High Sodium Intake Enhances Renal Nerve and Antinatriuretic Responses to Stress in Spontaneously Hypertensive Rats

JOHN P. KOEPKE AND GERALD F. DiBONA

SUMMARY The effects of high sodium intake (drinking 0.9% NaCl for 15 days) on the increased renal sympathetic nerve activity and decreased urinary sodium excretion resulting from stressful environmental stimulation (air jet to head) were examined in conscious spontaneously hypertensive rats (SHR) and normotensive Wistar-Kyoto rats (WKY). On a normal sodium intake in SHR, air stress increased renal sympathetic nerve activity 77% and decreased urinary sodium excretion 28% without altering effective renal plasma flow or glomerular filtration rate. By contrast, in conscious SHR on high sodium intake, the same air stress caused a greater increase in renal sympathetic nerve activity (103%) and a greater antinatriuresis (42%) along with reductions in effective renal plasma flow and glomerular filtration rate. Surgical renal denervation prevented the antinatriuretic responses to air stress in other conscious SHR on high or normal sodium intake. In conscious WKY, air stress had no effect on renal sympathetic nerve activity or urinary sodium excretion, regardless of normal or high sodium intake. We conclude that the enhanced renal sympathetic nerve activity and antinatriuretic responses to air stress in conscious SHR on high sodium intake are dependent on a centrally mediated facilitation of sympathetic neural outflow to the kidney. The greater antinatriuretic response to air stress in conscious SHR than in WKY may reflect a greater genetic predisposition in SHR to increase renal sympathetic nerve activity during air stress. (Hypertension 7: 357-363, 1985)

KEY WORDS • renal sympathetic nerve activity • dietary sodium • environmental stress

STRESSFUL environmental stimulation has been used to study the neural control of renal excretory function in conscious spontaneously hypertensive rats (SHR) and dogs. Decreased urinary sodium excretion results from exposure of conscious SHR to air stress (see the preceding article by J. P. Koepke and G. F. DiBona on pages 350-356 of this issue), conscious dogs to aversive conditioning, and conscious humans to mental competition. The antinatriuretic response to aversive conditioning or air stress occurs in the absence of changes in glomerular filtration rate, which suggests an increased renal tubular sodium reabsorption (see the preceding article). Moreover, the antinatriuretic response to air stress is associated with increased renal sympathetic nerve activity and is abolished by surgical renal denervation or by intracerebroventricular administration of β-adrenergic receptor antagonists (see the preceding article). In addition, the increased renal sympathetic nerve activity and antinatriuresis resulting from stressful environmental stimulation is greater in conscious SHR than in normotensive Wistar-Kyoto rats (WKY). Similarly, humans with a parental history of hypertension respond to mental competition with a greater antinatriuresis than humans with no parental history of hypertension. Thus, the effects of air stress on urinary sodium excretion are mediated by the renal sympathetic nerves and are more pronounced in animals or individuals with a genetic predisposition toward hypertension.

Similar to stressful environmental stimulation, high sodium intake increases the responsiveness of the sympathetic nervous system to neurogenic stimuli to a greater degree in animals with a genetic predisposition toward hypertension. Responsiveness of abdominal sympathetic nerve activity to posterior hypothalamic
stimulation is enhanced by high sodium intake in Dahl salt-sensitive rats and in deoxycorticosterone acetate (DOCA) hypertensive rats.\textsuperscript{5,6} High sodium intake may facilitate peripheral sympathetic neurotransmission as well. The responsiveness of vascular smooth muscle to norepinephrine is greater in stroke prone SHR on a high sodium intake than in those on a normal sodium intake.\textsuperscript{7,8}

In the present study, we tested the hypothesis that high sodium intake facilitates the antinatriuretic response to stressful environmental stimulation in conscious SHR and WKY. Moreover, we hypothesized that high sodium intake would facilitate the antinatriuretic response to stressful environmental stimulation to a greater degree in conscious SHR than in conscious WKY. Finally, we measured the renal sympathetic nerve activity response to stressful environmental stimulation in conscious SHR and WKY on normal and high sodium intakes to determine whether any facilitation of the antinatriuretic response could be attributed to enhanced renal sympathetic neural outflow from the central nervous system.

