Arterial baroreceptors control plasma vasopressin responses to graded hypotension in conscious dogs

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Arterial baroreceptors control plasma vasopressin responses to graded hypotension in conscious dogs. Am. J. Physiol. Regulatory Integrative Comp. Physiol. 278: R469–R475, 2000.—We studied the role of cardiac and arterial baroreceptors in the reflex control of arginine vasopressin (AVP) and renin secretion during graded hypotension in conscious dogs. The dogs were prepared with Silastic cuffs on the thoracic inferior vena cava and catheters in the pericardial space. Each experiment consisted of a control period followed by four periods of inferior vena cava constriction, during which mean arterial pressure (MAP) was reduced in increments of ~10 mmHg. The hormonal responses were measured in five dogs under four treatment conditions: 1) intact, 2) acute cardiac denervation (CD) by intrapericardial infusion of procaine, 3) after sinoaortic denervation (SAD), and 4) during combined SAD+CD. The individual slopes relating MAP to plasma AVP and plasma renin activity (PRA) were used to compare the treatment effects using a 2 × 2 factorial analysis. There was a significant (P < 0.01) effect of SAD on the slope relating plasma AVP to MAP but no effect of CD and no SAD × CD interaction. In contrast, the slope relating PRA and MAP was increased (P < 0.05) by SAD but was not affected by CD. These results support the hypothesis that stimulation of AVP secretion in response to graded hypotension is primarily driven by unloading arterial baroreceptors in the dog.

Angiotensin; antidiuretic hormone; cardiac receptors; atrial receptors; ventricular receptors; blood volume; blood pressure

We have proposed that the stimulation of arginine vasopressin (AVP) secretion in response to hypovolemia arises primarily from the unloading of arterial baroreceptors in the dog (20, 21). Although this hypothesis contrasts sharply with earlier concepts involving atrial receptors (17), it is supported by a number of observations. The acoustic blockade of the cardiac nerves by pericardial infusion of a local anesthetic has no effect on plasma AVP in euvolemic dogs with baroreceptors intact or after sinoaortic denervation (SAD), suggesting that cardiac receptors do not tonically inhibit AVP release (13, 18, 21). Also, we (12, 21) and others (18) have found no effect of cardiac denervation (CD) on the AVP response to hemorrhage, suggesting that stimulation of cardiac receptors is not an essential component of the response. In contrast, SAD results in a marked decrease in the slope of the relationship between plasma AVP and arterial pressure during hemorrhage (21). Finally, we have been unable to detect a significant rise in plasma AVP in response to either gradual constriction of the inferior vena cava (14), a model of central hypovolemia, or hemorrhage (12, 21) until there is a decline in arterial pressure. These observations suggest a strong relationship between mechanisms controlling arterial pressure and the secretion of AVP.

In a recent review, Shadt and Ludbrook (16) observed that integrated responses to progressive hemorrhage in conscious animals and humans can be categorized into two phases: an initial “sympathoexcitatory” phase, in which mean arterial pressure (MAP) is maintained at control levels by sympathetically mediated increases in peripheral vascular resistance, followed by a “sympathoinhibitory” phase characterized by a precipitous fall in MAP secondary to an acute decrease in sympathetic efferent tone. They also observed that the increase in plasma AVP during hemorrhage coincides with the appearance of the sympathoinhibitory phase, i.e., simultaneous with the abrupt decline in MAP. Thus the progressive hemorrhage model does not offer suitable conditions to examine the steady-state relationship between graded reductions in MAP and plasma AVP.

