Increased dietary sodium inhibits baroreflex-induced bradycardia during acute sodium loading

Steven L. Bealer

Department of Pharmacology and Toxicology, College of Pharmacy, University of Utah, Salt Lake City, Utah

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Bealer, Steven L. Increased dietary sodium inhibits baroreflex-induced bradycardia during acute sodium loading. Am J Physiol Regul Integr Comp Physiol 288: R1211–R1219, 2005.—The present study investigated the effects of increased dietary sodium on the modification of cardiac baroreflex responses induced by acute sodium loading. Changes in blood pressure and heart rate during intravenous phenylephrine and nitroprusside administration were compared using a four-parameter sigmoid logistic function before and after a 30-min infusion of 0.6 or 1.0 M NaCl in conscious male Sprague-Dawley rats consuming only tap water (Tap) or isotonic saline (Iso) for 2–3 wk. In Tap animals, infusion of 1.0 M NaCl increased the baroreflex-induced heart rate minimum, reduced heart rate range, and increased the operating blood pressure. In contrast, infusion of 0.6 M NaCl in Tap rats reduced both heart rate minimum and maximum. However, infusion of 0.6 M NaCl in Iso animals produced responses similar to that shown in Tap rats infused with 1.0 M NaCl. In addition, the decreased heart rate minimum in Tap rats after infusion of 0.6 M NaCl was prevented by intravenous administration of a vasopressin V1-receptor antagonist. Furthermore, cardiac parasympathetic responses were similar in Tap and Iso rats before and after 0.6 M NaCl infusion. However, in animals receiving intravenous atropine, 0.6 M NaCl decreased heart rate minimum and maximum in Tap but did not alter the response parameters in Iso rats. These results demonstrate that the facilitation of cardiac baroreflex responses normally observed during moderate sodium loading is mediated by vasopressin and that increased dietary sodium ingestion reverses this facilitation by reducing sympathetic nervous system withdrawal.

Hypertension; cardiac baroreceptor

INCREASED DIETARY SODIUM IS a risk factor for development of hypertension. One effect of a high-sodium diet that may contribute to chronically increased arterial pressure is reduced baroreflex-induced bradycardia (22, 23, 31). The mechanism through which enhanced sodium ingestion decreases cardiac buffering of transient increases in blood pressure is not completely understood. Either decreased parasympathetic activation or increased sympathetic nervous system (SymNS) activity could contribute to diminished bradycardia. Directly related to this question, previous studies demonstrated that increasing dietary sodium enhances SymNS-mediated pressor responses to a number of excitatory stimuli (27, 39). Together, these data are consistent with the proposal that increased dietary sodium enhances SymNS responses to sympathoexcitatory stimuli, which would decrease SymNS withdrawal during arterial baroreceptor stimulation and inhibit bradycardia.

Acute changes in sodium status produce concentration-dependent effects on baroreflex responses. For example, administration of small, nonpressor concentrations of sodium [either systemically (32) or centrally (5)] or water deprivation (6, 40) increases cardiac baroreflex responses in dogs and rats. The enhanced baroreflex sensitivity during moderate increases in systemic sodium and/or osmolality may be important for buffering transient changes in blood pressure, which could occur following water deprivation, exercise, or consumption of a hyperosmotic meal, because pressor systems could be potentially activated by increased sodium/osmolality, e.g., vasopressin release, activation of the SymNS, and/or volume expansion.

In contrast to moderate sodium loads, administration of both central (8, 24, 43) and systemic (3, 4) pressor concentrations of hypertonic solutions diminishes cardiac baroreflex responses. Furthermore, the decrease in baroreflex-induced bradycardia after systemic infusion of pressor concentrations of hypertonic saline is mediated by reduced withdrawal of cardiac sympathetic tone during baroreceptor stimulation (3).