**Materials and Methods**

Male SHR and normotensive WKY rats 12 to 14 weeks of age were obtained from Taconic Farms, Inc. (Germantown, NY). The SHR and WKY were maintained for 15 days on either a normal sodium intake (SHR-Na, WKY-Na) or a high sodium intake (SHR-HNa, WKY-HNa). Normal sodium intake rats were given tap water, and high sodium intake rats were given isotonic saline to drink; both normal sodium and high sodium intake rats were given standard rat chow (Na content, 163 mEq/kg).

One group, comprised of 16 SHR and 13 WKY, underwent ketamine HCl anesthesia (150 mg/kg i.p.; Bristol Laboratories, Syracuse, NY) and was surgically prepared 24 to 48 hours before experimentation with catheters (Silastic 602-135, Dow Corning, Midland, MI) in the jugular vein and right carotid artery. The venous and arterial catheters were tunneled to the back of the neck, filled with heparinized saline (1000 U/ml), and plugged with stainless steel pins. Through a suprapubic incision, a stainless steel urinary bladder catheter (18 gauge, 12.5 cm long), modified from that of Gellai and Valtin,\textsuperscript{9} was sutured into the urinary bladder, exteriorized, and secured to adjacent tissues. The venous and arterial catheters were tunneled to the back of the neck and exteriorized, the flank incision was closed in layers, and 24 hours was allowed for recovery.

Another group of SHR (n = 14) underwent either renal denervation or sham renal denervation under ketamine anesthesia (150 mg/kg i.p.) 5 to 7 days before the experimental day. Through a midline laparotomy, bilateral renal denervation was performed by stripping the renal arteries and veins of adventitia, cutting the renal nerve bundles, and coating the vessels with a 10% solution of phenol in absolute ethanol, as previously described.\textsuperscript{11} Sham renal denervation was accomplished by exposing the renal arteries and veins, but leaving adventitia and renal nerve bundles intact. These rats also were implanted with jugular, carotid, and urinary bladder catheters 24 to 48 hours before experimentation.

On the experimental day, conscious SHR and WKY were placed in Lucite cylinders, which permitted forward and backward movement, and an isotonic saline infusion was started at a rate of 60 μL/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 arterial 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 i.v. norepinephrine (5 μg) as on the surgical day. If the quality of the renal nerve activity recording was similar to that observed when
the electrode was implanted, then the experiment commenced.

The isotonic saline infusion included inulin and para-aminohippurate (PAH) for determination of inulin and PAH clearances respectively. After 60 minutes of equilibration to the infusion, two consecutive 20-minute control periods were obtained, followed by a 20-minute stressful environmental stimulation period and then by two consecutive 20-minute recovery periods. For clearance experiments, 20 minute urine collections were made for each period, and venous blood samples (200 μL) 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. At the end of renal sympathetic nerve activity recording experiments, the quality of the renal nerve signal was again assessed with intravenous injections of norepinephrine (5 μg). Finally, the rat was killed and postmortem renal nerve activity was recorded 30 to 45 minutes later as a measure of background noise; this value was subtracted from all values of renal sympathetic nerve activity.

Urinary 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: 

\[
C_{\text{IN}} = \frac{V \times U_{\text{IN}}}{P_{\text{IN}}}
\]

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: 

\[
C_{\text{PAH}} = \frac{V \times U_{\text{PAH}}}{P_{\text{PAH}}}
\]

where \(U_{\text{PAH}}\) and \(P_{\text{PAH}}\) are urine and plasma PAH respectively. Fractional sodium excretion was estimated by 

\[
\text{FSE} = \frac{C_{\text{IN}}}{C_{\text{PAH}}} \times 100,
\]

where \(C_{\text{IN}}\) is sodium clearance. Fractional water excretion was determined by 

\[
\text{FW} = \frac{V}{C_{\text{IN}}} \times 100.
\]

Because the values of the two control periods were statistically similar, these values were averaged to give a single control period value. Similarly, the values from the two recovery periods were averaged to give a single recovery period value. All renal sympathetic nerve activity data were quantified for each experiment period. Statistical analyses were conducted with repeated measures analysis 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

