The Contribution of Vasopressin and Angiotensin to the Maintenance of Blood Pressure After Autonomic Blockade

MASAO HIWATARI, PETER L. NOLAN, AND COLIN I. JOHNSTON

SUMMARY The contribution of vasopressin and angiotensin II to the maintenance of blood pressure after short-term autonomic blockade was investigated in conscious Long-Evans and Brattleboro (vasopressin-deficient; hereditary diabetes insipidus) rats. After short-term autonomic blockade by atropine (1 mg/kg), propranolol (5 mg/kg), and pentolinium (5 mg/kg and 10 mg/kg/hr), the fall in blood pressure was significantly greater in Brattleboro rats than in Long-Evans rats (48 ± 3 vs 32 ± 2 mm Hg; p < 0.01). Administration of the vasopressin vascular receptor antagonist D(CH2)5Tyr-(Me)AVP (2 μg/kg) caused further blood pressure decreases only in Long-Evans rats, so that the final blood pressure in both groups was identical. Administration of enalaprilat (10 mg/kg), an angiotensin converting enzyme inhibitor, further reduced blood pressure in both strains. When enalaprilat was given first after autonomic blockade, it reduced blood pressure in Brattleboro rats but not in Long-Evans rats. Administration of the vasopressin antagonist after enalaprilat further reduced blood pressure only in Long-Evans rats. The fall in blood pressure following vasopressin blockade was greater than that occurring after angiotensin converting enzyme inhibition (14 ± 1 vs 6 ± 1 mm Hg; p < 0.05) in autonomic blockaded Long-Evans rats. Plasma levels of vasopressin in Long-Evans rats increased markedly after short-term autonomic blockade, whereas plasma renin and angiotensin II levels were unchanged. Plasma angiotensin II levels were increased by the vasopressin antagonist and decreased by enalaprilat. We conclude that, due to sympathetic nervous system blockade and consequent blunting of renal renin release, vasopressin has a greater capacity than the renin-angiotensin system for maintaining blood pressure after short-term autonomic blockade.

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KEY WORDS • renin • Brattleboro rat • hypertension • hypotension • converting enzyme inhibition • vascular tone

BLOOD pressure (BP) regulation is a multifactorial phenomenon involving numerous complex interactions.1-3 The three major pressor mechanisms influencing BP are the autonomic nervous system and the vasoactive peptides angiotensin and vasopressin. The importance of the autonomic nervous system in cardiovascular control mechanisms is well defined, and the role of the renin-angiotensin system in various physiological and hypertensive or hypotensive states has been the subject of considerable investigation.1-3 Arginine vasopressin (AVP) has been shown to play a substantial role in maintaining BP during hypotensive and volume-depleted states such as hemorrhage4-5 and dehydration.6 A possible pressor role for AVP also has been postulated in some hypertensive models.5,7-9

Although complicated interactions have been reported among these pressor mechanisms,1-3,5 the autonomic nervous system has been established as the dominant mechanism for BP maintenance. However, when the autonomic nervous system is blocked acutely, which results in prompt and marked hypotension, secondary pressor mechanisms may be activated to compensate for the decreased BP. The renin-angiotensin system is one such mechanism that may be activated after autonomic blockade since hypotension activates the renal baroreceptor and thus stimulates renin secretion. Conversely, elimination of the sympathetic outflow reduces renin release.7 Recently, inappropri-
ate secretion of AVP was demonstrated in patients with progressive autonomic failure who suffer from severe postural hypotension; the importance of AVP for BP maintenance after α1-adrenergic receptor blockade in rats also has been demonstrated. These reports suggest that AVP is another important pressor mechanism that may be activated after autonomic blockade. Maintenance of BP by AVP has recently been demonstrated in ganglion-blocked, anesthetized dogs.

The present study was designed to investigate the relative roles of the renin-angiotensin system and AVP after short-term blockade of the autonomic nervous system in conscious animals. Specific inhibitors of angiotensin converting enzyme and of vasopressin vascular receptors were used in this study, as was the Brattleboro rat, which is genetically deficient in endogenous AVP. To avoid the effects of anesthesia on hormonal, sympathetic, and cardiovascular functions, all experiments were performed in fully conscious rats.