Because dietary sodium enhances SymNS sympathoexcitatory responses to pressor stimuli (27, 39), it is possible that increasing sodium ingestion may reduce the threshold change in systemic sodium or osmolality necessary for SymNS activation and the resulting diminished baroreflex response. In this study, the hypothesis that increased dietary sodium reduces the SymNS contribution to baroreflex-induced bradycardia during acute, moderate sodium loading, which normally enhances bradycardic responses, was tested. A long-term decrease in the ability to buffer repeated, transient increases in blood pressure, resulting from high dietary sodium ingestion, could favor resetting of the baroreflex and contribute to maintenance of chronically increased arterial blood pressure.

MATERIALS AND METHODS

Animals

Male Sprague-Dawley rats weighing 225–250 g at the time of purchase were obtained from a commercial supplier (Charles River) and housed in individual cages with ad libitum access to food and drinking solution. The animals were maintained in a room with a 12:12-h light-dark cycle at 22°C. All protocols used in these studies were approved by the Institutional Animal Care and Use Committee at the University of Tennessee or University of Utah.

Increased Sodium Ingestion

Animals were provided with either tap water (Tap group) or isotonic saline (Iso group) as their sole drinking solution and standard laboratory rat chow (Harlan 8640, 0.4% sodium) ad libitum. Animals

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Address for reprint requests and other correspondence: S. L. Bealer, Dept. of Pharmacology/Toxicology, Univ. of Utah, 30 South 2000 East Rm. 201, Salt Lake City, UT 84112-5820 (E-mail: steve.bealer@deans.pharm.utah.edu).
were maintained on this regimen for 2–3 wk before surgery and testing.

**Surgical Procedure**

On the day before testing, animals were anesthetized with tri bromo methanol (Avertin, 300 mg/kg), and catheters (40-mm PE-10 poly ethylene cemented into PE-50) filled with heparinized (50 U/ml) isotonic saline were implanted into a femoral artery and both femoral veins. These catheters were used to monitor arterial blood pressure and heart rate and to infuse intravenous saline and vasoactive substances. The distal ends of the catheters were led subcutaneously and exited between the scapulae, where they were secured. All animals were then allowed to recover from the anesthetic and were returned to their home cages overnight.

**Baroreflex Testing**

Baroreflex function was determined by continuously recording blood pressure and heart rate during sequential intravenous infusions of nitroprusside and phenylephrine. The animals’ blood pressures were initially lowered to ~50 mmHg with sodium nitroprusside (10–80 μg·kg⁻¹·min⁻¹·iv) and then raised to ~180 mmHg with phenylephrine (1–20 μg·kg⁻¹·min⁻¹·iv) (13, 17). The rate of increase in blood pressure was maintained at ~1–2 mmHg/s. The mean blood pressure and heart rate values for sequential 2-s periods during the transition between maximum hypotension and hypertension were used to evaluate cardiac baroreflex responses.

Cardiac baroreflex sensitivity was evaluated by fitting the blood pressure and heart rate values to a sigmoid logistic function (18, 19), modified from Kent et al. (29), using the following equation: $$y = m_1 + (m_2 - m_1)/[1 + \exp(m_3 \times (x - m_0))]$$ (KaleidaGraph, Synergy Software). In this equation, y is heart rate, $$m_1$$ is minimum heart rate (HRmin), $$m_2$$ is maximum heart rate (HRmax), $$m_3$$ is slope coefficient, $$m_0$$ is mean arterial pressure at the midpoint of the curve (BP, 50), and x is blood pressure. If the calculated correlation coefficient (R) that quantifies the fit of the data points to the generated curve was <0.95 on either baroreflex test, the animal was eliminated from the data analyses. The heart rate range (HR_range) was calculated as $$m_2 - m_1$$, and the maximum gain ($$G_{max}$$) was estimated as $$-[(m_2 - m_1) \times m_3]/4$$ (29). The group mean values of the curve-fit parameters were calculated and used to generate an average cardiac baroreflex reflex function curve for each experimental condition.