Renal Function and Mean Arterial Pressure

High sodium intake augmented the antinatriuretic response to air stress in conscious SHR, but not in WKY (Figure 1). In fact, in WKY air stress had no effect on urine flow rate, urinary sodium excretion, effective renal plasma flow, or glomerular filtration rate regardless of normal sodium or high sodium intakes (Table 1). The decreased urinary sodium excretion resulting from air stress in SHR-HNa (−42%) was greater \((p < 0.01)\) than the antinatriuretic response in SHR-NNa (−28%). Whereas no changes in urine flow rate (−8%), effective renal plasma flow (−2%), and glomerular filtration rate (−1%) occurred in SHR-Na, these measures decreased during air stress in SHR-HNa (−37%, −24%, and −14% respectively). Accordingly, the effects of air stress on the fractional excretions of sodium and water in SHR-HNa (−34% change from 3.47 ± 0.63%, \(p < 0.01\), and −28% change from 3.22 ± 0.54%, \(p < 0.01\) respectively) were greater \((p < 0.05)\) than in SHR-NNa (−22% change from 2.85 ± 0.58%, \(p < 0.05\); and −2% change from 2.67 ± 0.57%, \(p = \text{not significant}\)). Urinary sodium excretion decreased \((p < 0.05)\) in sham renal denervated SHR on normal or high sodium intakes (30% from 2.2 ± 0.9 μEq/min/100 g body weight and 45% from 4.5 ± 1.0 μEq/min/100 g body weight respectively; \(n = 4\)). In contrast, chronic bilateral renal denervation completely abolished the decreases in renal excretory and hemodynamic function resulting from air stress in conscious SHR-Na and SHR-HNa. In fact, changes in sodium excretion during air stress after surgical renal denervation in SHR were not different from those in WKY.

High sodium intake had no effect on the mean arterial pressure or heart rate responses to air stress in either SHR or WKY. Mean arterial pressure and heart rate increased \((p < 0.01)\) in SHR-Na by 13 mm Hg from 149 ± 8 mm Hg and 25 beats/minute from 423 ± 2 beats/minute respectively compared with the increases \((p < 0.01)\) in SHR-HNa of 9 mm Hg from 154 ± 4 mm Hg and 27 beats/minute from 429 ± 20 beats/minute. During recovery, mean arterial pressure and heart rate returned to control levels in both SHR-Na (151 ± 8 mm Hg and 430 ± 14 beats/minute) and SHR-HNa (154 ± 3 mm Hg and 433 ± 20 beats/minute).

Mean arterial pressure and heart rate were increased \((p < 0.05)\) by air stress in WKY-Na (+4 mm Hg from 112 ± 6 mm Hg, and +15 beats/minute from 356 ± 20 beats/minute) and in WKY-HNa (+5 mm Hg from 117 ± 4 mm Hg and +15 beats/minute from 381 ± 13 beats/minute). Control measures of mean arterial pressure

![Figure 1. Sodium excretion responses to air stress in conscious SHR. SHR with renal denervation (SHR-DNX), and WKY on normal and high sodium diets. Values are the change from the average of control plus recovery periods to air stress periods. *p < 0.01.](http://hyper.ahajournals.org/lookup/fig/359/23/11891527/11891527)
TABLE 1. Renal Function Responses to Air Stress in Conscious Spontaneously Hypertensive Rats (SHR), SHR with Renal Denervation (SHR-DNX) and Wistar-Kyoto Rats (WKY) on Normal and High Sodium Diets

