-denervated rats is in fact the result of increased renal excretion of sodium and water secondary to SAD-induced hypertension. We examined the transient and steady-state effects of baroreceptor denervation on regulation of arterial pressure and sodium and water balance in conscious unrestrained rats. We hypothesized that SAD would result in an acute hypertensive response, followed by an increased sodium and water excretion and a return of arterial pressure to control levels. Finally, since hypertension has been reported after denervation of the aortic baroreceptors alone (11, 13, 15), experiments were also conducted in rats with partial arterial baroreceptor denervation (ABD).
METHODS

General Procedures

Male Sprague-Dawley rats were purchased (Biolab, St. Paul, MN) and housed in small groups in a temperature- and light-controlled animal housing facility until the time of study. Standard rat chow and water were provided ad libitum. At the beginning of the study, rats were brought to the laboratory for chronic instrumentation (see below) and subsequently housed in metabolic cages in a quiet, isolated laboratory with a 12:12 h day-night cycle (lights on at 0700 h). All procedures were approved by the institutional Animal Care Committee and were conducted in accordance with institutional and National Institutes of Health guidelines.

Surgical Procedures

Chronic catheterization. Rats were anesthetized (pentobarbital sodium; 50 mg/kg), atropinized (0.4 mg/kg), and administered antibiotic (gentamicin sulfate, 5 mg/kg, Elkins-Sinn, Cherry Hill, NJ) with a single intraperitoneal injection. After induction of anesthesia, rats were placed on a heated surgical table. Arterial and venous catheters (Dural Plastics, Dural, NSW, Australia) were advanced to abdominal aorta and vena cava, respectively, from the femoral vessels. The distal ends of these lines were tunneled subcutaneously to the head where they were secured to the skull with stainless steel screws and dental acrylic. The distal ends of the catheters were then passed through a lightweight flexible spring connected to a single-channel hydraulic swivel to which the venous catheter was attached. The incisions were closed, and the rats remained on the heated surgical table until they were mobile. Rats were then placed in individual metabolic cages with the swivel mounted above. This allowed the animals complete freedom of movement about the cage and permitted handling of the catheters without disturbing the rats. Two days were permitted for recovery from surgery and acclimatization to the laboratory environment, and studies were conducted with the rats in their home cages. Arterial catheters were drained and filled daily with heparinized saline (1,000 U/ml) to maintain patency.

Sham, aortic, and sinoaortic barodenervation. Arterial baroreceptor denervation was performed as described by Krieger (16). Briefly, on the day of the procedure, rats were anesthetized with pentobarbital (50 mg/kg iv) and atropinized (0.4 mg/kg iv). A ventral midline neck incision was made, and the sternocleidomastoid muscles were retracted. Aortic baroreceptors were denervated by sectioning bilaterally the cervical sympathetic trunks (caudal to the superior cervical ganglion), the superior laryngeal nerves, and, when present, the aortic depressor nerve. Combined SAD was performed by denervation of the aortic baroreceptors and then stripping the region of the carotid bifurcation. Sham denervation consisted of a midline incision and retraction of the sternocleidomastoid muscles bilaterally.

Experimental Protocol

After catheterization and housing, the daily sodium intake was fixed at ~3.5 meq/24 h (see RESULTS) for the duration of the study by a continuous intravenous infusion of 0.9% saline at ~24 ml/24 h. Rats were fed a sodium-deficient powdered diet (Research Diets, New Brunswick, NJ) and distilled water ad libitum. After 2 days of recovery, mean arterial pressure (MAP), heart rate (HR), and body fluid balance (see details below) were measured for 2 control days. Immediately after the second day of control measurements, rats underwent either a sham (n = 6), ABAD (n = 10), or SAD (n = 7) surgery. Measurements were continued for the next 7 days.

Cardiovascular measurements. MAP, the lability of MAP, and HR were measured each day between 0830 and 1200 h. MAP was measured by connecting the arterial catheter to a pressure transducer coupled to a Grass polygraph (model 7D). The pulsatile arterial pressure signal was input to a second amplifier with a low-pass filter to acquire an electrical mean of arterial pressure. The filtered analog signal was digitized with an analog-to-digital converter (model DT2801A, Data Translation, Marlboro, MA) and sampled at 1 Hz using an IBM AT compatible computer and commercial data acquisition and analysis software (ASYSTANT+, Macmillan Software, New York, NY). The MAP signal was monitored over a 30-min period (total of 1,800 samples), while the rats rested quietly in their cages. The average and SD of MAP were then calculated for each recording period. The SD of MAP was used as an index of the lability of arterial pressure. HR was determined by periodically increasing the chart speed and counting peaks on the pulsatile pressure tracing.

