Central \(\beta\)-Adrenergic Receptors Mediate Renal Nerve Activity During Stress in Conscious Spontaneously Hypertensive Rats

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SUMMARY The effects of intracerebroventricular (i.c.v.) administration of \(\beta\)-adrenergic receptor antagonists (\(d,\!L\)-propranolol or timolol, 30 \(\mu\)g in 2 \(\mu\)L of isotonic saline) on the increased renal sympathetic nerve activity and decreased urinary sodium excretion (\(U_NaV\)) responses to stressful environmental stimulation (air jet to head) in conscious spontaneously hypertensive rats (SHR) were examined. Before i.c.v. \(d,\!L\)-propranolol or timolol, air stress increased renal sympathetic nerve activity (68% from 10.6 ± 2.1 and 63% from 8.2 ± 0.9 integrator resets/min respectively). In contrast, after i.c.v. \(d,\!L\)-propranolol or timolol in the same conscious SHR, air stress had no effect on renal sympathetic nerve activity (+7% from 8.1 ± 1.7 and +7% from 5.5 ± 1.0 integrator resets/min respectively). Air stress decreased \(U_NaV\) in conscious SHR given i.c.v. saline vehicle (25% from 2.8 ± 0.5 \(\mu\)Eq/min/100 g body weight), but had no effect on effective renal plasma flow or glomerular filtration rate. In contrast, after i.c.v. \(d,\!L\)-propranolol or timolol, air stress had no effect on \(U_NaV\) (0% from 2.8 ± 0.5 and +9% from 3.3 ± 0.3 \(\mu\)Eq/min/100 g body weight respectively). Mean arterial pressure increased similarly during air stress with i.c.v. saline-vehicle or \(\beta\)-adrenergic receptor antagonists. Intravenous administration of the same doses of \(d,\!L\)-propranolol or timolol did not prevent the increased renal sympathetic nerve activity or decreased \(U_NaV\) responses resulting from air stress. These results suggest that central nervous system \(\beta\)-adrenergic receptors mediate the increased renal sympathetic nerve activity and decreased \(U_NaV\) responses resulting from stressful environmental stimulation in conscious SHR. (Hypertension 7: 350–356, 1985)

KEY WORDS • conscious spontaneously hypertensive rats • sympathetic nervous system • environmental stress
central nervous system may be intimately involved in the integrative control of this response.

Renal responses to stressful environmental stimulation in conscious SHR are very similar to renal responses observed in conscious dogs and humans. An antinatriuresis results from aversive conditioning in conscious dogs and from stressful competition in young men. In conscious dogs the antinatriuresis can occur in the absence of changes in glomerular filtration rate or effective renal blood flow and is abolished by surgical renal denervation. Moreover, not all dogs or humans respond to stressful environmental stimulation with antinatriuresis. Only in 21 of 30 conscious dogs and in young men with a parental history of hypertension did stressful environmental stimulation produce an antinatriuresis, which suggests that some individuals may be predisposed to respond to stressful environmental stimulation with sodium retention. Of specific interest was the finding in conscious dogs that the intravenous infusion of propranolol, but not timolol or oxprenolol, abolished the antinatriuretic response to aversive conditioning. Because propranolol crosses the blood-brain barrier much more readily than does timolol or oxprenolol, these results suggest that a central nervous system β-adrenergic receptor mechanism mediated the antinatriuretic response to stressful environmental stimulation.

Given the importance of the central nervous system in the neural control of the antinatriuretic response to stressful environmental stimulation in both conscious SHR and dogs, we sought to determine whether the increased renal sympathetic nerve activity and antinatriuresis resulting from stressful environmental stimulation in conscious SHR are mediated by a central nervous system β-adrenergic receptor mechanism. To accomplish this objective, we tested the effects of intracerebroventricular (i.c.v.) administration of β-adrenergic receptor antagonists (d,l-propranolol and timolol) on the increased renal sympathetic nerve activity and antinatriuresis resulting from stressful environmental stimulation in conscious SHR.

Materials and Methods

Male SHR, 3 to 4 months of age, were obtained from Taconic Farms, Inc. (Germantown, NY). The SHR were maintained on a normal sodium diet (sodium, 163 mEq/kg) and water.