**Protocols**

**Experiment 1: effect of sodium ingestion on baroreflex responses during moderate sodium loading.** On the morning of testing, animals were brought to the laboratory and the arterial catheter was connected to a pressure transducer and Maclab data acquisition system so that arterial blood pressure and heart rate could be continuously monitored. One femoral vein catheter was attached to a syringe filled with 0.6 or 1.0 M NaCl, which was placed in a remote syringe pump. The other venous catheter was connected to a 1-ml syringe for administration of nitroprusside and phenylephrine to generate baroreflex response curves. After connection of the catheters, the rats were left undisturbed for 45–60 min. Baseline blood pressure and heart rate were then determined as the mean value during a 5-min observation period, and control (preinfusion) baroreflex curves were generated with the procedures described above. After baroreflex testing was completed, blood pressure and heart rate were allowed to return to control values at which time intravenous infusions of 0.6 M NaCl (Tap) and 1.0 M NaCl (Tap rats) were initiated at 0.1 ml·kg⁻¹·min⁻¹·iv and continued for 30 min. Furthermore, arterial blood samples (200 μl) were obtained immediately before and immediately after the saline infusion for evaluation of hematocrit and plasma osmolality with a vapor pressure osmometer (Vapro S520; Westcore, Logan, UT). After 30 min of infusion, postinfusion blood pressure and heart rate were determined, and experimental (postinfusion) baroreflex curves were generated.

To evaluate whether restricting drinking fluid to isotonic saline altered thirst either before or in response to hypertonic saline loading, ad libitum water ingestion was determined during testing in some animals. Graduated cylinders filled with tap water were provided for Tap and Iso rats before and after infusion of 0.6 M NaCl. The volumes of water consumed during 30-min observation periods were recorded.

**Experiment 2: role of vasopressin in baroreflex responses after acute sodium loading.** Other Tap and Iso animals were prepared and tested using the procedures described in experiment 1. However, immediately before the start of the saline infusion period, these rats were treated with a specific vasopressin V₁ receptor antagonist (VP-X) ([deamino-Pen¹,Tyr(Me)³,Arg⁴]-vasopressin; Bachem; 10 μg/kg iv).

**Experiment 3: effects of dietary sodium on the parasympathetic and SymNS components of the baroreflex after acute sodium loading.** Similar baroreflex analyses were conducted on Tap and Iso animals treated with either 1 mg/kg iv atropine methylsulfate (Sigma) or 1 mg/kg iv atenolol (Sigma) administered to separate groups of rats. Atropine treatment blocks the parasympathetic component of the cardiac baroreflex response so that the SymNS contribution can be evaluated, and atenolol blocks cardiac SymNS influences so that the parasympathetic contribution to baroreflex responses can be observed. The doses of these agents employed in this study have been widely used previously in similar experiments (10, 20, 33, 45); these doses prevented changes in heart rate following administration of 1 μg/kg acetylcholine (Sigma) or 0.1 μg/kg isoproterenol (Sigma) in our preliminary studies. Drugs were injected 10 min before generation of the initial baroreflex curve, and, to ensure adequate blockade during the postinfusion baroreflex test, a second administration was given after 20 min of 0.6 M NaCl infusion.

**Statistical Analysis**

All data are presented as means ± SE. Comparisons between two means were made by Student’s t-test. Differences between multiple means were evaluated with a two-factor ANOVA for repeated measures, followed by a Newman-Kuels a posteriori test. $$P < 0.05$$ was considered significant.

**RESULTS**

Animals weighed between 297 and 380 g at the time of testing. The effects of saline infusion on plasma osmolality and hematocrit are illustrated in Fig. 1. There were no significant changes in plasma osmolality following the 30-min infusion of 0.6 M NaCl in either Tap or Iso rats, whereas administration of 1.0 M NaCl significantly increased this variable. However, all groups demonstrated a decrease in hematocrit levels.