<table>
<thead>
<tr>
<th>Value</th>
<th>SHR (n = 8)</th>
<th>SHR-DNX (n = 6)</th>
<th>WKY (n = 8)</th>
<th>SHR (n = 8)</th>
<th>SHR-DNX (n = 8)</th>
<th>WKY (n = 5)</th>
</tr>
</thead>
<tbody>
<tr>
<td>MAP (mm Hg)</td>
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<td></td>
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<td></td>
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<tr>
<td>C</td>
<td>149 ± 8</td>
<td>132 ± 9</td>
<td>112 ± 6</td>
<td>154 ± 4</td>
<td>134 ± 8</td>
<td>117 ± 4</td>
</tr>
<tr>
<td>Air</td>
<td>162 ± 10*</td>
<td>144 ± 7*</td>
<td>116 ± 6</td>
<td>163 ± 4*</td>
<td>148 ± 6*</td>
<td>123 ± 3</td>
</tr>
<tr>
<td>R</td>
<td>151 ± 8</td>
<td>130 ± 11</td>
<td>109 ± 5</td>
<td>154 ± 3</td>
<td>137 ± 7</td>
<td>117 ± 4</td>
</tr>
<tr>
<td>V (μL/min/100 g BW)</td>
<td></td>
<td></td>
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</tr>
<tr>
<td>C</td>
<td>15.8 ± 3.3</td>
<td>13.1 ± 1.2</td>
<td>15.4 ± 2.9</td>
<td>27.1 ± 5.1</td>
<td>19.7 ± 2.0</td>
<td>26.2 ± 7.4</td>
</tr>
<tr>
<td>Air</td>
<td>14.5 ± 3.2</td>
<td>18.1 ± 3.0</td>
<td>14.4 ± 2.6</td>
<td>17.1 ± 3.3*</td>
<td>24.1 ± 2.9</td>
<td>25.3 ± 7.0</td>
</tr>
<tr>
<td>R</td>
<td>15.8 ± 2.6</td>
<td>13.0 ± 1.5</td>
<td>16.8 ± 3.1</td>
<td>25.1 ± 3.8</td>
<td>22.4 ± 2.6</td>
<td>24.9 ± 7.1</td>
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<tr>
<td>UNaV (μEq/min/100 g BW)</td>
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<td></td>
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<tr>
<td>C</td>
<td>2.5 ± 0.6</td>
<td>2.3 ± 0.4</td>
<td>2.2 ± 0.5</td>
<td>4.3 ± 0.8</td>
<td>6.1 ± 1.1</td>
<td>3.9 ± 0.6</td>
</tr>
<tr>
<td>Air</td>
<td>1.8 ± 0.4*</td>
<td>2.5 ± 0.4</td>
<td>2.2 ± 0.5</td>
<td>2.5 ± 0.5*</td>
<td>6.1 ± 1.1</td>
<td>3.9 ± 0.5</td>
</tr>
<tr>
<td>R</td>
<td>2.7 ± 0.6</td>
<td>2.5 ± 0.5</td>
<td>2.4 ± 0.5</td>
<td>4.1 ± 0.7</td>
<td>6.1 ± 1.2</td>
<td>3.9 ± 0.6</td>
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<tr>
<td>ERPF (ml/min/100 g BW)</td>
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<td></td>
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<tr>
<td>C</td>
<td>4.4 ± 0.5</td>
<td>—</td>
<td>3.9 ± 0.4</td>
<td>3.8 ± 0.3</td>
<td>3.7 ± 0.2</td>
<td>4.6 ± 1.4</td>
</tr>
<tr>
<td>Air</td>
<td>4.3 ± 0.5</td>
<td>—</td>
<td>3.9 ± 0.4</td>
<td>2.9 ± 0.2†</td>
<td>3.7 ± 0.2</td>
<td>4.4 ± 1.4</td>
</tr>
<tr>
<td>R</td>
<td>4.4 ± 0.6</td>
<td>—</td>
<td>3.9 ± 0.3</td>
<td>3.2 ± 0.3</td>
<td>3.7 ± 0.2</td>
<td>4.6 ± 1.4</td>
</tr>
<tr>
<td>GFR (ml/min/100 g BW)</td>
<td></td>
<td></td>
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<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>C</td>
<td>0.87 ± 0.05</td>
<td>—</td>
<td>0.91 ± 0.07</td>
<td>0.89 ± 0.06</td>
<td>0.92 ± 0.13</td>
<td>0.96 ± 0.27</td>
</tr>
<tr>
<td>Air</td>
<td>0.86 ± 0.05</td>
<td>—</td>
<td>0.89 ± 0.07</td>
<td>0.77 ± 0.08†</td>
<td>0.91 ± 0.13</td>
<td>0.94 ± 0.25</td>
</tr>
<tr>
<td>R</td>
<td>0.90 ± 0.05</td>
<td>—</td>
<td>0.90 ± 0.07</td>
<td>0.83 ± 0.07</td>
<td>0.94 ± 0.11</td>
<td>0.95 ± 0.25</td>
</tr>
</tbody>
</table>

Values are means ± SEM.