Methods

Male Long-Evans rats (LE), weighing 260 to 380 g (16–28 weeks of age), and male homozygous Brattleboro rats with hereditary hypothalamic diabetes insipidus, weighing 230 to 330 g (16–26 weeks of age), were used. (The latter strain of rats will hereinafter be identified by the abbreviation DI.) All rats had free access to food and water throughout the experimental period.

With the rats under ether anesthesia, the left femoral artery and bilateral femoral veins were cannulated using polyethylene tubing. The catheters were tunneled subcutaneously and exteriorized at the nape of the neck. They were filled with heparinized (1000 U/ml) saline solution and sealed by heating. Rats were allowed at least 24 hours to recover from the operation. All studies were performed using fully conscious rats. During each experiment, rats were placed in rectangular boxes (30 × 17 × 17 cm) with no restriction of movement. The arterial catheter was connected to a Statham P23Db pressure transducer (Statham Instruments Inc., Oxnard, CA, USA) for BP measurement. Pulse period was monitored with a period meter (Model 440, Gould-Brush, Cleveland, OH, USA). Heart rate was calculated from the measured pulse period. One hour was allowed for stabilization, after which rats generally were resting.

The following drugs were used: atropine sulfate (David Bull Laboratories, Sydney, Australia); dl-propranolol hydrochloride (Sigma Chemical Corp., St. Louis, MO, USA); pentolinium tartrate (Sigma); enalaprilat, diacid form of enalapril maleate (enalaprilic acid, MK-422, Merck Sharp & Dohme Research Laboratories, West Point, PA, USA); [1-(β-mercapto-β,β-cyclopentamethylenepropionic acid), 2-(O-methyl)-tyrosine] arginine vasopressin [α(CH)23Tyr-(Me)AVP, Peninsula Laboratories, Belmont, CA, USA]; and [1-(β-mercapto-β,β-cyclopentamethylenepropionic acid), 8-α-arginine] vasopressin [α(CH)23DAVP, supplied by Dr. M. Manning]. All drugs were dissolved in 0.9% NaCl solution.

Experimental Groups

Group 1

Eight LE and eight DI received intravenous bolus injections of atropine (1 mg/kg), propranolol (5 mg/kg), and pentolinium (5 mg/kg) followed by constant infusion of pentolinium (10 mg/kg/hr). This treatment produced a total pharmacological, autonomic blockade that was tested by (1) blockade of the pressor response to temporary bilateral carotid occlusion in anesthetized rats and (2) blockade of heart rate response to intravenous infusion of phenylephrine (10 μg/kg/min) and sodium nitroprusside (50 μg/kg/min) in conscious rats. After blockade, the BP and pulse period were monitored continuously for 30 minutes. In another group of LE trunk blood was collected by decapitation for the measurement of plasma renin activity (PRA) and plasma levels of angiotensin II (ANG II) and AVP 10 minutes after administration of saline (n = 12) or total autonomic blockade (n = 7).

Group 2

Using the same methods as in Group 1, total autonomic blockade was established in eight LE and eight DI. Ten minutes later, the vasopressin vascular receptor antagonist atropine sulfate (α(CH2)3Tyr(Me)AVP (2 μg/kg) was injected intravenously as a single bolus. Ten minutes later, a single bolus of the angiotensin converting enzyme inhibitor enalaprilat (10 mg/kg) was injected intravenously. In a separate group of rats with total autonomic blockade, these doses of (α(CH2)3Tyr(Me)AVP and enalaprilat were shown to block the pressor responses to 100 ng/kg of AVP (intravenous bolus) by 95% and to 300 ng/kg of angiotensin I (intravenous bolus) by 100%, respectively, for up to 30 minutes after administration. The BP and pulse period were recorded throughout the experiments.

Group 3

Protocol for Group 3 was the same as that for Group 2, except that the order of administration of α(CH2)3Tyr(Me)AVP and enalaprilat was reversed. Another 13 LE also received the drugs for total autonomic blockade followed 10 minutes later by a bolus injection of α(CH2)3DAVP (3 μg/kg; n = 7) or enalaprilat (n = 6). Ten minutes later, blood samples were collected by decapitation for analysis of PRA and levels of ANG II and AVP. In these rats, α(CH2)3DAVP was used as a vasopressin vascular receptor antagonist instead of α(CH2)3Tyr(Me)AVP because the latter cross-reacts with the antibody used in the radioimmunoassay to measure AVP.

