Central Adrenergic Receptor Control of Renal Function in Conscious Hypertensive Rats

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SUMMARY The role of central nervous system α-adrenergic and β-adrenergic receptors in the increased renal sympathetic nerve activity and antinatriuresis resulting from environmental stress (air stress) in conscious spontaneously hypertensive rats (SHR) was examined. Intracerebroventricular administration of the α2-adrenergic receptor agonist clonidine (1, 5, and 15 μg) prevented the effects of air stress on renal sympathetic nerve activity and urinary sodium excretion. Clonidine, 5 and 15 μg, lowered baseline mean arterial pressure and renal sympathetic nerve activity and increased baseline urine flow rate and urinary sodium excretion; clonidine, 1 μg, had no effect on these baseline levels. Intravenous administration of 5 μg, but not 1 μg of clonidine, abolished the renal responses to air stress. Intracerebroventricular administration of α2-adrenergic receptor antagonists (yohimbine, rauwolscine) reversed the effects of clonidine. α2-adrenergic receptor blockade alone, α1-adrenergic receptor blockade (20 μg prazosin), or combined α1-adrenergic and α2-adrenergic receptor blockade (30 μg phenoxycbenzamine) had no effect on the renal sympathetic nerve activity or antinatriuretic responses to air stress. Intracerebroventricular, but not intravenous, administration of the β2-adrenergic receptor antagonist ICI 118551 (30 μg) prevented the increased renal sympathetic nerve activity and antinatriuretic responses to air stress. In contrast, intracerebroventricular administration of the β1-adrenergic receptor antagonist atenolol (30 μg) had no effect on the renal responses to air stress. These results indicate that the increased renal sympathetic nerve activity and antinatriuresis resulting from environmental stress in conscious SHR can be prevented by pharmacological stimulation of central α2-adrenergic receptors or by blockade of central β2-adrenergic receptors.

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KEY WORDS • renal sympathetic nerves • environmental stress • spontaneously hypertensive rats • central nervous system • urinary sodium excretion

THE neural control of renal function has been demonstrated in conscious rats and dogs using environmental stress to activate renal sympathetic nerve activity.1–4 The antinatriuretic response to environmental stress (air stress) in conscious spontaneously hypertensive rats (SHR) occurs in the absence of changes in glomerular filtration rate or effective renal plasma flow, which indicates an increase in renal tubular reabsorption of sodium.5,6 These renal responses in SHR are associated with increased renal sympathetic nerve activity and are abolished by surgical renal denervation.6,7 In contrast to the effects of air stress on renal function in SHR, the renal effects in normotensive Wistar-Kyoto rats (WKY) are of smaller magnitude, which suggests that a genetic predisposition to develop hypertension is an important determinant of the renal sympathetic nerve activity and antinatriuretic responses to environmental stress in SHR.1–3 A similar phenomenon has been observed in humans: Stressful mental competition decreased urinary sodium excretion only in young men with a parental history of hypertension.3 Thus, environmental stress in conscious rats may provide a model to examine not only the physiological but also the pathophysiological significance of the neural control of renal function in hypertension.6

Central nervous system catecholaminergic mechanisms have been implicated in the renal sympathetic nerve activity and antinatriuretic responses to environmental stress.4,7 In conscious dogs, the antinatriuretic
response to avoidance conditioning is abolished by β1, β2-adrenergic receptor antagonists that readily cross the blood-brain barrier (propranolol), but not by those that cross much less readily (timolol, oxprenolol). In conscious SHR, the intracerebroventricular (i.c.v.) administration of propranolol or timolol prevents the increased renal sympathetic nerve activity and antinatriuresis resulting from environmental stress in conscious animals.

High dietary sodium intake enhances the neural outflow to the kidneys during air stress in conscious SHR. In normotensive WKY, however, high dietary sodium intake has no effect on the renal responses to air stress. The mechanism of the facilitated central neurotransmission in SHR on high dietary sodium intake is unknown but may be related to an increased density of central α1-adrenergic receptors. High sodium intake can augment the density of renal α1-adrenergic receptors in hypertensive but not normotensive rats. Moreover, α1-adrenergic receptor agonists, such as clonidine and guanabenz, exert their antihypertensive effects in part by lowering effenter sympathetic activity.

One goal of the present study was to examine the contribution of central nervous system α1-adrenergic and α2-adrenergic receptors to the renal responses resulting from air stress in conscious SHR. A second goal was to determine the β1 versus β2 selectivity of the central nervous system β-adrenergic receptor mechanism in the increased renal sympathetic nerve activity and antinatriuresis resulting from air stress in conscious SHR.