**Experiment 1: Effect of Sodium Ingestion on Baroreflex Responses During Moderate Sodium Loading**

Control blood pressures and heart rates in experiment 1 Tap or Iso animals before and after infusion of NaCl are presented in Table 1 and in Fig. 2. Before the infusion period, there were no differences in either basal mean arterial pressure or basal heart rate as a function of drinking solution. Furthermore, infusion of 1.0 M NaCl in Tap animals resulted in an increase in blood pressure but no reflex-induced bradycardia. In contrast, infusion of 0.6 M NaCl in Tap animals decreased heart rate, whereas blood pressure remained constant. However, in Iso rats subjected to 0.6 M NaCl infusion, blood pressure tended to increase during infusion ($$P = 0.07$$, 1 animal in the
Table 1. Control BPs and HRs and response parameters describing logistic function curves relating BP and HR before and after intravenous infusion of 0.6 or 1.0 M NaCl in Tap and Iso rats

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<tr>
<th></th>
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<th>Control HR</th>
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<tr>
<td>Tap</td>
<td>0.6 M NaCl (n = 7)</td>
<td>125±3</td>
<td>380±10</td>
<td>534±7</td>
<td>284±8</td>
<td>249±5</td>
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<tr>
<td></td>
<td>1.0 M NaCl (n = 6)</td>
<td>118±4</td>
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<td>513±12</td>
<td>296±12</td>
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<td>-4.1±0.4</td>
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<tr>
<td>Iso</td>
<td>6 M NaCl (n = 9)</td>
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<td>373±10</td>
<td>508±12</td>
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</tr>
<tr>
<td>Tap</td>
<td>0.6 M NaCl</td>
<td>130±7</td>
<td>367±11</td>
<td>505±10</td>
<td>306±6*</td>
<td>198±9*</td>
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<tr>
<td></td>
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<td>138±3*</td>
<td>381±16</td>
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<tr>
<td>Iso</td>
<td>0.6 M NaCl</td>
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<td>367±11</td>
<td>505±10</td>
<td>306±6*</td>
<td>198±9*</td>
<td>-3.0±0.4</td>
</tr>
</tbody>
</table>

Values are means ± SE; n = no. of rats. BP, blood pressure; BP-50, mean arterial pressure at midpoint of logistic function curve; G\textsubscript{max}, maximum gain; HR, heart rate (min, minimum; max, maximum); Iso, rats that consumed isotonic saline; Tap, rats that consumed tap water. * and †P < 0.05, 0.01 compared with preinfusion. § and $P < 0.05, 0.01 compared with 0.6 M NaCl Tap group postinfusion.
infusion period prevented both the fall in control heart rate during saline infusion and the decrease in HRmax and HRmin characteristic of 0.6 M NaCl infusion in Tap animals but had no effect on the increase in HRmin observed in Iso rats (Table 3; Fig. 3).

Experiment 3: Effects of Dietary Sodium on the Parasympathetic and SymNS Components of the Baroreflex After Acute Sodium Loading

Atenolol significantly decreased basal heart rate to a similar degree in Tap and Iso rats but had no effect on blood pressure (Table 2). Blood pressures and heart rates immediately preceding baroreflex testing (control), baroreflex curves, and curve parameters obtained during blockade of cardiac SymNS responses are shown in Fig. 4 and Table 4. Administration of atenolol significantly decreased control heart rate in both Tap and Iso animals but did not alter blood pressure. Furthermore, the preinfusion parasympathetic baroreflex curve parameters were similar between Tap and Iso rats and were not altered in either group by administration of 0.6 M NaCl.