Group 4

Seven LE and seven DI received α(CH2)3Tyr-(Me)AVP, enalaprilat, and the drugs for total autonomic blockade in this order in 10-minute intervals; BP and pulse period were monitored.
Group 5

Protocol for Group 5 was the same as that for Group 4, except that the order of administration of \( \text{D(CH}_2\text{)}_5\text{Tyr(Me)}\text{AVP} \) and enalaprilat was reversed.

Hormone Measurement

The blood samples for hormonal analysis were collected by decapitation. For the measurement of PRA and plasma ANG II levels, about 2.5 ml of trunk blood was collected in chilled tubes containing 250 \( \mu \)l of 1:10 British anti-Lewisite ethylenediaminetetraacetic acid with 25 units of heparin through a chilled, heparinized funnel. Blood samples for AVP assay were collected into chilled tubes, and after centrifugation, the plasma was separated and stored at \(-20^\circ\text{C}\).

The PRA was measured by an enzyme kinetic technique using a radioimmunoassay for angiotensin I generated by incubating 90 \( \mu \)l of rat plasma at 37 \( ^\circ\text{C} \) and pH 6.2 for 60 minutes. Plasma concentration of ANG II was measured by radioimmunoassay after incubation and elution of plasma with fuller’s earth. Plasma concentration of AVP was measured in 1-ml aliquots of acetone-petroleum ether-extracted plasma with a sensitive and specific radioimmunoassay for AVP.

The mean recovery of AVP was 83.2 \( \pm \) 2.8% and was linear over the range of 0 to 20 pg/ml. The assay sensitivity was 0.6 pg/ml, and the intraassay and interassay variability were 8.4% and 11.6% respectively.

Because \( \text{D(CH}_2\text{)}_5\text{Tyr(Me)}\text{AVP} \) cross-reacts (cross-reactivity = 50.0%) with the antibody used in the radioimmunoassay to measure AVP, we used \( \text{D(CH}_2\text{)}_5\text{DAVP} \) (which does not cross-react; cross-reactivity = 0.12%) to evaluate the effect of a vasopressin vascular receptor antagonist on AVP. These two vasopressin analogues have almost the same weak antidiuretic action and similar antivasopressor potencies. A 3-\( \mu \)g/kg dose of \( \text{D(CH}_2\text{)}_5\text{DAVP} \), used to examine the effect of a vasopressin vascular receptor antagonist on AVP secretion, produced a degree of antagonism to the vasopressin effect of AVP similar to that of 2 \( \mu \)g/kg of \( \text{D(CH}_2\text{)}_5\text{Tyr(Me)}\text{AVP} \) administered in the cardiovascular studies.

Statistical Methods

All values are expressed as means \( \pm \) SEM. Statistical analysis was performed by one-way or two-way analysis of variance for repeated measurements. Difference between the mean values was considered to be significant when \( p < 0.05 \).

Results

Group 1

The effects of total autonomic blockade on mean arterial pressure (MAP) and heart rate in LE and DI (Group 1) are shown in Figure 1. Total autonomic blockade caused an abrupt and marked hypotension in both groups, with the maximum falls in MAP achieved within 2 minutes. The BP had recovered slightly after 10 minutes but remained suppressed for the following 20 minutes. The DI had a greater fall in BP after autonomic blockade. The MAP for LE was significantly higher than that for DI throughout the 30-minute period after total autonomic blockade (\( p < 0.01 \)). Heart rate in DI declined progressively throughout the first 10 minutes after total autonomic blockade and then remained stable for the following 20 minutes. Heart rate in the LE fell only slightly after total autonomic blockade, a change that was not statistically significant. The heart rate after total autonomic blockade in LE was significantly higher than that in DI (\( p < 0.05 \)).

Group 2

The results after total autonomic blockade and administration of the vasopressin vascular receptor antagonist \( \text{D(CH}_2\text{)}_5\text{Tyr(Me)}\text{AVP} \) in LE and DI (Group 2) are shown in Figure 2. Administration of \( \text{D(CH}_2\text{)}_5\text{Tyr(Me)}\text{AVP} \) after total autonomic blockade caused a prompt and significant decrease in MAP in LE (from 75 \( \pm \) 2 to 61 \( \pm \) 3 mm Hg; \( p < 0.01 \)) 5 minutes after injection, whereas it had no effect on BP in DI. The MAP levels for LE and DI were identical after sequential total autonomic blockade and vasopressin vascular receptor antagonist administration. Administration of enalaprilat significantly decreased MAP further in LE (62 \( \pm \) 2 to 50 \( \pm \) 3 mm Hg; \( p < 0.01 \)) as well as DI (63 \( \pm \) 3 to 52 \( \pm \) 3 mm Hg; \( p < 0.05 \)). There was no significant difference between the final MAP levels in the two strains (LE, 53 \( \pm \) 3 mm Hg; DI, 52 \( \pm \) 3 mm Hg). Neither the vasopressin vascular receptor antagonist nor enalaprilat caused any change in heart rate after total autonomic blockade in either strain.
Group 3