Sodium and water balance measurements. Daily sodium balance was calculated as the difference between 24-h sodium intake and urinary sodium excretion (UN·V). Total sodium intake was calculated daily from the infusion rate and sodium concentration of infused saline. UN·V was determined from the 24-h urinary flow rate (V) and urine sodium concentration (UN). In addition, residual sodium remaining on the funnels of the metabolism cages was collected by rinsing each with 100 ml of distilled water, which was then analyzed for sodium. Total sodium excretion was then calculated as the sum of UN·V plus residual sodium collected from the funnels. Sodium concentrations of the infusate and urine were measured with an ion-specific electrode (Nova Biomedical, Waltham, MA). Water balance (ml/24 h) was calculated as the difference between water intake (ad libitum + infused) and V.

Test of baroreflex sensitivity. Five days after sham, ABAD, or SAD, the sensitivity of the arterial baroreflex control of HR was tested (after measurement of the daily variables). Baroreflex activity was assessed by determining the response of HR to acute increases and decreases of arterial pressure. Arterial pressure was elevated by bolus injection of one to two doses of phenylephrine (0.1–1.0 µg/kg, Winthrop-Breon Laboratories, New York, NY) and decreased by bolus injection of one to two doses of nitroprusside (0.1–1.0 µg/kg, Elkins-Sinn). Responses were measured as the peak change in MAP and HR. Because of the increased lability of MAP after ABAD and SAD, special care was taken to ensure that injections were not made until MAP was stable. Both vasoactive
agents were dissolved in sterile 0.9% saline. The volume of injections ranged from 0.1 to 0.3 ml.

**Statistical Analysis**

Values for the 2 control days were averaged together to obtain a single control value for each group. The effect of sham, ABD, and SAD on daily measured variables was analyzed by a one-way analysis of variance (ANOVA) for repeated measures in one dimension (time). A significant F ratio was followed by Duncan's multiple-range test. The sensitivity of the baroreceptor reflex was determined by linear regression analysis using the least squares method. The slope of the regression equation was used as an indicator of the "gain" of the baroreflex control of HR. Statistical significance for all tests was set a P < 0.05. All values are reported as means ± SE.

**RESULTS**

**Barodenervation Tests**

We used two separate methods to quantitatively determine the effectiveness of our barodenervation procedures. First, we compared between the three groups the lability of MAP as determined from the SD of the daily MAP recordings (overall average of 7 days after sham, ABD, or SAD). The lability of MAP was significantly different between the three groups, progressing from sham (5.1 ± 0.3 mmHg) to ABD (8.7 ± 0.5 mmHg) to SAD (12.1 ± 1.0 mmHg) rats. Second, we tested the sensitivity of baroreflex control of HR 5 days after sham or barodenervation (Fig. 1). As expected, the slope of the regression equation relating changes in HR to changes in MAP was the steepest in sham rats (−2.31 beats min⁻¹ mmHg⁻¹). Denervation of the aortic baroreceptors significantly attenuated the gain of the baroreflex (ABD slope = −0.80 beats min⁻¹ mmHg⁻¹), and denervation of both the aortic and carotid baroreceptors completely abolished the baroreflex control of HR (SAD slope = −0.2 beats min⁻¹ mmHg⁻¹). The slope for the SAD group was not significantly different from a slope of zero but was significantly different from ABD rats.

**Cardiovascular Responses to Barodenervation**

Sham denervation had no statistically significant effect on any variables measured in this study. For clarity, the responses to ABD (Figs. 2, 4, and 5) and SAD (Figs. 3, 6, and 7) are shown separately, but the single sham group is represented in all of the figures. The cardiovascular effects of ABD are shown in Fig. 2. MAP was significantly elevated the first day after ABD, but returned to control levels within the next 2 days. The lability of MAP (expressed as SD of MAP) was nearly doubled for up to 4 days after ABD but returned to control levels within 1 wk after denervation. ABD increased HR from a control level of 381.4 ± 13.2 to 445.6 ± 8.2 beats/min the first day after barodenervation. HR gradually declined over the next 6 days to levels not significantly different from control.