Materials and Methods

Male SHR, 12 to 13 weeks of age, were used (Laboratory Supply, Indianapolis, IN, USA). The SHR were maintained on standard laboratory rat chow and water. All experimental procedures were performed in accordance with guidelines established by the University of Iowa College of Medicine and the National Institutes of Health for the use and care of laboratory animals.

The SHR were anesthetized with ketamine HCL (Ketaset), 150 mg/kg, or sodium pentobarbital (Nembutal), 50 mg/kg, 24 to 48 hours before the experiment began and surgically implanted with catheters in the right jugular vein, carotid artery, and lateral cerebral ventricle. The venous and arterial catheters (Tygon) were tunneled to the back of the neck and exteriorized, the arterial catheter was flushed and attached to a pressure transducer (Statham P23Db, Oxnard, CA, USA), and a 3-cm polyethylene catheter was at-
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...tached to the urinary bladder catheter and led to a collection beaker. For some experiments, inulin (30 mg/100 g body weight/hr) and para-aminobipirurate (PAH; 3-4 mg/100 g body weight/hr) were infused to measure inulin and PAH clearances. The renal sympathetic nerve activity recording electrode cable was connected to a high impedance probe (Grass N1), which in turn was connected to the bandpass amplifier. The quality of the renal nerve activity recording was tested with intravenously administered norepinephrine (3 \( \mu \)g) and acetylcholine (1 \( \mu \)g) as described previously to ensure the absence of noise due to mechanical movement, respiration, or heart rate. If the quality of the renal sympathetic nerve activity recording was similar to that observed when the electrode was implanted, then the experiment commenced.

After urine flow rate and urinary sodium excretion stabilized (45-60 minutes), two consecutive sets of experimental periods (control, stress, recovery; 10 minutes each) were examined. The i.c.v. microinjection of vehicle (2 \( \mu \)l through a 10-\( \mu \)l Hamilton syringe) occurred 10 minutes before the control period of the first set of experimental periods, and the i.c.v. microinjection of a-2-adrenergic or \( \beta \)-adrenergic receptor agonists or antagonists occurred immediately after the first recovery period and 10 minutes before the control period of the second set of experimental periods. In some experiments, drugs were injected intravenously rather than intracerebroventricularly. Separate groups of SHR were used for each drug protocol. This design has been shown to result in increases in renal sympathetic nerve activity and arterial pressure and decreases in urine flow rate and urinary sodium excretion during air stress of similar magnitude between the first and second sets of experimental periods in the same conscious SHR. In time-control experiments for the effects of i.c.v. drug injection in the absence of stress, air stress was delivered only during the first set of experimental periods, i.e., drug injection occurred as already described, and air stress was omitted from the second set of experimental periods. Environmental stress (air stress) consisted of an air jet located 4 to 5 cm in front of the rat and delivered to the top of the rat’s head. At the end of each experiment, the quality of the renal sympathetic nerve activity recordings was reassessed with intravenous injections of norepinephrine (3 \( \mu \)g) and acetylcholine (1 \( \mu \)g). The SHR then were killed and postmortem renal nerve activities were recorded for 30 to 45 minutes as a measure of background noise. These values (<1 integrator reset/min) were subtracted from all experimental values of renal sympathetic nerve activity.

Drugs used for i.c.v. administration were \( \alpha \)-adrenergic receptor agonists (1, 5, 15 \( \mu \)g clonidine HCl; 5 \( \mu \)g guanabenz acetate) and antagonists (30 \( \mu \)g yohimbine HCl; 30 \( \mu \)g rauwolscine HCl), an \( \alpha \)-adrenergic receptor antagonist (20 \( \mu \)g prazosin HCl), an \( \alpha \)-adrenergic and \( \alpha \)-adrenergic receptor antagonist (30 \( \mu \)g phenoxybenzamine HCl), \( \beta \)-adrenergic receptor antagonist (30 \( \mu \)g ICI 118551 HCl), and a \( \beta \)-adrenergic receptor antagonist (30 \( \mu \)g atenolol HCl). Vehicle was isotonic saline, except for prazosin (distilled water) and phenoxybenzamine (ethanol 10% and polypropylene glycol 10% in distilled water).