While they were under ketamine HCl (Bristol Laboratories, Syracuse, NY) anesthesia (150 mg/kg, intraperitoneally), catheters were inserted (Silastic 602-135, Dow Corning, Midland, MI) in the left jugular vein and right carotid artery in one group of SHR (n = 36) 24 to 48 hours before experimentation. The venous and arterial catheters were tunneled to the back of the neck, filled with heparinized saline (1000 U/ml; Elkins-Sinn, Cherry Hill, NJ), and plugged with stainless steel pins. Through a supraumbilical incision, a stainless steel urinary bladder catheter (18 gauge, 12.5 cm long), modified from that of Gellai and Valtin, was sutured into the urinary bladder, exteriorized, and secured by suturing to adjacent muscle, subcutaneous tissue, and skin. The urinary bladder catheter was obturated, and rats voided through the urethra until the experiment began. With the skull surface level between bregma and lambda, the right lateral cerebral ventricle was stereotaxically (Model 900, Kopf, Tujunga, CA) implanted with a stainless steel cannula (23 gauge, 15 cm long) according to the following coordinates: 0.3 mm posterior to bregma, 1.4 mm lateral to midline, and 4.5 mm subdural. Verification of cannula location in the cerebroventricular system was accomplished either by observing spontaneous flow of cerebrospinal fluid after removal of the obturator (30 gauge) or by injecting dye into the lateral cerebral ventricular cannula with subsequent postmortem brain section. The venous catheter was used for saline infusions and blood sampling, the arterial catheter was used for arterial pressure and heart rate recordings, the urinary bladder catheter was used for urine collections, and the intracerebroventricular cannula was used for drug injections.

A second group of SHR (n = 23) was surgically prepared (pentobarbital sodium, 50 mg/kg, intraperitoneally) with renal nerve electrodes to record multifiber renal sympathetic nerve activity and with catheters in the jugular vein, carotid artery, and lateral cerebral ventricle. Through a left flank incision, the left kidney was exposed with a retroperitoneal approach. With the use of a dissection microscope (25X) a renal nerve branch was dissected from the aortic renal junction and placed on a bipolar silver or platinum wire (Cooner Wire Company, Chatsworth, CA) electrode. Renal sympathetic nerve activity was amplified (×10,000–50,000) and filtered (low, 30; high, 3,000 Hz) with a Grass P511 Bandpass Amplifier (Grass Instrument Co., Quincy, MA). The amplified and filtered signal was channeled to a Tektronix 5113 Oscilloscope (Tektronix, Inc., Beaverton, OR) and Grass Model 7DA Polygraph for visual evaluation, to an audio amplifier/loudspeaker (Grass Model AM 8 Audio Monitor) for auditory evaluation, and to a rectifying voltage integrator (Grass Model 7P10) and frequency discharge counter (Scope Raster/Stepper Model 140A, W-P Instruments, Inc., New Haven, CT). The voltage-integrated frequency discharge and renal neurogram signals were displayed on the Grass Polygraph. The quality of the renal sympathetic nerve signal was assessed during operation by examining the magnitude of decrease in recorded renal sympathetic nerve activity during sinoaortic baroreceptor loading with the injection of norepinephrine (5 μg i.v.) and the magnitude of increase in recorded renal sympathetic nerve activity during sinoaortic baroreceptor unloading with the injection of acetylcholine (1 μg i.v.). When an optimal renal sympathetic nerve activity signal was observed, the recording electrodes were fixed to the renal nerve branch with Sil-Gel 604 (Wacker Chemie, Munich, W. Germany). The electrode cable was tunneled to the back of the neck and exteriorized, the flank incision was closed in layers, and 24 hours was allowed for recovery.
On the experimental day, conscious SHR were placed in Lucite cylinders, which permitted forward and backward movement, and an isotonic saline infusion was started at a rate of 60 \( \mu \text{L/minute} \). The arterial catheter was flushed and attached to a pressure transducer (P23Db, Statham, Oxnard, CA) zeroed at the center of the cylinder. For experiments with urine collections, a 3-cm polyethylene catheter was attached to the urinary bladder catheter and led to a collection beaker. For renal sympathetic nerve activity recording experiments, the renal nerve recording electrode cable was connected to a high-impedance probe (Grass HIP 511), which in turn was connected to the bandpass amplifier. The quality of the renal nerve activity recording was tested with administration of norepinephrine (5 \( \mu \text{g i.v.} \)), as on the surgical day. If the quality of the renal sympathetic nerve activity recording was similar to that observed when the electrode was implanted, then the experiment commenced.