The cardiovascular responses to SAD (Fig. 3) were qualitatively similar to those observed after ABD. The
NEUROGENIC HYPERTENSION AND RENAL FUNCTION

**SINOAORTIC - DENERVATED**

![Graph showing mean arterial pressure over days after denervation](image)

**AORTIC - DENERVATED**

![Graph showing sodium intake and excretion over days after denervation](image)

**Heart Rate**

- Increase of MAP measured 24 h after denervation (+19.0 ± 4.0 mmHg) was not significantly different from the response seen in ABD rats (+20.0 ± 3.7 mmHg). MAP then returned to control levels within 3 days after SAD.
- The lability of MAP increased nearly threefold after SAD and, unlike in ABD rats, remained elevated for the duration of the study. Finally, similar to ABD rats, a pronounced tachycardia was observed the first day after SAD (+90.1 ± 13.7 beats/min), but it was not maintained longer than 4 days after denervation.

**Effects of Barodenervation on Sodium and Water Balance**

To facilitate measurements of sodium balance, sodium intake was held relatively constant in all groups (Figs. 4 and 6) by intravenous infusion. Due to a technical problem, one sham rat received only 25% of the normal volume of saline on day 1, resulting in a greater variability and lower sodium intake for the sham group on day 1. Despite the transient (2-day) hypertensive response to ABD, no significant change in $U_{NaV}$ or sodium balance (Fig. 4) was observed. To the contrary, instead of the predicted loss of sodium (i.e., a negative sodium balance), a statistically insignificant increase in sodium balance was observed 2-4 days after ABD (Fig. 4). Thereafter, sodium balance returned to control levels. ABD had no significant effect on ad libitum water intake, urine output, or water balance (Fig. 5).

In contrast to ABD rats, a significant natriuresis was observed the first day after SAD, resulting in a decreased sodium balance 1 day after barodenervation (Fig. 6). However, within the next 24 h, this pattern was reversed.
and a significant retention of sodium (positive sodium balance) was observed. Similar to ABD rats, sodium balance remained slightly positive after barodenervation but returned to control levels within a few days (6 days after SAD). The net effect of both ABD and SAD on cumulative sodium balance is shown in Fig. 7. After ABD, there was a tendency for a net accumulation of sodium over time. Although SAD resulted in a transient sodium loss by day 1, cumulative sodium balance progressively increased thereafter. Despite an overall trend of sodium retention after ABD and SAD, none of these changes were statistically significant.

In regard to water balance (Fig. 8), the only statistically significant effect of SAD was a decreased water balance 1 day after denervation. This resulted from small, insignificant changes in ad libitum water intake (decrease) and urine output (increase) on day 1.

**DISCUSSION**

The major objective of this study was to determine the temporal relationships between arterial pressure and body fluid balance after baroreceptor denervation in the rat. We hypothesized that baroreceptor denervation would produce a transient hypertension and that the normalization of arterial pressure would be associated with an increased renal excretion of sodium and water (pressure natriuresis and diuresis). The major findings of the present study can be summarized as follows. First, the hypertensive response to partial (ABD) and complete (SAD) arterial baroreceptor denervation was similar in
Arterial pressure increased -20 mmHg the first day but returned to control levels within 3 days after barodenervation. However, the normalization of arterial pressure was not associated with a "pressure natriuresis" response. To the contrary, there was no change in sodium balance the first day after ABD and, as arterial pressure declined over the next 2 days, there was a tendency for sodium retention. A significant natriuresis was observed the first day after SAD, however, this was followed by a 4-day period of sodium retention. As a result, there was a tendency toward a positive (although statistically insignificant) cumulative sodium balance after ABD and SAD rather than the predicted sodium loss. It is important to note that the moderate sodium retention observed after ABD and SAD occurred at the same time that arterial pressure was either slightly elevated or normal.

Response of Arterial Pressure and Renal Function to Barodenervation

Our original hypothesis was that the normalization of arterial pressure after barodenervation would be associated with a net sodium loss, as a result of pressure natriuresis. There are at least three explanations for failure to observe such a response in the present study.

First, a key assumption in our hypothesis was that the "renal function curve" is not altered by baroreceptor denervation. However, studies in conscious dogs suggest this assumption may not be valid. In these studies, acute bilateral carotid occlusion (BCO) resulted in a 40-mmHg rise of arterial pressure and a modest natriuresis. However, when renal arterial pressure was not allowed to increase during BCO, sodium excretion decreased by ~70% (19). This observation strongly suggests that acute unloading of high-pressure baroreceptors increases renal sympathetic nerve activity resulting in antinatriuresis (rightward shift in the renal function curve). This response was presumably the result of a direct effect of renal nerves on sodium and water reabsorption (9) and possibly via activation of the renin-angiotensin-aldosterone axis. Therefore, the natriuretic response to acute unloading of high-pressure baroreceptors is dependent on the balance of natriuretic (increased arterial pressure) and antinatriuretic (elevated renal sympathetic nerve activity) stimuli. This concept, based on the acute response of conscious dogs to BCO, is supported by the results of the present study in conscious rats. That is, failure to observe a net sodium loss after chronic baroreceptor denervation suggests that surgical denervation of baroreceptors also shifts the renal function curve to a higher operating pressure, thereby offsetting the predicted natriuretic response to an elevated arterial pressure.