Intravenous administration of atropine produced tachycardia in both Tap and Iso animals without affecting blood pressure (Table 2). Values for these variables immediately before each baroreflex test are provided in Table 5. Logistic function curves and associated parameters describing the baroreflex responses in Tap and Iso animals treated with atropine are illustrated in Fig. 5 and provided in Table 4. Infusion of 0.6 M NaCl in atropine-treated Tap animals reduced heart rate, similar to that shown in untreated Tap animals (Table 1). Furthermore, hypertonic infusion in atropine-treated Tap rats resulted in decreased HRmin and HRmax, with no change in HRrange, Gmax, or BP-50. These effects were also observed in untreated Tap animals after infusion of 0.6 M NaCl (Table 1). Infusion of 0.6 M NaCl did not alter either control heart rate or any characteristic of the baroreflex response curves in Iso animals. Although HRmin did not increase in atropine-treated Iso animals following 0.6 M NaCl infusion, as it did in untreated Iso rats, it was significantly greater than in Tap rats following hypertonic infusion. This is similar to the relationship seen in the untreated Tap and Iso animals after 0.6 M NaCl infusion (Table 1).

DISCUSSION

Results from the present study demonstrate that increasing dietary sodium alters cardiac responses during systemic administration of moderate volumes of NaCl. Specifically, during infusion of 0.6 M NaCl, heart rate decreased in Tap animals, with no change in blood pressure. However, in Iso animals receiving a similar infusion of 0.6 M NaCl, there was a strong tendency for blood pressure to rise, but no bradycardia was observed. This response pattern was similar to that observed in Tap rats infused with 1.0 M NaCl, where there was a significant hypertensive response and no fall in heart rate. Furthermore, characterization of the entire cardiac baroreflex function demonstrated that HRmin and HRmax were both decreased in Tap animals infused with 0.6 M NaCl, with no change in HRrange, operating set point, or Gmax. However, similar infu-

Table 2. Basal BP and HR before and 10 min after intravenous administration of the vasopressin antagonist VP-X, atenolol, or atropine in Tap and Iso rats

<table>
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<td>Tap</td>
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<tr>
<td>Pre</td>
<td>117±4</td>
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<td>111±3</td>
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<tr>
<td>Post</td>
<td>113±4</td>
<td>383±11</td>
<td>110±5</td>
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<tr>
<td>Iso</td>
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<tr>
<td>Pre</td>
<td>113±4</td>
<td>356±6</td>
<td>114±5</td>
</tr>
<tr>
<td>Post</td>
<td>114±2</td>
<td>365±11</td>
<td>111±5</td>
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Values are means ± SE. BP are given in mmHg; HR are given in beats/min. Pre, before administration; Post, after administration. *P < 0.01 compared with Pre.
sions in animals consuming increased dietary sodium produced a significant increase in HR_{min} and BP-50 and decreased HR_{range} but no alteration in HR_{max} or G_{max}. This response profile was similar to that observed in Tap animals infused with 1.0 M NaCl. These data demonstrate that increased dietary sodium reverses the potentiation of baroreflex-induced bradycardia normally associated with moderate sodium loading. Indeed, the responses observed in Iso animals were similar to those produced by systemic administration of much larger, pressor concentrations of NaCl (3, 4).

Previous studies reported that, although enhanced dietary sodium does not increase control blood pressure in normotensive rats, it potentiates pressor responses to central administration of excitatory neurotransmitters (27, 39). Results from the present study showed a similar relationship between dietary sodium and cardiac baroreflexes, i.e., that control responses were normal but were inhibited in response to another stimulus. Together, these results are consistent with the proposal that, although increased sodium ingestion alone does not produce hypertension in normal animals, it alters a number of cardiovascular responses to other stimuli in a direction favoring increased arterial pressure. This could predispose animals to develop hypertension by chronically enhancing pressor responses and diminishing baroreflex buffering in response to

Table 3. Control BPs and HRs and response parameters describing logistic function curves relating BP and HR before and after intravenous infusion of 0.6 M NaCl in Tap and Iso animals treated with the vasopressin antagonist before baroreflex testing

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<td>Tap (n = 6)</td>
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<td>387±8</td>
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<tr>
<td>Tap</td>
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<td>405±18</td>
<td>514±20</td>
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<td>Iso</td>
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<td>369±9</td>
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<td>307±11*</td>
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Values are means ± SE; n = no. of rats. *P < 0.01 compared with Pre.