Urine volume was determined gravimetrically. Urine sodium concentration was measured by flame photometry (model 143; Instrumentation Laboratories, Lexington, MA, USA). Urine and plasma inulin and PAH concentrations were determined by the anthrone and ethylenediaime methods, respectively. Glomerular filtration rate and effective renal plasma flow were estimated by the clearances of inulin and PAH.

Statistical analyses were conducted with repeated measures analysis of variance (BMDP 2 PV) for main effects and interactions and Tukey's Honestly Significant Different tests for pairwise comparisons among means. Statistical significance was defined as a \( p \) level less than 0.05.

Results

**\( \alpha \)- and \( \alpha \)-Adrenergic Receptors**

Before \( \alpha \)-adrenergic receptor agonist administration, 10 minutes of air stress increased mean arterial pressure, decreased urine flow rate, and increased renal sympathetic nerve activity in conscious SHR (Figure 1). These measures returned to control levels during the 10 minute recovery period.

After the i.c.v. administration of the \( \alpha \)-adrenergic receptor agonist clonidine, 1 \( \mu \)g, the urine flow rate, urinary sodium excretion, and renal sympathetic nerve activity responses to air stress in conscious SHR were abolished, although mean arterial pressure still increased during air stress (see Figure 1). In contrast, the intravenous administration of 1 \( \mu \)g of clonidine did not block the renal responses to air stress in SHR (see Figure 1).

Similar to results obtained with clonidine, 1 \( \mu \)g i.c.v., the i.c.v. administration of the \( \alpha \)-adrenergic receptor antagonist guanabenz, 5 \( \mu \)g, abolished the increased renal sympathetic nerve activity and antinatriuretic responses to air stress in conscious SHR (Figure 2). Neither clonidine, 1 \( \mu \)g i.c.v., nor guanabenz, 5 \( \mu \)g i.c.v., altered baseline levels of mean arterial pressure, urine flow rate, urinary sodium excretion, or renal sympathetic nerve activity. Moreover, in time-control experiments (\( n = 5 \)) for the effects of clonidine, 1 \( \mu \)g i.c.v., on renal function in the absence of air stress, no changes occurred during the three time-control periods in urinary sodium excretion (2.7 ± 0.5, 2.5 ± 0.5, 2.8 ± 0.6 \( \mu \)Eq/min/100 g body weight) or renal sympathetic nerve activity (7.4 ± 1.4, 6.8 ± 1.2, 6.7 ± 1.3 integrator resets/min); before time-control periods, air stress still decreased urinary sodium excretion (32% from 2.8 ± 0.8 \( \mu \)Eq/min/100 g body weight) and increased renal sympathetic nerve activity (60% from 6.7 ± 1.1 integrator resets/min).

The i.c.v. administration of the \( \alpha \)-adrenergic receptor antagonist yohimbine, 30 \( \mu \)g, before clonidine, 1 \( \mu \)g i.c.v. (Figure 3), or guanabenz, 5 \( \mu \)g i.c.v. (Figure 4), prevented these \( \alpha \)-adrenergic receptor agonists...
Figure 1. Intracerebroventricular (i.c.v.) and intravenous administration of 1 μg of clonidine. Intracerebroventricular administration abolished the urine flow rate (V), urinary sodium excretion (U$_{Na}V$), and renal sympathetic nerve activity (RSNA) responses but not mean arterial pressure (MAP) responses to air stress in conscious SHR. BW = body weight; Cont = control; Recov = recovery. *p < 0.05, compared with control values.

Figure 2. Intracerebroventricular administration of guanabenz, 5 μg, prevented air stress from decreasing urine flow rate (V) and urinary sodium excretion (U$_{Na}V$) and increasing renal sympathetic nerve activity (RSNA) in SHR. See Figure 1 for key to abbreviations. *p < 0.05, compared with control values.

Figure 3. Intracerebroventricular (i.c.v.) administration of yohimbine, an α$_2$-adrenergic receptor antagonist, before clonidine, 1 μg i.c.v., prevented the α$_2$-adrenergic receptor agonist from blocking the antidiuretic, antinatriuretic, and renal sympathetic nerve activity (RSNA) responses to air stress in conscious SHR. See Figure 1 for key to abbreviations. *p < 0.05, compared with control values.
from blocking the antidiuretic, antinatriuretic, and renal sympathetic nerve activity responses to air stress in SHR. Administration of yohimbine, 30 μg i.c.v., alone had no effect on the increased mean arterial pressure and renal sympathetic nerve activity, antidiuresis, and antinatriuresis resulting from air stress (Figure 5).