For experiments with urine collections, the isotonic saline infusion included inulin and para-aminohippurate (PAH) in quantities sufficient for determination of inulin clearance and PAH clearance respectively. After 60 minutes of equilibration, a 20-minute stressful environmental stimulation period was preceded by a 20-minute control period and followed by a 20-minute recovery period. For renal clearances, a 20-minute urine collection was made for each period and venous blood samples (200 \( \mu \text{L} \)) were taken at the midpoints. Stressful environmental stimulation consisted of an air jet delivered to the top of the rat’s head through a tube located 4 to 5 cm in front of the rat. Intracerebroventricular injections of isotonic saline (vehicle; 2 \( \mu \text{L} \)), d,l-propranolol (30 \( \mu \text{g} \) in 2 \( \mu \text{L} \) of vehicle), d-propranolol (30 \( \mu \text{g} \) in 2 \( \mu \text{L} \) of vehicle), or timolol (30 \( \mu \text{g} \) in 2 \( \mu \text{L} \) of vehicle) were administered with a 10-\( \mu \text{L} \) Hamilton syringe 20 minutes before the control period in separate groups of SHR.

For experiments with renal sympathetic nerve activity recordings, the effects of air stress were examined after administration of isotonic saline (vehicle; 2 \( \mu \text{L} \), i.c.v.) and after \( \beta \)-adrenergic receptor antagonist injection (d,l-propranolol, timolol; 30 \( \mu \text{g} \) in 2 \( \mu \text{L} \) of vehicle, i.c.v.) in the same SHR. The 60-minute equilibration period was followed by two consecutive sets of experimental periods (i.e., control, air stress, and recovery; 10 minutes each) with an intracerebroventricular injection of saline occurring 20 minutes before the control period of the first set and an intracerebroventricular injection of \( \beta \)-adrenergic receptor antagonist or vehicle (time-control) occurring immediately after the first recovery period and 20 minutes before the control period of the second set of experimental periods. At the end of renal sympathetic nerve activity recording experiments, the quality of the renal sympathetic nerve signals were again assessed with intravenous injections of norepinephrine (5 \( \mu \text{g} \)) and acetylcholine (1 \( \mu \text{g} \)). Finally, the SHR were killed and postmortem renal nerve activities were continuously recorded for 30 to 45 minutes as a measure of background noise; these values (less than 1 integrator reset/min) were subtracted from all experimental values of renal sympathetic nerve activity.

At the same point in time and dosage as the injection of d,l-propranolol and timolol (i.e., 20 minutes before the control period; 30 \( \mu \text{g} \) in 2 \( \mu \text{L} \) of isotonic saline, i.c.v.), the effects of the intravenous injection of d,l-propranolol or timolol on the renal sympathetic nerve activity and urinary sodium excretion responses to air stress were examined in separate groups of conscious SHR.

Urine volume was determined gravimetrically. Urine sodium concentration was measured by flame photometry (Model 143, Instrumentation Laboratories, Lexington, MA). Urine and plasma inulin and PAH concentrations were determined by the anthrone and ethylenediamine methods respectively. Glomerular filtration rate was measured as inulin clearance: $C_{\text{In}} = (V \times U_{\text{In}})/P_{\text{In}}$, where $U_{\text{In}}$ and $P_{\text{In}}$ are urine and plasma inulin concentrations, respectively, and $V$ is urine flow rate. Effective renal plasma flow was determined by PAH clearance: $(V \times U_{\text{PAH}})/P_{\text{PAH}}$, where $U_{\text{PAH}}$ and $P_{\text{PAH}}$ are urine and plasma PAH respectively. Fractional sodium excretion was estimated by the equation $C_{\text{Na}}/C_{\text{In}} \times 100$, where $C_{\text{Na}}$ is sodium clearance.

Statistical analyses were conducted with repeated-measures analyses of variance (BMDP 2V) for main effects and interactions and Scheffe’s test for pairwise comparisons among means. Statistical significance was defined as $p < 0.05$.