The effects on MAP and heart rate of enalaprilat following total autonomic blockade in LE and DI (Group 3) are summarized in Figure 3. After total autonomic blockade, enalaprilat reduced MAP in DI from 61 ± 3 to 50 ± 3 mm Hg (p < 0.01) but had no significant hypotensive effect on MAP (from 72 ± 3 to 67 ± 3 mm Hg) in LE. The subsequent administration of a vasopressin vascular receptor antagonist caused a significant decrease in MAP in LE (from 69 ± 3 to 53 ± 2 mm Hg; p < 0.01) but was without effect in DI (from 51 ± 22 to 53 ± 3 mm Hg). Again, final MAP levels in the LE and DI were not significantly different (54 ± 2 and 54 ± 3 mm Hg respectively) and matched the final MAP levels when the order of administration was reversed (Group 2). By comparing the results from Groups 2 and 3, it is evident that in autonomically blocked LE the decrement in MAP caused by vasopressin vascular receptor antagonist (−14 ± 1 mm Hg) was significantly greater than that caused by enalaprilat (−6 ± 1 mm Hg; p < 0.05). Similar to the results obtained in Group 2, neither enalaprilat nor vasopressin vascular receptor antagonist following total autonomic blockade significantly changed heart rate in Group 3.

Group 4

Administration of vasopressin vascular receptor antagonist alone did not change MAP or heart rate in either LE or DI (Group 4; Figure 4). Treatment with
enalaprilat after administration of vasopressin vascular receptor antagonist caused a significant decrease in MAP in both LE and DI (from 108 ± 3 to 96 ± 4 mm Hg in LE, \( p < 0.01 \); from 111 ± 2 to 103 ± 2 mm Hg in DI, \( p < 0.05 \)), and this was accompanied by an increased heart rate (from 355 ± 12 to 391 ± 13 beats/min in LE; from 347 ± 8 to 393 ± 15 beats/min in DI; both \( p < 0.05 \)). Subsequent total autonomic blockade caused further reductions in both MAP and heart rate in LE and DI.

**Group 5**

The results in Group 5 are summarized in Figure 5. The injection of enalaprilat alone had no effect on MAP or heart rate in LE but caused a significant decrease in MAP (from 105 ± 3 to 94 ± 3 mm Hg; \( p < 0.01 \)) in DI, which was associated with an increase in heart rate (from 342 ± 7 to 380 ± 9 beats/min; \( p < 0.05 \)). Additional administration of the vasopressin vascular receptor antagonist did not affect MAP or heart rate in either strain. Administration of vasopressin vascular receptor antagonist together with enalaprilat, however, caused a significant decrease in MAP (from 108 ± 2 to 98 ± 2 mm Hg; \( p < 0.01 \)) in LE, which was accompanied by tachycardia (346 ± 10 to 383 ± 10 beats/min; \( p < 0.05 \)). When total autonomic blockade followed enalaprilat and vasopressin vascular receptor antagonist, MAP and heart rate fell markedly in both LE and DI. There was no significant difference in the final MAP levels between LE and DI.

In LE, the hypotensive effect of combined treatment with vasopressin vascular receptor antagonist and enalaprilat before total autonomic blockade was significantly less than their combined effects after total autonomic blockade (11 ± 1 mm Hg, Groups 4 and 5; \( n = 14 \), vs 20 ± 2 mm Hg, Groups 2 and 3, \( n = 16 \); \( p < 0.01 \)), which suggests that activation of the sympathetic nervous system buffered the fall in BP.