Higher doses of clonidine (5 and 15 μg i.c.v.) also abolished the renal responses to air stress in conscious SHR and altered baseline levels of mean arterial pressure, urine flow rate, urinary sodium excretion, and renal sympathetic nerve activity (Table I). Glomerular filtration rate and effective renal plasma flow were unaffected by the i.c.v. administration of clonidine, 15 μg. Before clonidine they averaged (n = 6) 1.17 ± 0.13 and 4.92 ± 0.40 ml/min/100 g body weight, respectively. During the clonidine, 15 μg i.c.v., control period, glomerular filtration rate and effective renal plasma flow were 1.22 ± 0.22 and 4.80 ± 0.43 ml/min/100 g body weight, respectively. The mean arterial pressure response to air stress was abolished only after i.c.v. injection of 15 μg of clonidine (see Table I). Similar to results obtained with clonidine, 5 μg i.c.v., intravenous administration of 5 μg of clonidine prevented the antidiuretic, antinatriuretic, and renal sympathetic nerve activity responses to air stress in SHR. Before administration of clonidine, 5 μg i.v., air stress decreased (p < 0.05) urine flow rate (19% from 25.1 ± 11.6 μl/min/100 g body weight) and urinary sodium excretion (36% from 2.5 ± 0.7 μEq/min/100 g body weight) and increased renal sympathetic nerve activity (75% from 7.2 ± 1.1 integrator resets/min). After administration of clonidine, 5 μg i.c.v., in the same SHR, air stress had no effect on urine flow rate, urinary sodium excretion, or renal sympathetic nerve activity (+ 14% from 27.8 ± 3.5 μl/min/100 g body weight; −12% from 4.2 ± 0.9 μEq/min/100 g body weight; +19% from 4.9 ± 1.0 integrator resets/min, respectively). The α₂-adrenergic receptor antagonists yohimbine or rauwolscine (30 μg i.c.v.), administered 10 minutes before clonidine, 15 μg i.c.v., reversed the effects of clonidine on mean arterial pressure and renal responses to air stress (see Table I). However, neither yohimbine nor rauwolscine prevented clonidine, 15 μg i.c.v., from increasing baseline levels of urinary sodium excretion (see Table I). Similarly, i.c.v. administration of the α₁-adrenergic receptor antagonist prazosin or the α₁-adrenergic and α₂-adrenergic receptor antagonist phenoxycobenzamine did not affect the mean arterial pressure or renal responses to air stress in conscious SHR (see Table I).

**Figure 4.** After intracerebroventricular (i.c.v.) administration of yohimbine, guanabenz, 5 μg i.c.v., did not block the urine flow rate (V), urinary sodium excretion (UNaV), or renal sympathetic nerve activity (RSNA) responses to air stress in conscious SHR. See Figure 1 for key to abbreviations. *p < 0.05, compared with control values.

**Figure 5.** Intracerebroventricular (i.c.v.) administration of yohimbine had no effect on the increased mean arterial pressure (MAP) and renal sympathetic nerve activity (RSNA) or decreased urine flow rate (V) and urinary sodium excretion (UNaV) resulting from air stress. See Figure 1 for key to abbreviations. *p < 0.05, compared with control values.

**β₁- and β₂-Adrenergic Receptors**

Air stress increased mean arterial pressure, decreased urinary sodium excretion, and increased renal sympathetic nerve activity before β₂-adrenergic recep-
**TABLE 1. Effects of Air Stress on Mean Arterial Pressure, Urinary Sodium Excretion, and Renal Sympathetic Nerve Activity Before and After /3-Adrenergic Receptor Agonist and Antagonist Administration (i.c.v.) in Conscious SHR**

<table>
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<th>Variable</th>
<th>MAP (mm Hg)</th>
<th>Urine flow rate (µEq/min/100 g body wt.)</th>
<th>Uu/V (µEq/min/100 g body wt.)</th>
<th>RSNA (integrator resets/min)</th>
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<tr>
<td></td>
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<td>Vehicle</td>
<td>Drug</td>
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<td>170 ± 7†</td>
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<td></td>
<td>R</td>
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<td>145 ± 8*</td>
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<td>148 ± 8†</td>
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<tr>
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<td>169 ± 3††</td>
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<td>21.3 ± 4.4</td>
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</tbody>
</table>

Values are means ± SEM. Clonidine, prazosin, and phenoxybenzamine were administered at the end of the first recovery period and 10 minutes before the second control period. Yohimbine and rauwolscine were administered 10 minutes before clonidine.