The object of the present study was to establish the relationship between plasma AVP and graded reductions in MAP in intact (i.e., both arterial and cardiac receptors functional), conscious dogs. Graded thoracic inferior vena cava constriction (IVCC), a model of central hypovolemia, was used to produce step reductions in MAP. The participation of cardiac receptors in the response was tested by repeating the IVCC protocol during pericardial infusion of procaine, an acute reversible model of CD (13). The participation of arterial baroreceptors was tested by repeating the IVCC protocol after SAD. On the basis of our working hypothesis, we predicted that SAD would significantly alter the relationship between arterial pressure and plasma AVP but CD would have no effect. We also measured plasma renin activity (PRA), an index of renin secretion, to determine if removal of cardiac or arterial baroreflex signals altered the renin response to graded decreases in MAP.

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METHODS

General procedures. Experiments were performed on five adult mongrel dogs (4 females and 1 male) weighing between 19 and 24 kg. The dogs were housed in a room maintained at 22 ± 2°C and 70% humidity with a 12:12-h light-dark cycle. Each day between 1600 and 1800, the dogs were administered oral prophylactic antibiotic treatment with sulfamethoxazole (800 mg) and trimethoprim (160 mg) and fed a mixture of dry chow and canned food sufficient to maintain a constant body weight. The food was consumed within 10 min of presentation, and sodium intake on this diet averaged 2–3 meq·kg^{-1}·day^{-1}. Water was available ad libitum.

Patency and sterility of the vascular catheters were maintained by filling them with a mixture of heparin (1,000 U/ml, Elkins-Sinn, Cherry Hill, NJ) and penicillin G potassium (20,000 U/ml, Eli Lilly, Indianapolis, IN), which was replaced a minimum of every 72 h. To ensure that the dogs were free of infection throughout all aspects of the study, rectal temperatures were taken on a weekly basis and on the morning before experiments. Rectal temperatures were always <39°C, indicating that the dogs were free of infection throughout the duration of the study.

Surgical procedures. In all surgical procedures, the dogs were sedated with acepromazine maleate (0.2 mg/kg iv; Tech America, Elwood, KS) and anesthetized with pentobarbital sodium (25 mg/kg iv; Fort Dodge Laboratories, Fort Dodge, IA). During the 7-day postoperative period after each surgical procedure, the dogs were treated with enrofloxacin (Baytril, Mobay, Shawnee, KS; 2.5 mg/kg) twice daily to provide antibacterial coverage and oxyphrine (Numophar, Du Pont Pharmaceuticals) as required to provide analgesia. The first procedure was a right thoracotomy (4th interspace) to implant a Silastic cuff (Hazen Everett, Teenack, NJ) on the inferior vena cava and place catheters in the right atrium and pericardial space. The chest was then closed, and negative intrapleural pressure was established to completely reflate the lungs. Additional Tygon catheters were introduced into a femoral artery and vein and advanced to the abdominal aorta and inferior vena cava, respectively. All catheters were tunneled subcutaneously to exit between the shoulder blades and were protected by placement in a pouch sewn to the underside of a nylon jacket (Alice King Chatham Medical Arts, Los Angeles, CA). At least 2 wk were allowed for recovery.

After completion of the experiments in the intact and acute CD conditions, the dogs were anesthetized and the carotid sinus region was exposed via a ventral midline neck incision. The internal carotid arteries were ligated and cut together with all other vessels originating from the external carotid proximal to the lingual artery. The adventitia between the cranial thyroid artery and the lingual artery was stripped and painted with 5% phenol in ethanol bilaterally. At least 2 wk were allowed for recovery from this procedure. Finally, the dogs were anesthetized and the aortic arch was exposed via a left thoracotomy at the fourth intercostal space. All visible nerves in the region of the arch were cut, and the adventitia of the descending aorta to the level of the second thoracic artery was stripped. In addition, the adventitia of the brachiocephalic and subclavian trunks was stripped to the level of the second bifurcation of each vessel. Finally, the vessels were painted with 5% phenol solution. The chest was then closed, and negative pressure was reestablished to ensure complete expansion of the lungs. At least 3 wk were allowed before experimentation was resumed.