The effects of the various treatment regimens on PRA and plasma levels of ANG II and AVP are summarized in Table 1. Total autonomic blockade increased plasma AVP levels 30-fold from 1.8 ± 0.4 to 52.3 ± 8.3 pg/ml (\( p < 0.01 \)), while PRA and plasma ANG II concentrations were unchanged. Additional treatment with \( \alpha(CH_2)_5DAVP \), which led to falls in BP, was associated with significant increases in PRA (\( p < 0.05 \)) and plasma ANG II levels (\( p < 0.01 \)) with no further rise in plasma AVP levels. When enalaprilat followed total autonomic blockade pretreatment, PRA increased (\( p < 0.01 \)) and plasma ANG II concentration decreased (\( p < 0.05 \)), while plasma AVP levels did not significantly increase.

### Table 1

<table>
<thead>
<tr>
<th>Treatment</th>
<th>No. of rats</th>
<th>PRA (ng ANG I/ml/hr)</th>
<th>ANG II (pg/ml)</th>
<th>AVP (pg/ml)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control</td>
<td>12</td>
<td>4.0 ± 0.4</td>
<td>29.6 ± 3.2</td>
<td>1.8 ± 0.4</td>
</tr>
<tr>
<td>TAB</td>
<td>7</td>
<td>5.3 ± 1.1</td>
<td>31.7 ± 2.6</td>
<td>52.3 ± 8.3</td>
</tr>
<tr>
<td>TAB + VPA</td>
<td>7</td>
<td>9.8 ± 0.9*†</td>
<td>45.5 ± 4.4†§</td>
<td>57.7 ± 10.2†</td>
</tr>
<tr>
<td>TAB + enalaprilat</td>
<td>6</td>
<td>38.3 ± 9.3†§</td>
<td>20.7 ± 1.6†§</td>
<td>46.2 ± 7.3†</td>
</tr>
</tbody>
</table>

Values are means ± SEM.

Total autonomic blockade (TAB) was performed by combined treatment with atropine (1 mg/kg), propranolol (5 mg/kg), and pentolinium (5 mg/kg + 10 mg/kg/hr). Enalaprilat (10 mg/kg) or \( \alpha(CH_2)_5DAVP \) (3 μg/kg) was injected 10 minutes following TAB. Blood samples were obtained by decapitation 10 minutes after each treatment.

**ANG I** = angiotensin I; **ANG II** = angiotensin II; **AVP** = arginine vasopressin; **PRA** = plasma renin activity; **VPA** = vasopressin vascular receptor antagonist.

*\( p < 0.05 \), †\( p < 0.01 \) (control); ‡\( p < 0.05 \), ‡§\( p < 0.01 \) (control vs TAB).
Discussion

The present study provides strong evidence that AVP has a greater capacity to maintain systemic arterial pressure after short-term blockade of the autonomic nervous system than has the renin-angiotensin system. This contention is supported by measurements of plasma AVP and ANG II levels, which show a significant increase in plasma AVP after total autonomic blockade with no change in plasma ANG II levels. Furthermore, the fall in BP in DI, which lack AVP, was significantly greater than that in LE. It appears, therefore, that under these conditions AVP is brought into play before the renin-angiotensin system to compensate for the fall in BP. This occurrence probably is due to blunting of the renal release of renin by inhibiting the renal sympathetics following autonomic blockade.

In doses as low as $10^{-12}$ mol/L, which are similar to physiological levels, AVP can cause contraction of isolated vasculature in vitro. In vivo, however, much higher concentrations of AVP are required to increase BP, which suggests that the vasoconstrictor activity of AVP is buffered by other mechanisms. Cowley et al. and Pullan et al. have shown that the pressor effect of AVP is greatly attenuated by a baroreflex-mediated decrease in the sympathetic nervous activity. Consequently, the pressor effect of AVP is potentiated after baroreceptor denervation or pharmacological autonomic blockade. Plasma AVP levels attained after total autonomic blockade in the present study ($52 \pm 8$ pg/ml) would be sufficient to elicit a marked vasoconstrictor response. The MAP levels after total autonomic blockade were significantly lower in DI than in LE, and the difference in MAP disappeared after additional administration of the vasopressin vascular receptor antagonist t(Ch$_2$)$_3$Tyr(Me)AVP, which suggests that the vasoconstrictor effect of AVP accounts for the difference in MAP between DI and LE after total autonomic blockade. In LE, the vasopressin vascular receptor antagonist caused a further fall in BP after total autonomic blockade than did the converting enzyme inhibitor enalaprilat. These results indicate that AVP is quantitatively more important than the renin-angiotensin system in BP maintenance after total autonomic blockade.