MAP = mean arterial pressure; Uu/V = urinary sodium excretion; RSNA = renal sympathetic nerve activity; C = second control period; A = air stress; R = first recovery period.

*p < 0.05, mean of C+R of vehicle compared with mean of C+R of drug; **p < 0.05 compared with C values.

Discussion

The control of urinary sodium excretion by the renal sympathetic nerves is stronger in conscious SHR than in conscious normotensive WKY during exposure to environmental stress. In conscious SHR, environmental stress increases renal sympathetic nerve activity and decreases urinary sodium excretion, both before and after i.c.v. administration of the /3-adrenergic receptor antagonist atenolol in conscious SHR (Figure 7). These measures returned to control levels during the recovery periods. In addition, atenolol had no effect on baseline levels of mean arterial pressure, urine flow rate, urinary sodium excretion, or renal sympathetic nerve activity (see Figure 7).
sive rats (crossbred SHR × WKY).22 These studies suggest that increased renal sympathetic nerve activity and renal sodium retention mediate the pathophysiology of hypertension resulting from long-term exposure to environmental stress in conscious rats with a genetic predisposition to hypertension. In consideration of this working hypothesis, the present study was designed to characterize central α-adrenergic and β-adrenergic receptor mechanisms in the increased renal sympathetic nerve activity and antinatriuresis resulting from short-term exposure to environmental stress in conscious SHR.

Stimulation of central nervous system α2-adrenergic receptors prevents the increased renal sympathetic nerve activity and antinatriuresis from air stress in conscious SHR. This conclusion is based on two main findings. First, only the i.c.v., not the intravenous, administration of 1 μg of clonidine abolished the renal sympathetic nerve activity and urinary sodium excretion responses to air stress, which demonstrates the action of clonidine in the central nervous system. Second, pretreatment with α2-adrenergic receptor antagonists (yohimbine, rauwolscine) reversed the effects of the α2-adrenergic receptor agonists, which demonstrates the specificity for central α2-adrenergic receptors in the renal responses to air stress. Since i.c.v. administration of yohimbine alone had no effect on the increased renal sympathetic nerve activity and antinatriuretic responses to air stress, basal activity of these central α2-adrenergic receptors may be very low. Similarly, i.c.v. administration of the α1-adrenergic receptor antagonist prazosin or the α1- and α2-adrenergic receptor antagonist phenoxybenzamine had no effect on the renal responses to air stress. Whether blockade of central α-adrenergic receptors in areas other than those affected by i.c.v. administration can alter the renal responses to air stress in conscious SHR is not known. In fact, the natriuresis resulting from injection of norepinephrine into the ventromedial hypothalamus was potentiated by yohimbine and blocked by prazosin; however, the antagonists alone had no effect on baseline levels of urinary sodium excretion.23 In any case, the present results support the conclusion that stimulation of central α2-adrenergic receptors can prevent the increases in renal sympathetic nerve activity and decreases in urinary sodium excretion resulting from environmental stress in conscious SHR.

Blockade of central nervous system β2-adrenergic receptors with ICI 118551 abolishes the increased renal sympathetic nerve activity and antinatriuretic responses to air stress in conscious SHR. This conclusion is supported by the finding that i.c.v., but not intravenous, administration of ICI 118551 abolished
the renal responses to air stress in conscious SHR. Similarly, i.c.v., but not intravenous, administration of propranolol or timolol abolished the renal responses to air stress in conscious SHR, which further implicates central nervous system \(\beta\)-adrenergic receptors in the responses.\(^4\) ICI 118551 is a selective and specific \(\beta\)-adrenergic receptor antagonist with no partial agonist activity and with membrane-stabilizing properties similar to those of propranolol.\(^24\) In a previous study, the i.c.v. administration of \(d\)-propranolol (30 \(\mu\)g), which is devoid of \(\beta\)-adrenergic receptor blocking but not membrane-stabilizing properties, did not alter the renal responses to air stress,\(^4\) which suggests that the same dose of ICI 118551 in the present study probably was not acting through a membrane-stabilizing action. In contrast to \(\beta\)-adrenergic receptor blockade, i.c.v. administration of atenolol, which is a \(\beta\)-adrenergic receptor antagonist equipotent to propranolol\(^22\) had no effect on the renal responses to air stress. Whether higher doses of atenolol or blockade of central \(\beta\)-adrenergic receptors other than those blocked by i.c.v. administration would alter the renal responses to air stress in conscious SHR is not known. Consistent with the present results is the study of Camargo et al.,\(^25\) in which injection of the \(\beta\)-adrenergic and \(\beta\)-adrenergic receptor agonist isoproterenol into the septal area of conscious rats decreased urinary sodium excretion. This antinatriuretic response was prevented by blockade of \(\beta\)-adrenergic (butoxamine) but not \(\beta\)-adrenergic (practolol) receptors; stimulation of \(\beta\)-adrenergic receptors with terbutaline or salbutamol decreased urinary sodium excretion similar to isoproterenol. Thus, these results indicate that central nervous system \(\beta\)-adrenergic receptors control urinary sodium excretion through the renal sympathetic nerves in conscious rats.