Verification of cardiac nerve blockade and effectiveness of SAD. Blockade of cardiac efferent nerves during pericardial infusion of procaine was tested by measuring heart rate (HR) responses to bolus administration of nitroglycerine (NG; 15 µg/kg, American Critical Care, McGraw Park, IL) and phenylephrine (PE; 5 µg/kg, Winthrop-Breon Laboratories, New York, NY) before and during acute CD. Cardiac afferent nerve blockade was tested by bolus injection of veratridine (50 µg) into the right atrium before and during acute CD. Effectiveness of SAD was determined by measuring the HR responses to bolus injections of NG and PE. HR responses reported below are based on a 10-s sample corresponding to the peak of the change in MAP. In the intact condition, PE increased MAP 38 ± 3 mmHg and HR decreased 28 ± 3 beats/min, whereas NG decreased MAP 26 ± 3 mmHg and HR increased 55 ± 12 beats/min. During acute CD, PE increased MAP 54 ± 4 mmHg with no change in HR (0 ± 0 beats/min) and NG decreased MAP 63 ± 8, again with no change in HR (1 ± 1 beat/min). After SAD, PE increased MAP 49 ± 8 mmHg, with no change in HR (1 ± 3 beats/min), and NG decreased MAP 50 ± 5 mmHg, with no change in HR (1 ± 1 beat/min). HR fell 39 ± 6 beats/min in response to veratridine in the intact condition, did not change during CD, and fell 81 ± 13 beats/min after SAD.

After all studies were completed, the dogs were killed with an overdose of pentobarbital sodium to examine the hearts for central nervous system autonomic afferent and efferent fibers from the thoracic cavity and the right atrium were isolated and tied together. The right atrial appendages were tied together, and the right atrial appendage of the heart was tied off. The pericardium was opened, and the heart was removed and immersed in 0.3 M EDTA for measurement of PRA or heparin for measurement of plasma osmolality and AVP. The order of experiments was randomized, and at least 4 days were allowed between experiments.

Methods of measurement. Arterial and right atrial pressures (RAP) were measured using Cobe transducers and recorded on a Grass model 7d polygraph. The pressure transducers were adjusted to heart level for each dog. The output from the polygraph was fed to a Buxco cardiovascular analyzer (model CVA-1, Buxco Electronics) connected to an online data-acquisition system (Keithly, Series 500) that stored the results for analysis. Plasma osmolality was determined by freezing-point depression (Advanced model 3W). Plasma AVP was determined by RIA after extraction with phenylephrine (PE; 5 µg/kg, Winthrop-Breon Laboratories, New York, NY) before and during acute CD. Cardiac afferent nerve blockade was tested by bolus injection of veratridine (50 µg) into the right atrium before and during acute CD. Effectiveness of SAD was determined by measuring the HR responses to bolus injections of NG and PE. HR responses reported below are based on a 10-s sample corresponding to the peak of the change in MAP. In the intact condition, PE increased MAP 38 ± 3 mmHg and HR decreased 28 ± 3 beats/min, whereas NG decreased MAP 26 ± 3 mmHg and HR increased 55 ± 12 beats/min. During acute CD, PE increased MAP 54 ± 4 mmHg with no change in HR (0 ± 0 beats/min) and NG decreased MAP 63 ± 8, again with no change in HR (1 ± 1 beat/min). After SAD, PE increased MAP 49 ± 8 mmHg, with no change in HR (1 ± 3 beats/min), and NG decreased MAP 50 ± 5 mmHg, with no change in HR (1 ± 1 beat/min). HR fell 39 ± 6 beats/min in response to veratridine in the intact condition, did not change during CD, and fell 81 ± 13 beats/min after SAD.