Fig. 3. Sigmoid logistic function curves for cardiac baroreflex responses obtained from experiment 2 Tap rats (A) or Iso rats (B) before (pre) and after (post) intravenous infusion of 0.6 M NaCl and treated with the vasopressin V_{1} antagonist. Circles represent control blood pressures and heart rates. Curve parameters are shown in Table 3.

Fig. 4. Sigmoid logistic function curves for cardiac baroreflex responses obtained from experiment 3 Tap animals (A) or Iso animals (B) before (pre) and after (post) intravenous infusion of 0.6 M NaCl and treated with atenolol. Circles represent control blood pressures and heart rates. Curve parameters are shown in Table 4.
Table 4. Control BPs, HRs, and baroreflex response parameters describing logistic function curves relating BP and HR before and after intravenous infusion of 0.6 M NaCl in Tap and Iso animals treated with atenolol

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<td>TAP (n = 5)</td>
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<tr>
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Values are means ± SE; n = no. of rats.

Table 5. Control BPs, HRs, and baroreflex response parameters describing logistic function curves relating BP and HR before and after intravenous infusion of 0.6 M NaCl in Tap and Iso animals treated with atropine

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<td>Tap (n = 5)</td>
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<td>Tap</td>
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Values are means ± SE; n = no. of rats. *P < 0.05 compared with preinfusion. †P < 0.05 compared with postinfusion Tap rats with same drug treatment.
shown in Table 5. Circles represent control blood pressures and heart rates. Curve parameters are derived in the present experiments. However, the HRmax was observed in Tap animals following systemic infusion of 0.6 M NaCl may be due to release of vasopressin induced by increased systemic sodium and/or osmolality. This interpretation is supported by the results of experiment 2 demonstrating that changes in baroreflex function following 0.6 M NaCl in Tap animals are prevented by treatment with VP-X. These data indicate that increased SymNS tone in Iso animals infused with 0.6 M NaCl overcomes the facilitatory effects of vasopressin on baroreflex function and attenuates the fall in heart rate.

There are a large number of studies demonstrating that a primary mechanism of vasopressin enhancement of baroreflex responses is a centrally mediated increase in sympathoinhibition (15, 21, 35, 42). However, other mechanisms, independent of central control of SymNS tone, may contribute to the effects of vasopressin on baroreflex responses. For example, vasopressin sensitizes baroreceptor afferents projecting to the central nervous system (1, 14). In addition, a direct inhibitory effect of systemic vasopressin on sympathetic ganglionic transmission has been proposed (26, 38), although this response has not been consistently obtained (37). Therefore, it is possible that vasopressin may alter baroreflex responses in Tap animals following 0.6 M NaCl through mechanisms independent of central control of SymNS tone, probably by sensitizing baroreceptor afferents. However, due to the prominent, well-documented effect of vasopressin on central sympathoinhibition, it is likely that this is a contributing factor in the enhanced bradycardia in Tap animals following saline infusion.

In the present study, the baroreflex function curves did not go through the control blood pressure and heart rate values in all experimental conditions. However, this is characteristic of the relationship between control values and baroreflex curves when the sigmoid function is based on data generated during continuous transition between hypotension and hypertension (17). The differences between control blood pressure and heart rate and the generated baroreflex curve in the present study were similar in magnitude to previously reported data using similar techniques to evaluate baroreflexes (17).

Studies investigating the effects of dietary sodium on cardiovascular regulation typically use sodium diets, which increase ingestion 10- to 20-fold. In our experiments, Iso rats typically drank 50–60 ml of fluid/day. This represents an increase of approximately two- to threefold over animals consuming tap water and regular laboratory chow (27). This is considerably less than the volume of sodium consumed by rats placed on chow containing 4 or 8% sodium. Furthermore, the volume of sodium administered during infusion of 0.6 M NaCl was approximately equivalent to that ingested during a large meal of standard laboratory chow. Therefore, we feel that these are functionally relevant challenges for evaluating effects of dietary sodium and systemic sodium loading on baroreflex responses.