**Results**

**Intracerebroventricular \( \beta \)-Adrenergic Receptor Antagonists**

The effects of intracerebroventricular administration of d,l-propranolol on the mean arterial pressure, renal neurogram, integrated renal sympathetic nerve activity, and renal sympathetic nerve discharge frequency responses to air stress are illustrated for one conscious SHR in Figure 1. Before intracerebroventricular administration of d,l-propranolol (Figure 1, top panel), the onset of air stress was associated with increases in mean arterial pressure, activity of renal neurogram, integrated renal sympathetic nerve activity, and renal sympathetic nerve discharge frequency. The offset of air stress was associated with a return of these measures to control levels. After i.c.v. d,l-propranolol (Figure 1, bottom panel), air stress still increased mean arterial pressure, but air stress had no effect on renal sympathetic nerve activity.

In the time-control group (Figure 2, top panel), air stress increased renal sympathetic nerve activity after both intracerebroventricular injections of saline (61% from 9.2 ± 2.7 integrator resets/min and 58% from 9.2 ± 2.5 integrator resets/min respectively); renal sympathetic nerve activity returned to control levels during the recovery periods (9.0 ± 2.0 integrator resets/min and 9.1 ± 2.3 integrator resets/min respectively). Before i.c.v. d,l-propranolol (Figure 2, middle panel), air stress increased renal sympathetic nerve
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Figure 1. Effects of air stress on mean arterial pressure (MAP), renal neurogram, integrated renal sympathetic nerve activity (RSNA), and frequency discharge renal nerve activity before (i.c.v. saline; top panel) and after β-adrenergic receptor blockade (i.c.v. d,l-propranolol; bottom panel) in one SHR.

Figure 2. Intracerebroventricular administration of d,l-propranolol or timolol abolished the renal sympathetic nerve activity (RSNA) responses to air stress (AIR) in conscious SHR. C = control; R = recovery; *p < 0.05 compared with C; †p < 0.05 compared with R.

The antinatriuretic response to air stress in conscious SHR was abolished by intracerebroventricular β-adrenergic receptor blockade (Figure 3). With intracerebroventricular administration of saline, air stress decreased urinary sodium excretion 25% from 2.8 ± 0.5 μEq/min/100 g body weight (BW). In contrast, after intracerebroventricular administration of d,l-propranolol or timolol, air stress had no effect on urinary sodium excretion (0% from 2.8 ± 0.5 μEq/min/100 g BW and +9% from 3.3 ± 0.3 μEq/min/100 g BW respectively). Furthermore, the antinatriuretic response to air stress was not abolished by intracerebro-
Mean arterial pressure increased ($p < 0.05$) similarly among saline-, $d$,l-propranolol-, and timolol-treated groups of conscious SHR during air stress (7 mm Hg from 155 ± 8 mm Hg, 6 mm Hg from 150 ± 6 mm Hg, and 10 mm Hg from 148 ± 7 mm Hg respectively; see Figure 3). Heart rate increased ($p < 0.05$) during air stress after intracerebroventricular administration of saline (20 beats/min from 353 ± 12 beats/min), $d$,l-propranolol (20 beats/min from 330 ± 14 beats/min), and timolol (19 beats/min from 328 ± 11 beats/min). Both mean arterial pressure and heart rate returned to control period values during recovery periods.

**Intravenous $\beta$-Adrenergic Receptor Antagonists**

Unlike intracerebroventricular administration, intravenous injection of $d$,l-propranolol or timolol did not abolish the renal sympathetic nerve activity or antinatriuretic responses to air stress in conscious SHR. With i.v. $d$,l-propranolol, air stress increased renal sympathetic nerve activity 76% from 7.1 ± 1.0 integrator resets/minute ($p < 0.05$, $n = 4$) and decreased urinary sodium excretion 27% from 2.5 ± 0.8 $\mu$Eq/min/100 g BW ($p < 0.05$, $n = 4$). Both renal sympathetic nerve activity and urinary sodium excretion returned to control period levels during the recovery period (7.4 ± 1.4 integrator resets/min and 2.3 ± 0.7 $\mu$Eq/min/100 g BW). Similar to i.v. $d$,l-propranolol, intravenous administration of timolol failed to prevent the increased renal sympathetic nerve activity (56% from 5.5 ± 1.0 integrator resets/minute; $p < 0.05$, $n = 4$) and decreased urinary sodium excretion (38% from 1.8 ± 0.2 $\mu$Eq/min/100 g BW; $p < 0.05$, $n = 4$). Renal sympathetic nerve activity and urinary sodium excretion returned to control values during the recovery period (5.4 ± 1.0 integrator resets/min and 1.8 ± 0.3 $\mu$Eq/min/100 g BW respectively).