Central administration of clonidine (5 and 15 \(\mu\)g) and ICI 118551 lowered baseline levels of renal sympathetic nerve activity and increased baseline levels of urinary sodium excretion. Clonidine, 5 and 15 \(\mu\)g i.c.v., also lowered mean arterial pressure. The mean arterial pressure and renal sympathetic nerve activity responses to clonidine were prevented by \(\alpha\)-adrenergic receptor blockade (yohimbine, rauwolscine), which suggests that these responses were mediated by a central \(\alpha\)-adrenergic receptor mechanism. In contrast, clonidine, 15 \(\mu\)g i.c.v., still produced a natriuresis after central \(\alpha\)-adrenergic receptor blockade; however, the natriuresis was not as great as that resulting from clonidine, 15 \(\mu\)g i.c.v., alone. Since glomerular filtration rate and effective renal plasma flow were not altered by clonidine, 15 \(\mu\)g i.c.v., changes in renal hemodynamics do not explain the natriuresis. The natriuresis resulting from clonidine (15 \(\mu\)g i.c.v.) more likely was due to 1) inhibition of renal sympathetic nerve activity\(^26\) by a central \(\alpha\)-adrenergic receptor mechanism and 2) clonidine-induced inhibition of vasopressin release from the central nervous system or peripheral inhibition of the action of vasopressin on renal tubules through leakage from the cerebral ventricles.\(^27\)\(^28\)

The ability of clonidine, 5 \(\mu\)g i.v., to alter baseline levels of urine flow rate and urinary sodium excretion supports the possibility that the i.c.v. administration of the same or higher dose could have peripheral effects if leakage from the cerebral ventricles occurred. The natriuresis resulting from ICI 118551 probably is not mediated by changes in renal hemodynamics, since mean arterial pressure was not affected and a previous study showed that central administration of propranolol did not affect glomerular filtration rate or effective renal blood flow.\(^4\) More likely, the natriuresis was a result of a lowered renal sympathetic nerve activity and consequent decrease in renal tubular reabsorption of sodium.\(^26\)

Other studies point to specific central nervous system areas where adrenergic receptors may be important in the renal sympathetic nerve activity and antinatriuretic responses to environmental stress in conscious SHR. Norepinephrine administration into the ventromedial hypothalamus, lateral hypothalamus, septal area, and third ventricle of conscious rats increases urinary sodium excretion; the natriuresis is prevented by central \(\alpha\)-adrenergic receptor blockade and potentiated by \(\alpha\)-adrenergic receptor blockade.\(^22\)\(^29\)\(^31\) In contrast, isoproterenol administration into the lateral hypothalamus, septal area, and third ventricle decreases urinary sodium excretion in conscious rats; the antinatriuresis is abolished by combined \(\beta\)-adrenergic and \(\beta\)-adrenergic, or \(\beta\)-adrenergic, but not \(\beta\)-adrenergic receptor blockade.\(^25\)\(^29\)\(^31\) Radioisotopic binding studies have verified the presence of \(\alpha\)-adrenergic and \(\beta\)-adrenergic receptors in these as well as other areas in the central nervous system. These studies along with the present results implicate an inhibitory role for central \(\alpha\)-adrenergic receptors and an excitatory role for central \(\beta\)-adrenergic receptors on urinary sodium excretion. Although the specific neurotransmitter affecting these receptors was not determined in this study, it is interesting to speculate about a role for epinephrine, given that its potency at \(\alpha\)-adrenergic and \(\beta\)-adrenergic receptors is greater than that of norepinephrine.\(^33\)

The present study also suggests that a change in renal sympathetic nerve activity is an important efferent mechanism. Moreover, these studies suggest possible central nervous system loci that may be important in the renal sympathetic nerve activity and antinatriuretic responses to environmental stress in conscious SHR.

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**References**

Central adrenergic receptor control of renal function in conscious hypertensive rats.
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