C = control; R = recovery; MAP = mean arterial pressure; V = urine flow rate; UNaV = urinary sodium excretion; ERPF = effective renal plasma flow; GFR = glomerular filtration rate; BW = body weight; SHR-DNX = SHR with renal denervation; WKY = Wistar-Kyoto rats.

*p < 0.01, †p < 0.05 compared with control.

and heart rate in SHR-NNa and WKY-NNa were similar to control measures in SHR-HNa and WKY-HNa respectively. Bilateral renal denervation or sham renal denervation did not affect the mean arterial pressure or heart rate responses to air stress in SHR-NNa or SHR-HNa.

High sodium intake elevated control measures of urine flow rate and sodium excretion (p < 0.05), but had no effect on control measures of effective renal plasma flow, glomerular filtration rate, or mean arterial pressure. In SHR-HNa, control urine flow rate and sodium excretion were each 72% higher than in SHR-NNa. Control urine flow rate and sodium excretion, respectively, were 70% and 77% greater in WKY-HNa than WKY-NNa. Similarly, in SHR with bilateral surgical renal denervation, HNa increased control urine flow rate and sodium excretion by 50% and 165%, respectively, relative to renal denervated SHR or NNa.

Renal Sympathetic Nerve Activity

Air stress increased renal sympathetic nerve activity only in SHR, but had no effect on renal sympathetic nerve activity in WKY (Figure 2). High sodium intake augmented (p < 0.05) the renal sympathetic nerve activity response to air stress only in SHR. In SHR-HNa, renal sympathetic nerve activity increased 77%, whereas in SHR-HNa renal sympathetic nerve activity increased 103%. In contrast, air stress failed to elicit a renal sympathetic nerve activity response in WKY on either high or normal sodium intake.
In these rats, air stress increased (p < 0.01) mean arterial pressure in SHR-NNa (+10 mm Hg), SHR-HNa (+9 mm Hg), WKY-NNa (12 mm Hg), and WKY-HNa (9 mm Hg; Table 2). The increases in mean arterial pressure during air stress were similar between rats on either high or normal sodium intake. Mean arterial pressure and heart rate returned to control levels during the recovery period.

**Discussion**

Stressful environmental stimulation in conscious SHR increased renal sympathetic nerve activity and decreased urinary sodium excretion without altering effective renal plasma flow or glomerular filtration rate. The antinatriuretic effect was abolished by bilateral surgical renal denervation. These findings suggest that the antinatriuretic response to stressful environmental stimulation increased renal tubular sodium reabsorption, which in turn was mediated by increased effenter renal sympathetic nerve activity. In sharp contrast, stressful environmental stimulation had no effect on renal sympathetic nerve activity or urinary sodium excretion in conscious WKY. These results support the study of Lundin and Thoren, in which stressful environmental stimulation caused a much greater increase in renal sympathetic nerve activity and antinatriuresis in conscious SHR than in conscious WKY. A new finding of the present study is that a high sodium intake enhances the magnitude of the renal sympathetic nerve activity and antinatriuretic responses to stressful environmental stimulation in conscious SHR. This enhancement was selective in that the mean arterial pressure and heart rate responses were not increased; however, high sodium intake had no additional effect on renal sympathetic nerve activity or urinary sodium excretion responses to stressful environmental stimulation in conscious WKY.

Therefore, it appears that conscious SHR are not only more sensitive to the effects of stressful environmental stimulation on renal sympathetic nerve activity and urinary sodium excretion than are conscious WKY, but also are more sensitive to the effects of high sodium intake. That is, high sodium intake and stressful environmental stimulation interact to cause greater renal sympathetic nerve activity and antinatriuretic responses than stressful environmental stimulation alone.

The enhanced antinatriuretic response to stressful environmental stimulation in conscious SHR on high sodium intake was not mediated by a circulating humoral factor. This view is supported by the finding that surgical renal denervation abolished the antinatriuretic response in conscious SHR on normal and high sodium intakes. Similarly, a greater renal sympathetic nerve activity response to stressful environmental stimulation in conscious SHR on high rather than normal sodium intake supports the view that the enhanced antinatriuretic response was mediated by the renal sympathetic nerves.