Experimental protocols. Experiments were conducted between 0800 and 1300 in a quiet room with the dog in a sling (Alice King Chatham Medical Arts), which provided support but minimal restraint. Each experiment began with a 20-min control period to establish baseline values for MAP and HR, followed by pericardial infusion of either 2% procaine (Abbott Laboratories, North Chicago, IL) or 0.9% saline (initially 1 ml/min for 10 min and then reduced to 0.2 ml/min for the duration of the experiment). Twenty minutes after the beginning of the pericardial infusion, either IVCC was begun to reduce MAP in four steps of −10 mmHg each and maintained for 10 min or a time control experiment was performed. Blood samples (10 ml each) were collected at the beginning and end of the control period, 1 min before the first period of IVCC and at the end of each period of IVCC. Blood samples were replaced with an equal volume of saline. The blood samples were immediately aliquoted into chilled tubes containing 0.3 M EDTA for measurement of PRA or heparin for measurement of plasma osmolality and AVP. The order of experiments with arterial baroreceptors intact and after SAD was randomized, and at least 4 days were allowed between experiments.

Verification of cardiac nerve blockade and effectiveness of SAD. Blockade of cardiac efferent nerves during pericardial infusion of procaine was tested by measuring heart rate (HR)
as nanograms of ANG I generated per milliliter of plasma during a 3-h incubation at pH 6.0 (RIANEN RIA Kit, Du Pont, Wilmington, DE). The intra- and interassay coefficients of variability were 5% and 12%, respectively.

Data analysis. A one-way repeated-measures ANOVA was used to analyze hemodynamic changes in response to IVCC within each treatment condition (25). A difference was considered significant if \( P < 0.05 \). Dunnett’s test (26) was used to compare responses during IVCC with the control means. A two-way repeated-measures ANOVA was used to compare changes in RAP across treatments (25). The effects of the treatments on hypotension-induced secretion of AVP and renin were compared using two approaches. In the first approach, the individual slopes relating the plasma level of each hormone to MAP were estimated using the least-squares method (26). The slopes in each of the four treatment conditions were compared using a 2 \times 2 factorial analysis (25). In the second approach, the pooled data for each treatment condition were used to determine the relationship between plasma hormone concentration and MAP. The slopes derived from the pooled responses were then compared. The values for plasma AVP during hypotension displayed excessive heterogeneity (Bartlett’s test) and were transformed logarithmically before analysis.

RESULTS

Time-control experiments. In the intact condition, there were no significant changes in MAP, HR, plasma AVP, or PRA during the 90-min experiment (Fig. 1). In contrast, acute CD caused significant increases in both HR and MAP, but no change in plasma AVP, and a small but significant decline in PRA. At least 3 wk after SAD, resting MAP and plasma AVP were similar to the intact state, but HR was significantly elevated and PRA was marginally different (\( P = 0.051 \)). Nevertheless, these variables were stable over the 90-min time-control experiment. As observed previously (21), pericardial infusion of procaine in SAD dogs led to a greater increase in MAP compared with the intact condition but no change in plasma AVP. However, there was a significant decline in PRA during pericardial procaine, as was observed during pericardial procaine with the arterial baroreceptors functional. The most likely explanation for the decreases in PRA in both the CD and SAD+CD conditions was the increase in MAP associated with pericardial administration of procaine.

Hemodynamic and hormonal responses to graded IVCC. The hemodynamic responses to graded IVCC are shown in Fig. 2. The values for MAP and HR plotted at the zero period are the 5-min averages before beginning IVCC and correspond to the averages at 40 min in the time-control series. The means corresponding to IVCC periods 1–4 represent the average over the 5-min period preceding the blood sample. The decreases in MAP in each period were similar within each treatment, and the absolute levels of MAP reached during the fourth period of IVCC were similar in all four conditions. However, the magnitude of the change in MAP in the SAD+CD condition was greater (\( P < 0.05 \)) because MAP was much higher at the beginning of IVCC. HR increased significantly in response to the initial reduction in MAP (first period of IVCC) in the intact condition and remained significantly elevated.