**Discussion**

Our results indicate that central nervous system $\beta$-adrenergic receptors mediated the increased renal sympathetic nerve activity and decreased urinary sodium excretion resulting from stressful environmental stimulation in the conscious SHR. This conclusion is supported by the findings that intracerebroventricular injection, but not intravenous injection, of the nonselective $\beta$-adrenergic receptor antagonists $d$,l-propranolol or timolol completely abolished the renal sympathetic nerve activity and antinatriuretic responses to air stress in conscious SHR. Also, i.v. $d$-propranolol, which is devoid of $\beta$-adrenergic receptor blocking properties, failed to abolish the antinatriuretic response, which indicates that $d$,l-propranolol blocked the renal sympathetic nerve activity and the antinatriuretic responses to air stress by a $\beta$-adrenergic receptor mechanism. These results are supported by a previous study of the effects of aversive conditioning on urinary sodium excretion in conscious dogs. In that study the intravenous administration of $d$,l-propranolol, which accumulates to a high degree in the central nervous system, completely abolished the antinatriuretic response to aversive conditioning in conscious SHR.

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**Table 1. Renal Hemodynamic Responses to Air Stress**

<table>
<thead>
<tr>
<th>Condition</th>
<th>ERPF</th>
<th>GFR</th>
<th>FENa</th>
</tr>
</thead>
<tbody>
<tr>
<td>Saline</td>
<td>4.0</td>
<td>1.0</td>
<td>2.00</td>
</tr>
<tr>
<td>Propranolol</td>
<td>4.0</td>
<td>1.0</td>
<td>2.00</td>
</tr>
<tr>
<td>Timolol</td>
<td>4.0</td>
<td>1.0</td>
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**Figure 3. Intracerebroventricular administration of $d$,l-propranolol or timolol abolished the antinatriuretic response ($U_{\text{Na}}$) to air stress in conscious SHR, but had no effect on the mean arterial pressure response (MAP). Cont = control; E = air stress; Recov = recovery; * $p < 0.05$ compared with Cont.**

**Figure 4. Effective renal plasma flow (ERPF) and glomerular filtration rate (GFR) were unaffected by air stress with or without intracerebroventricular $\beta$-adrenergic receptor blockade. Fractional sodium excretion ($FENa$) decreased during air stress in conscious SHR after intracerebroventricular administration of saline (vehicle). Cont = control; E = air stress; Recov = recovery; * $p < 0.05$ compared with Cont.**
dogs. In contrast, intravenous administration of timolol, which concentrates in the central nervous system much less readily than \(d,l\)-propranolol,\(^6,^{15}\) did not abolish the antinatriuretic response to aversive conditioning. Moreover, surgical renal denervation abolished the antinatriuretic response to stressful environmental stimulation in both conscious SHR (see the following article) and dogs.\(^2\) Therefore, these studies suggest that a central nervous system \(\beta\)-adrenergic receptor mechanism mediates the renal sympathetic nerve activity responses to stressful environmental stimulation in both conscious SHR and dogs.

Renal \(\beta\)-adrenergic receptors may be excluded as an important mechanism in the renal sympathetic nerve activity and antinatriuretic responses to air stress in the conscious SHR of the present study. Only intracerebroventricular (not intravenous) administration of \(\beta\)-adrenergic receptor antagonists prevented the renal sympathetic nerve activity and antinatriuretic responses to air stress. Consistent with these findings are the results from conscious dogs showing that \(d,l\)-propranolol, but not timolol, blocked the antinatriuretic response to aversive conditioning,\(^5\) even though both drugs concentrate highly in the kidney.\(^6\)

Central nervous system \(\beta\)-adrenergic receptors may regulate renal tubular sodium reabsorption through the renal sympathetic nerves during stressful environmental stimulation in conscious animals. Previous studies in conscious SHR (see the following article) and dogs\(^2\) have shown that chronic surgical renal denervation completely abolished the antinatriuretic response to stressful environmental stimulation. Moreover, the antinatriuretic response was found in this study as well as others (see the following article)\(^4\) to be associated with increased renal sympathetic nerve activity, which is known to increase renal tubular sodium reabsorption.\(^17\)

In the present study, the increased renal sympathetic nerve activity and decreased urinary sodium excretion resulting from air stress in conscious SHR occurred in the absence of changes in effective renal plasma flow or glomerular filtration rate. Consequently, the fractional excretion of sodium decreased during air stress, which suggests that renal tubular sodium reabsorption increased. Given that central nervous system \(\beta\)-adrenergic receptor blockade abolished these responses, these observations indicate that central nervous system \(\beta\)-adrenergic receptors may regulate the increased renal tubular reabsorption of sodium resulting from stressful environmental stimulation in conscious animals.