A second possible explanation for the absence of natriuresis after barodenervation is that the set point of the pressure-natriuresis relationship "resets," such that when arterial pressure is chronically elevated the natriuretic response is not sustained. If such secondary resetting were to occur, however, the ability of this control
system to chronically regulate arterial pressure would be severely limited. Moreover, to our knowledge, there is no direct evidence for secondary resetting of the pressure-natriuresis mechanism.

Finally, it is conceivable that the normalization of arterial pressure after barodenervation was due to decreases in sodium and water balance too small to be detected by our measurements. However, we are confident that the sensitivity of the methods used in the present study was sufficient to detect relatively small changes in body fluid balance. By precisely controlling and measuring daily sodium intake and making meticulous collections of urine, we were able to recover 94% of the daily sodium intake in the urine samples. As a result, all three groups of rats were in a steady state of zero sodium balance before sham or barodenervation procedures. With this degree of precision, a significant natriuresis was observed the first day after SAD, resulting in a statistically significant negative sodium balance. However, within 24 h the response was reversed from natriuresis to antinatriuresis, resulting in a statistically significant positive sodium balance. In other words, our methods were sensitive enough to document sodium retention at a point in time when SAD rats were hypertensive. This observation alone provides convincing evidence that sodium retention occurred 2 days after SAD despite an elevated arterial pressure. Similarly, a moderate sodium retention was observed after ABD, although this was not statistically significant. To further determine whether small but insignificant changes in daily sodium balance were responsible for the normalization of arterial pressure after barodenervation, we calculated the net cumulative sodium balance for both ABD and SAD rats. If pressure natriuresis was responsible for the return of arterial pressure to control levels, then cumulative sodium balance would be negative at the same point in time that arterial pressure returned to control. However, 1 wk after ABD or SAD there was a tendency for a positive net cumulative sodium balance in both groups. Again, however, these changes were not statistically significant. Overall, taking into consideration the fact that both daily and cumulative sodium balance tended to be positive after ABD and SAD, it is unlikely that increased precision of the measurements of body fluid balance would have revealed an opposite response, i.e., a negative sodium balance after barodenervation.

A more direct approach to this question would be to chronically servo-control renal arterial pressure after barodenervation. This type of “open-loop” analysis would enable one to maintain renal perfusion pressure constant after barodenervation, thereby preventing pressure natriuresis. Theoretically, if pressure natriuresis was entirely responsible for the absence of hypertension in barodenervated animals, “clamping” renal arterial pressure at normal levels would result in a sustained hypertension of greater magnitude. Indeed, preliminary studies utilizing this technique in chronically instrumented baboons suggest that pressure natriuresis may contribute to the normalization of arterial pressure after barodenervation in this species (21). The results of the present study suggest that maintenance of a constant renal perfusion pressure after barodenervation would increase the magnitude and duration of the transient hypertensive period but would not ultimately prevent the normalization of arterial pressure. Under servo-controlled conditions, the antinatriuretic response to increased renal nerve activity would be enhanced, since it would not be opposed by an elevated renal arterial pressure. This would result in an even greater retention of sodium that was observed in the present study, and presumably result in a transient hypertensive period of greater magnitude and longer duration. However, as discussed below, our results suggest that the elevated renal sympathetic activity in response to barodenervation is not sustained chronically and therefore the hypertension is not maintained. We hypothesize that the normalization of arterial pressure after barodenervation in the rat is ultimately due to the return of sympathetic tone to control levels, rather than pressure natriuresis.

Our results appear to contradict previous investigations of body fluid volume regulation after barodenervation in the rat. Alexander reported a transient (<1 wk) decrease in plasma volume after SAD (1). Fink and coworkers (11) have reported that plasma volume was contracted for as long as 1 mo after ABD. However, it is important to note that a subsequent study found that contraction of plasma volume after ABD was due to a reduced water intake rather than pressure diuresis (24). Kline and coworkers (15) also reported adipsia after ABD in rats, however, a similar response was observed in sham rats in that study. We did not observe a decrease in ad libitum water intake after either ABD or SAD. Comparisons of water intake after ABD or SAD between our study and others is complicated by the fact that >50% of the daily water intake was administered by intravenous infusion in the present investigation.