However, HR did not increase further in response to greater decreases in MAP. There was no change in HR in response to hypotension in the CD, SAD, and SAD+CD conditions. There was a significant decline in RAP (\( P < 0.01 \)) in response to the first period of IVCC in all four treatment conditions. The decreases in RAP in the four conditions were not different (\( P = 0.38 \)).
The hormonal responses to graded hypotension are shown in Fig. 3. Plasma AVP increased significantly during the first period of IVCC in the intact and CD conditions, rising 20 ± 10 and 23 ± 14 pg/ml above control, respectively. Plasma AVP did not change significantly in the SAD and SAD+CD conditions during the first period of IVCC even though the decreases in MAP were similar to those in the intact and CD conditions. In the second period of IVCC, small but significant increases in plasma AVP were detected in the SAD (3 ± 1 pg/ml) and the SAD+CD (5 ± 2 pg/ml) conditions. Significant increases in PRA appeared in the first period of IVCC in the CD condition, during the second period in the SAD+CD condition, and during the third period of IVCC in the intact and SAD conditions (Fig. 3). There were no significant changes in plasma osmolality during IVCC in any of the treatment conditions (data not shown).

The effects of SAD and CD on the relationship between plasma AVP and MAP are shown in (Fig. 4). Note that the regression lines shown in the figure were constructed from the mean of the individual slopes and intercepts, which are shown in Fig. 4, bottom. The individual slopes were compared using a 2 × 2 factorial analysis (25). There was a significant effect of SAD (P < 0.01), no effect of CD (P = 0.89), and no interaction between the factors (P = 0.92). This analysis indicates there was a much smaller AVP response in the SAD condition at any level of hypotension, and the response was not altered by acutely blocking cardiac reflexes.

To ensure that the comparisons based on individual responses did not introduce a bias, we reanalyzed the data by performing a regression on all the data points within each treatment (Table 1). Comparison of the slopes obtained using this approach indicated that intact and CD conditions were not different, but both differed significantly (P < 0.01) from the SAD and SAD+CD conditions. Thus this analysis produced the same conclusions as those obtained by comparing individual responses.

Reflex control of PRA using the 2 × 2 factorial approach to compare individual slopes relating PRA to MAP detected a significant effect of SAD (P < 0.05) but no effect of CD (P = 0.11) and no interaction between the two treatments (P = 0.56; Fig 5). Again, note that the lines in Fig. 5 are based on the mean of the
individual slopes and intercepts (shown in Fig. 5, bottom), not the individual data points. This analysis suggests that there is a greater increase in PRA for the same reduction in MAP after SAD. When the pooled data within each treatment were reanalyzed, the regression of PRA on MAP in the intact condition did not reach statistical significance \((P = 0.22; \text{Table 1})\), although significance was attained in the other three conditions. Furthermore, in two of five dogs, the individual slope relating PRA to MAP was not statistically significant in the intact condition.

### DISCUSSION

We hypothesized that arterial baroreceptor firing provides the principal afferent signal controlling AVP release in response to hypovolemia and hypotension \((20, 21)\). The present study focused on the participation of arterial baroreceptors in the control of AVP secretion during hypotension. If reductions in arterial baroreceptor firing during graded hypotension cause the increase in AVP secretion in intact animals, then the hypothesis predicts that SAD should reduce the slope relating plasma AVP to MAP. The data shown in Fig. 3 clearly support this prediction. Furthermore, the data also show that the AVP response during acute CD was not different from the intact response, suggesting that cardiac receptors are not involved in the stimulation of AVP secretion in this model of hypotension. If arterial baroreceptors are the only source of stimulation to mechanisms controlling AVP secretion in response to hypotension, SAD should eliminate the response. The results do not support this prediction. However, the increment in plasma AVP was reduced by at least 80% in the SAD condition compared with the intact response at each level of hypotension. Therefore, we conclude that the normal rise in plasma AVP in response to hypotension is largely dependent on the presence of functional signals from the arterial baroreceptors in the dog.