The renin-angiotensin system does contribute to BP maintenance after total autonomic blockade. Indeed, administration of enalaprilat following total autonomic blockade and vasopressin vascular receptor antagonist significantly decreased MAP in LE, and enalaprilat was also effective in lowering MAP after total autonomic blockade in DI. The fall in BP in DI alone after enalaprilat administration is in keeping with the higher levels of angiotensin found in this strain of rat. Therefore, both AVP and the renin-angiotensin system contribute to BP regulation after short-term blockade of the autonomic nervous system, and removal of one of these systems may be compensated, at least in part, by the other, as has been postulated in certain physiological states. Autonomic blockade by interfering with renal sympathetic efferents would markedly blunt renal renin release, and this may explain the dominant role of AVP after autonomic blockade. The renin-angiotensin system and AVP are reported to be equally important for BP maintenance during water deprivation and in chemically sympathectomized rats. Our results after total autonomic blockade agree with those of Houck et al., who studied BP regulation in anesthetized dogs after ganglionic blockade with hexamethonium.

To investigate whether AVP and the renin-angiotensin system are necessary for the maintenance of BP if the influence of the autonomic nervous system is intact, a vasopressin vascular receptor antagonist and enalaprilat were administered before total autonomic blockade. This procedure reduced MAP, which suggests that the autonomic nervous system alone is not able to maintain BP within normal levels after the influences of AVP and the renin-angiotensin system have been removed. In untreated rats, however, the MAP did not differ between LE and DI, and the vasopressor vascular receptor antagonist alone did not change MAP in intact LE. This finding may indicate that AVP does not in normal settings of BP maintenance during normal conditions but may play a substantial role when other pressor mechanisms are absent or impaired. Alternatively, AVP may have a marked tonic vasoconstrictor effect that, when removed, is compensated for by changes in activity of the autonomic nervous system or the renin-angiotensin system.

Plasma ANG II levels in LE did not change after total autonomic blockade despite systemic hypotension. Conceivably, the hypotensive stimulus to renin secretion was opposed by the loss of sympathetic neural tone and the elevated plasma AVP levels, both of which would act to reduce renin secretion. Vasopressin vascular receptor antagonist given after total autonomic blockade was associated with significantly increased PRA and plasma ANG II concentrations, which indicates compensatory activation of the renin-angiotensin system after the influence of AVP had been removed. Blockade of the renin-angiotensin system with enalaprilat after total autonomic blockade decreased plasma ANG II levels without causing any further change in plasma AVP levels. Since ANG II stimulates the secretion of AVP, the decrease in plasma ANG II levels after treatment with enalaprilat could act to reduce AVP secretion, while the decrease in MAP would stimulate AVP release. These opposing influences resulted in no significant change in circulating AVP levels.

Although there was no difference in heart rate between DI and LE before total autonomic blockade, the heart rate of DI after total autonomic blockade was significantly lower than that of autonomically blocked LE. This result is in accord with the low intrinsic heart rate reported previously by Gardiner and Bennett, although it is in contrast to the resting tachycardia in DI observed by other investigators. We have not investigated the exact mechanism underlying the low intrinsic heart rate in DI, although hypokalemia and a decreased resting membrane potential in excitable cells have been reported in DI. These phenomena could account for the low intrinsic heart rate in DI.
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sympatholytic drugs cause greater falls in BP in hypertensive patients than in normotensive subjects. This finding is often interpreted as implying sympathetic hyperactivity in hypertension; however, the same result is obtained when other classes of antihypertensive drugs are used. The results in the present studies also throw considerable doubt on this interpretation, as the fall in BP after autonomic blockade is determined not only by removal of sympathetic tone but also by the relative activation of the renin-angiotensin system and AVP. Our results clearly demonstrate the importance of AVP and the renin-angiotensin system in compensating for the loss of autonomic neural control of BP. They also suggest that AVP could act as a majorpressor hormone in hypertensive patients whose BP is uncontrolled by sympatholytic drugs and converting-enzyme inhibitors.

In summary, this study has provided evidence for the relative importance of AVP and the renin-angiotensin system in maintaining BP after total autonomic blockade in conscious rats. From these studies in LE and DI with vasopressin vascular receptor antagonist, we conclude that AVP is the primary compensatory mechanism initiated to maintain arterial pressure after short-term blockade of the autonomic nervous system.

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