The present study employed ingestion of isotonic saline solution to increase dietary sodium intake, which prevents animals from compensating for osmotically induced thirst by increasing water consumption. It is conceivable that altered thirst sensation, either before or as a result of hypertonic saline infusion, could alter the observed cardiovascular responses. However, in the present study, neither group of animals ingested any water before or after the 0.6 M NaCl infusion. This indicates that dietary sodium and not differential thirst stimulation contributed to the baroreflex-induced responses. In sup-
port of this interpretation, previous studies have reported similar effects of increased dietary intake on SymNS activation regardless of whether the sodium was presented in isotonic fluid (39) or chow (27).

Infusion of hypertonic solutions can produce volume expansion following translocation of water from the intracellular into the extracellular space. Subsequent stimulation of the cardiopulmonary receptors could potentially contribute to the effects observed in these experiments. However, previous studies have demonstrated that expanding extracellular fluid volume with isotonic saline containing the same amount of sodium as 2.5 M NaCl administered over 30 min did not alter baroreflex sensitivity (4). Therefore, it is unlikely that volume expansion resulting from a 30-min infusion of 0.6 M NaCl could contribute to the effects of acute saline infusion on baroreflex responses.

In these present studies, there were no measurable increases in plasma osmolality following infusion of 0.6 M NaCl for 30 min. However, hematocrit was significantly reduced in both Tap and Iso animals. These data suggest that the increase in osmolality resulting from 0.6 M NaCl infusion was diluted by translocation of water from the intracellular compartment to the extracellular and vascular spaces. In addition to plasma dilution following fluid movement from the intracellular compartment, the infused ions are filtered and excreted by the kidneys during the infusion period. Therefore, the increase in measured plasma osmolality is never equivalent to the predicted increase when calculating infused amount and extracellular fluid volume. Indeed, the differences between the volumes of NaCl administered during intravenous infusions of concentrations ranging from 1.0 M to 2.5 M and the measured increases in plasma osmolality are greater than the amount of NaCl that we administered during infusion of 0.6 M NaCl (12, 25, 40). We feel that, through dilution and concomitant renal excretion, animals have the capability to buffer the increased osmolality during infusion of 0.6 M NaCl, and the decrease in hematocrit indicates that an effective osmotic stimulus was administered.

In summary, these studies have demonstrated that, although cardiac baroreflex sensitivity was not affected in control conditions, a moderate increase in sodium ingestion reverses the increase in baroreflex sensitivity normally evoked by modest sodium loading.

Perspectives

Increased dietary sodium has long been known to be a risk factor for the development of hypertension. Although the specific mechanisms involved have not been completely elucidated, increased SymNS activity (9, 36) and decreased baroreflex sensitivity (22, 45) appear to contribute to increased arterial pressure in salt-sensitive hypertension.

Although increased dietary sodium does not typically cause hypertension in intact, normotensive animals, it clearly alters central SymNS mechanisms of blood pressure regulation in a manner that enhances susceptibility to chronic increases in arterial pressure (27, 39). The present studies have provided data supporting this proposal and demonstrate a functional effect of this response on baroreflex sensitivity. Specifically, the changes in cardiac baroreflex responses observed in Iso rats suggest that central SymNS centers are sensitized to the excitatory effects of systemic sodium administration, and a consequence of this enhanced SymNS response in the central nervous system is diminished SymNS withdrawal and reduced baroreflex buffering of increases in blood pressure during moderate systemic sodium loading. It is possible that increases in sodium ingestion diminish baroreflex responses under other environmental conditions that alter SymNS tone, such as stress.

Chronic, diminished baroreflex sensitivity during transient periods of hyperosmolality (i.e., during exercise, postprandially, or during brief periods of water deprivation), and perhaps with other environmental conditions that raise blood pressure, could eventually lead to increased blood pressure variability and diminished heart rate variability, which are both independent risk factors for development of hypertension (30).

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