### Table 1. Relationship between MAP, plasma AVP, and PRA in intact and denervated dogs based on all data pairs within each treatment condition

<table>
<thead>
<tr>
<th>Condition</th>
<th>AVP</th>
<th>PRA</th>
</tr>
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<tbody>
<tr>
<td></td>
<td>Slope Intercept (r^2)</td>
<td>Slope Intercept (r^2)</td>
</tr>
<tr>
<td>Intact</td>
<td>-7.66* 704 0.56</td>
<td>-0.03 4.4 0.07</td>
</tr>
<tr>
<td>CD</td>
<td>-5.70* 656 0.61</td>
<td>-0.06* 8.1 0.54</td>
</tr>
<tr>
<td>SAD</td>
<td>-1.10* 106 0.51</td>
<td>-0.14* 14.8 0.54</td>
</tr>
<tr>
<td>SAD+CD</td>
<td>-1.62* 187 0.63</td>
<td>-0.10* 13.4 0.53</td>
</tr>
</tbody>
</table>

Each regression was based on 25–27 pairs of data points obtained in each treatment condition. MAP, mean arterial pressure; AVP, arginine vasopressin; PRA, plasma renin activity; CD, cardiac denervated; SAD, sinoaortic denervated. * Significant slope \((P < 0.05)\).
There are, however, competing ideas as to the source of the stimulus to AVP secretion during hypovolemia and hypotension. Wang et al. (23, 24) proposed that ventricular receptors provide the principal volemic stimulus to AVP secretion. They observed that ventricular denervation produced a dramatic reduction in the AVP response to hemorrhage, suggesting that activation of ventricular receptors caused the increase in AVP secretion. Previously, Oberg and Thoren (11) identified a population of ventricular receptors with vagal afferents that were activated by severe hemorrhage and caused bradycardia and the inhibition of sympathetic outflow to kidney and muscle in the cat. Oberg and Thoren (11) suggested that the receptors were stimulated by distortion caused by intense ventricular contraction at low ventricular volumes. Subsequent studies in dogs and other species have also reported that stimulation of ventricular receptors by a variety of means can cause bradycardia and a fall in sympathetic activity (6). Thus activation of ventricular receptors results in a response that is quite similar to the sympathoinhibitory response to hypovolemia. Therefore, the concept that these same receptors initiate both the sympathoinhibitory phase and the massive stimulation of AVP secretion is very appealing. However, a study by Morita and Vatner (10) showed that cervical vagotomy did not prevent the decrease in renal nerve activity during severe hemorrhage in conscious dogs. Furthermore, a report by Shen et al. (18) and two studies from this laboratory (12, 21) were unable to demonstrate a significant effect of CD on either the ability to maintain MAP or the AVP response to hemorrhage. Thus, at present, there is no obvious way to reconcile the results of Wang et al. (23, 24), which clearly point toward a ventricular receptor mechanism, and the results of others, which do not support an important cardiac component in the AVP response to either hemorrhage (12, 18, 21) or hypotension (Fig. 3).

The stimulus to AVP secretion in response to hypotension after SAD or combined SAD + CD is unknown (Fig. 3). The increases in response to left atrial infusion of AVP at a dose of 10.2 μg/kg min were small, but there was an obvious increase in plasma AVP in four of five dogs when MAP fell <60 mmHg (Fig. 4). Because the denervation of the arterial baroreceptors would also eliminate afferents from carotid and aortic chemoreceptors, they could not have contributed to the response. It has been reported that stimulation of the central end of the thoracic vagus and stimulation of various somatic sensory nerves cause increases in plasma AVP in anesthetized dogs (9). More recently, Gieroba and Blessing (3) reported that stimulation of the abdominal vagus stimulates large increases in plasma AVP in anesthetized rabbits, and the effect was blocked by vagal section or injection of muscimol in the A1 neurons of the caudal ventrolateral medulla. The same A2 neurons are also thought to be involved in hemorrhage-induced secretion of vasopressin. Although speculative, it is possible that these abdominal afferents convey signals from gut receptors activated by ischemia and this is the source of AVP stimulation in baroreceptor-denervated dogs.