Our finding that arterial pressure was not chronically elevated after SAD is in agreement with previous studies in the rat (17, 23), rabbit (20), dog (7), and monkey (6). Our results are in conflict, however, with reports of chronic hypertension after SAD in rats (1, 2, 5, 16, 22), rabbits (8), and baboons (4). We used the same barodenervation technique (16) used by others studying the rat (1, 2, 5, 16, 17, 22). The effectiveness of our technique was tested in two ways. First, we determined the effect of ABD and SAD on the lability of arterial pressure. ABD resulted in a ~1.7-fold increase in lability, nearly identical to a 1.6-fold increase previously reported after ABD in the rat (10). We observed a 2.5-fold increase in the lability of arterial pressure after SAD, which is similar to what has been previously reported in several species (3-5, 7, 17, 22). A second test of the completeness of our barodenervation methods was to determine the gain of baroreflex control of HR. As reported by others, the gain of this reflex was reduced by ABD (11) and abolished by SAD (23). It is important to note that the baroreflex test was conducted 5 days after barodenervation, when arterial pressure had returned to control. Therefore, it is not likely that normalization of arterial pressure can be explained by a return of baroreflex activity.

In the present investigation, arterial pressure was measured at the same time each day, in conscious unrestrained rats, using computerized techniques. As previ-
ously shown (7), it is essential to obtain a large number of samples to accurately measure arterial pressure in SAD animals because of the large variability of the signal. We did not measure arterial pressure over a 24-h period, since previous investigations in both ABD (10) and SAD (5) rats have shown no difference between daily intermittent measurements and 24 h recordings.

In contrast to previous studies in the rat (10, 11, 15, 24, 25), we did not find that ABD resulted in a sustained hypertension. A likely explanation for this discrepancy is the use of direct computerized measurement of arterial pressure in our study vs. either indirect measurement in restrained rats (15) or noncomputerized measurements (10, 11, 24, 25) in other studies.

Hypothetical Role of Sympathetic Tone in Normalization of Arterial Pressure in Barodenervated Rats

Our results suggest that the failure of either ABD or SAD to produce a sustained hypertension in the rat was not due to pressure natriuresis mechanisms. An alternative hypothesis, as discussed in the introduction, is that the effective increase in sympathetic activity was not maintained chronically. This hypothesis is supported by the data summarized in Fig. 9 and the following assumptions. First, it is assumed that vascular tone and HR are directly related to sympathetic nerve activity (SNA) and that sodium excretion is inversely related to SNA. The second assumption is that barodenervation increases sympathetic activity to the peripheral vasculature, heart, and kidney. Based on these assumptions and the data shown in Fig. 9, we propose the following. The first day after barodenervation, both arterial pressure and HR were increased. However, depending on the magnitude of the opposing effects, increased renal arterial pressure, and increased renal SNA, sodium excretion either did not change significantly (ABD) or (assuming MAP increased more initially after SAD than ABD) increased after SAD. Over the next 2 days, sympathetic activity began to decrease but still remained elevated above control. Hence, the vasoconstrictor response diminished and arterial pressure began to fall as did HR. However, the effects of increased renal nerve activity on sodium excretion became evident, since renal perfusion pressure had returned to near normal and no longer opposed the sympathetically mediated antinatriuresis. Finally, within 4 to 5 days after denervation, sympathetic tone returned to normal, and therefore arterial pressure, HR, and sodium excretion also returned to control levels.

This hypothesis is supported by other studies in conscious rats. Plasma catecholamines are elevated 1 wk after SAD but return to normal by 3 wk after barodenervation (2). Two to six weeks after SAD, HR is normal (17) or only slightly elevated (3). Arterial pressure, cardiac output, and peripheral vascular resistance are not different between sham and SAD rats (23), and the depressor response to ganglionic blockade in SAD rats is not different from sham rats (3). Similarly, we have found that the depressor response to total autonomic blockade is increased the first day after barodenervation (when sympathetic activity is assumed to be elevated) but has returned to control 4 days later (18). Taken together, these observations strongly suggest that sympathetic tone returns to normal after barodenervation. However, without direct recordings of sympathetic nerve discharge, it is not possible to determine whether actual nerve activity is diminished over time or whether other factors alter the release of or vascular response to noradrenaline.

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