Our results suggest that an increased sensitivity of central nervous system pathways mediated the enhanced antinatriuretic response to stressful environmental stimulation in conscious SHR on high sodium intake. This conclusion is based on the finding that the increased renal sympathetic nerve activity resulting from stressful environmental stimulation was greater in SHR on a high sodium intake than in those on a normal sodium intake. Consistent with these findings are the results of Bunag and associates showing that the abdominal sympathetic nerve responses to posterior or ventromedial hypothalamic stimulation are greater in DOCA-salt and Dahl salt-sensitive rats than in control rats. Similarly, in normotensive rats made to drink isotonic saline for 5 weeks, the increased abdominal sympathetic nerve activity resulting from stimulation of the ventromedial hypothalamus was greater than in rats given water to drink. Thus, high sodium intake may increase the sensitivity of the hypothalamic-pituitary-adrenal axis.
These results indicate that the effects of high sodium intake on mean arterial pressure and heart rate were unaffected by the high sodium intake resulting from stressful environmental stimulation. In stroke prone SHR, the vascular smooth muscle response to norepinephrine was augmented by a high sodium intake, which suggests that high sodium intake may increase the sensitivity of the peripheral vasculature to circulating norepinephrine. Moreover, high sodium intake in stroke prone SHR increased the release of norepinephrine and impaired peripheral neuronal norepinephrine uptake, which resulted in higher baseline plasma norepinephrine concentrations and exaggerated increases in plasma norepinephrine concentrations during cold exposure. Whether renal sympathetic nerve terminals or ganglia are affected in similar fashion by high sodium intake in SHR, and whether the antinatriuretic response to stressful environmental stimulation is mediated in part by such a mechanism, remain to be determined.

A genetic predisposition to respond to stressful environmental stimulation with increased renal sympathetic nerve activity and antinatriuresis may underlie the greater responsiveness in conscious SHR than in WKY. In the present study, WKY were unaffected by stressful environmental stimulation, and in a previous study, both WKY and SHR had a greater response to similar stressful environmental stimulation than in the present study, but the antinatriuresis in SHR was much greater than in WKY. In addition, the high sodium intake enhanced the differences in responsiveness to stressful environmental stimulation between SHR and WKY, which increased the antinatriuretic response in SHR but had no additional effects in WKY. A similar phenomenon has been observed in humans. Psychological stress decreased urinary sodium excretion in young adult men with borderline hypertension or a family history of hypertension but had no effect on urinary sodium excretion in young adult men with no family history of hypertension. Although the effects of high sodium intake on the antinatriuretic response to stressful environmental stimulation in these individuals is unknown, salt loading in human adolescents with a family history of hypertension enhances the arterial pressure response to psychological stress, which implies that high sodium intake may enhance the antinatriuretic response in humans as well.

In the conscious SHR and WKY of the present study, 15 days on the high sodium intake had no effect on the increases in mean arterial pressure and heart rate resulting from stressful environmental stimulation. Similarly, control levels of mean arterial pressure and heart rate were unaffected by the high sodium intake. These results indicate that the effects of high sodium intake on the renal functional and electrophysiological responses to stressful environmental stimulation were not due to widespread and nonselective augmentation of responses mediated by the sympathetic nervous system. Rather, these results suggest that high sodium intake selectively augmented the renal neural and functional responses to stressful environmental stimulation, while it did not affect the mean arterial pressure and heart rate responses.

The pathophysiology of hypertension is accelerated by high sodium intake alone or by stressful environmental stimulation alone, but the combination of high sodium intake and stressful environmental stimulation is more effective in producing hypertension than is either factor alone. The development of hypertension was more rapid and severe in SHR exposed to territorial stress plus a high sodium intake (3% NaCl for drinking) than when either territorial stress or high sodium intake was presented alone. In similar fashion, hypertension was produced in conscious dogs over several weeks only when they were exposed to aversive conditioning plus high sodium intake. Whether high sodium intake and stressful environmental stimulation exacerbate the pathophysiology of hypertension by increased renal sympathetic nerve activity resulting in antinatriuresis and increased sodium retention, as observed during short-term exposure to these stimuli in the present study, remains to be examined.

Acknowledgments

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References

High sodium intake enhances renal nerve and antinatriuretic responses to stress in spontaneously hypertensive rats.

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