It is well established that reflex mechanisms can alter the level of renal sympathetic nerve activity and are involved in the control of renin secretion (2, 20). However, there appears to be general agreement that increases in renin secretion obtained in response to hypotensive hypovolemia are not dependent on either cardiac or arterial baroreceptor afferents (15, 21, 23). The intrarenal baroreceptor mechanism is likely to be responsible for the increased secretion in response to decreased renal perfusion pressure, although participation of the macula densa mechanism has not been excluded. Thus we did not expect to find remarkable differences in PRA among the treatments in this study. To our surprise, there was a significant increase in PRA in the intact condition when evaluated by ANOVA (Fig. 3), but the slope of the relationship between PRA and MAP was not significant on the basis of pooled regression of all the data points. Furthermore, the magnitude of the increase in PRA in the SAD condition was greater than that in the intact state, even though the MAP were identical. The difference in PRA between the CD and SAD + CD conditions was almost as large, but the MAP were not as evenly matched so we will focus on the former treatments for discussion.

A plausible explanation for the smaller increase in PRA in the intact condition compared with the response after SAD is that plasma AVP, which was much higher in the intact condition, acted to inhibit renin secretion. A number of studies reported that AVP is inhibitory to renin secretion (1, 4). Recently, Gregory and colleagues (4, 5) reported that both renal denervation and SAD + CD prevented the inhibition of renin secretion in response to infusion of AVP in conscious dogs. These observations suggest that AVP can inhibit renin secretion via an effect on reflex control of renal nerve activity. However, it is very likely that renal nerve activity in an intact dog was increasing during graded hypotension, not decreasing, and certainly greater than renal nerve activity in the SAD condition. Thus it is not plausible to argue that AVP was inhibiting renin secretion reflexly in the present study. However, there is also the possibility that AVP acted directly on intrarenal mechanisms to inhibit renin secretion. Johnson et al. (7) reported that intrarenal infusion of AVP at a dose that does not cause a rise in MAP inhibits renin secretion in conscious dogs. Furthermore, Vandonen (22) observed inhibition of renin secretion by AVP in the isolated rat kidney. Thus the large increases in plasma AVP during the last two periods of hypotension in the intact and CD conditions may explain the relatively small increments in PRA compared with the SAD condition.

In summary, the results of this study provide additional evidence that arterial baroreceptors play an important role in the control of AVP secretion. With baroreceptors functioning normally, step decreases in MAP caused graded increases in plasma AVP. After SAD, the increases in plasma AVP were reduced by 80% or more in response to identical decreases in MAP. Furthermore, acute CD did not alter the relationship between MAP and plasma AVP in baroreceptor intact dogs or after SAD. Taken together, these results indi-
icate that functional arterial baroreceptors are essential for a normal AVP response to hypotension in the dog. In contrast, the results provide no evidence that either cardiac or arterial baroreceptors play an essential role in the stimulation of renin secretion in response to graded hypotension.

Perspectives

The concept that atrial receptors with vagal afferents are a major influence in the control of blood volume via alterations in renin and AVP secretion is firmly entrenched in the experimental literature. The general acceptance of this theory is evident from the fact that “volume” receptors and “atrial” receptors are often used synonymously. The present study, based on a model of central hypovolemia, together with previous studies from this laboratory (12, 14, 21), suggests the need for a reevaluation of this hypothesis. The results do not rule out the possibility that unloading atrial receptors can stimulate secretion of AVP and renin, rather they show that other mechanisms can fully account for the changes in AVP and PRA observed during reductions in atrial and arterial pressure. The observation that SAD does permanently alter the pattern of AVP secretion during hypotension implies that arterial baroreceptor reflexes may be much more important than previously thought, at least in the dog.

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