In sharp contrast to the renal sympathetic nerve activity and urinary sodium excretion responses, the increases in mean arterial pressure and heart rate resulting from air stress in these conscious SHR were not affected by intracerebroventricular administration of \(\beta\)-adrenergic receptor antagonists. This finding is in agreement with a similar lack of effect of \(d,l\)-propranolol or timolol on the increased mean arterial pressure (but not the antinatriuretic) response to aversive conditioning in conscious dogs.\(^5\) Whether higher doses or long-term administrations of \(\beta\)-adrenergic receptor antagonists would alter the mean arterial pressure or heart rate responses to air stress is not known. Nevertheless, this finding indicates that a degree of selectivity exists for the effects of \(\beta\)-adrenergic receptor blockade on the renal sympathetic nerve activity and urinary sodium excretion responses — as compared with the mean arterial pressure and heart rate responses — to stressful environmental stimulation in conscious animals.

Central administration of \(\beta\)-adrenergic receptor antagonists lowered basal levels of renal sympathetic nerve activity in conscious SHR in the present study. Yet renal sympathetic nerve activity was still elevated relative to postmortem background noise levels. Similarly, after central \(\beta\)-adrenergic receptor blockade, baroreceptor loading with intravenous injection of noradrenaline still caused reflex reductions in renal sympathetic nerve activity, and baroreceptor unloading with intravenous acetylcholine still caused reflex increases in renal sympathetic nerve activity. Therefore, it seems that central \(\beta\)-adrenergic receptors contribute only in part to basal renal sympathetic nerve activity, and their blockade does not prevent baroreceptor-reflex-dependent alterations in renal nerve traffic.

A renal functional role of central nervous system \(\beta\)-adrenergic receptors has been demonstrated by other studies. Administration of \(d,l\)-propranolol into the third cerebral ventricle of conscious normotensive rats has been shown to result in an increased urinary sodium excretion.\(^18\) In conscious normotensive rats stimulation of \(\beta\)-adrenergic receptors in the medial septal area with isoproterenol elicited dose-dependent decreases in urinary sodium excretion, which were blocked by \(\beta_2\)-adrenergic receptor blockade.\(^19\) Reflex increases in renal sympathetic nerve activity elicited by electrically stimulating the central cut end of the sciatic nerve were diminished by intravenous administration of \(d,l\)-propranolol but not oxprenolol.\(^20\) As \(d,l\)-propranolol crosses the blood-brain barrier more readily than does oxprenolol, the central nervous system actions of \(d,l\)-propranolol were considered important in this response. These studies suggest that central nervous system \(\beta\)-adrenergic receptors may regulate urinary sodium excretion by way of the renal sympathetic nerves. The present study provides more convincing evidence that increased renal sympathetic nerve activity can alter urinary sodium excretion through a central nervous system \(\beta\)-adrenergic receptor mechanism.

The regulation of renal sympathetic nerve activity and urinary sodium excretion by central \(\beta\)-adrenergic receptors may be important in the pathophysiology of hypertension. The same air stress stimulus as employed in the present study failed to have any effect on renal sympathetic nerve activity or urinary sodium excretion in conscious Wistar-Kyoto rats (see the following article). Thus, SHR may be more genetically predisposed to respond to environmental stress with increased renal sympathetic nerve activity and antinatriuresis than are Wistar-Kyoto rats. An activation of central nervous system \(\beta\)-adrenergic receptors during exposure to environmental stress may be an important
factor contributing to the pathophysiology of hypertension in conscious SHR.

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References
16. Street JA, Hemsworth BA, Roach AG, Day MD. Tissue levels of several radio labelled beta adrenoceptor antagonists after intravenous administration in rats. Arch Int Pharmacodyn Ther 1979;237:180-190
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