Baroreflex regulation of renal sympathetic nerve activity and heart rate in renal wrap hypertensive rats

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Vitela, M., M. Herrera-Rosales, J. R. Haywood, and S. W. Mifflin. Baroreflex regulation of renal sympathetic nerve activity and heart rate in renal wrap hypertensive rats. Am J Physiol Regul Integr Comp Physiol 288: R856–R862, 2005; doi:10.1152/ajpregu.00620.2004.—Despite its usefulness as a nongenetic model of hypertension, little information is available regarding baroreflex function in the Grollman, renal wrap model of hypertension in the rat. Baroreflex regulation of renal sympathetic nerve activity (RSNA) and heart rate (HR) were studied in male Sprague-Dawley rats hypertensive (HT) for 1 or 4–6 wk after unilateral nephrectomy and figure-8 ligation around the remaining kidney or normotensive (NT) after sham surgery. Rats were anesthetized with Inactin and RSNA, and HR was recorded during intravenous infusions of sodium nitroprusside or phenylephrine to lower or raise mean arterial pressure (MAP). Response curves were analyzed using a logistic sigmoid function. In 1- and 4-wk HT rats the midpoints of RSNA and HR reflex curves were shifted to the right (P < 0.05). Comparing NT to 1- or 4-wk HT rats, the gain of RSNA-MAP curves was no different; however, gain was reduced in the HR-MAP curves at both 1 and 4 wk in HT rats (P < 0.05). In anesthetized rats the HR range was small; therefore, MAP and HR were measured in conscious rats during intravenous injections of three doses of phenylephrine and three doses of sodium nitroprusside. Linear regressions revealed a reduced slope in both 1- and 4-wk HT rats compared with NT rats (P < 0.05). The results indicate that baroreflex curves are shifted to the right, to higher pressures, in hypertension. After 1–4 wk of hypertension the gain of baroreflex regulation of RSNA is not altered; however, the gain of HR regulation is reduced.

baroreceptor; renal hypertension; cardiovasular regulation

METHODS

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The unilateral nephrectomy, figure-8 renal wrap, or Grollman (14), model of hypertension has been widely used to investigate the effects of hypertension on neurohumoral regulation of cardiovascular function (6, 11, 15, 19, 20, 23, 24, 27, 30, 31, 33, 37, 39, 42). The renal wrap model of hypertension is nongenetically determined; therefore, appropriate control subjects exist. In addition, renal wrap hypertension is associated with elevated sympathetic outflow (20, 24, 33, 39), it is dependent upon intact renal sympathetic innervation to the kidney (27), it is a sodium-dependent form of hypertension (15, 20) and it has also been shown to be ANG II-dependent (6, 37).

Although the above characteristics are also observed in renal artery clip, or Goldblatt, models of hypertension, comparatively little information is available regarding baroreflex regulation of sympathetic and parasympathetic function in the renal wrap model of hypertension in the rat. Therefore, we examined baroreflex regulation of renal sympathetic nerve activity (RSNA) and heart rate (HR) in anesthetized normotensive (NT) and renal wrap hypertensive (HT) rats at 1 and 4–6 wk after the induction of hypertension. Because the range of HR regulation was severely blunted in the anesthetized and paralyzed rats, we also examined baroreflex-mediated changes in HR in conscious rats. The results indicate that within 1 wk, baroreflex curves relating mean arterial pressure (MAP) to RSNA and HR are shifted to the right and centered on a new, higher midpoint. The gain of baroreflex regulation of RSNA is normal, whereas the gain of HR regulation is reduced. The changes in the reflex curves are not different when examined after 4–6 wk of hypertension.

METHODS

General. Successful experiments were performed on adult, male Sprague-Dawley rats (375–500 g, Charles River Labs, Willington, MA). Rats were housed two per cage in a fully accredited American Association for Accreditation of Laboratory Animal Care laboratory animal room with free access to normal rat chow (1% sodium) and water. All rats were given at least 1 wk to acclimate before being used for any procedures and had access to normal rat chow and water at libitum. The Institutional Animal Care and Use Committee of the University of Texas Health Science Center at San Antonio approved all experimental protocols.

Chronic hypertensive model. Hypertension was induced using a one-kidney renal wrap procedure. Rats were anesthetized with medetomidine (0.5 mg/kg ip; Pfizer, New York, NY) and ketamine (75 mg/kg ip; Fort Dodge Lab., Fort Dodge, IA). A figure-8 Grollman renal wrap and contralateral nephrectomy were performed on these animals (14). Sham-operated animals received unilateral nephrectomy and no contralateral renal wrap. Anesthesia was terminated by atipamezole (1 mg/kg ip; Pfizer) at the conclusion of the surgical procedures.

Baroreflex curves in anesthetized rats. Either 7–10 days or 4–6 wk after the initial surgery, hypertensive and sham-operated animals were anesthetized with Inactin (100 mg/kg ip) and placed on a thermostatically controlled heating pad. Body temperature was monitored using a rectal probe and maintained at 36–38°C throughout the experiment. After placement of venous catheters in the femoral and jugular veins and cannulation of the trachea, the rat was artificially ventilated with room air supplemented with 100% O2. Additional anesthetic was
given as needed (10 mg iv) to maintain stable arterial pressure and HR at rest and during pinch of the hind paw. Gallamine triethiodide (20 mg·kg⁻¹·0.5 h⁻¹, iv) or pancuronium bromide (1 mg/kg iv, supplemented by an iv infusion of 0.5 mg·kg⁻¹·h⁻¹) given for paralysis. A femoral artery was cannulated, and arterial pressure was measured using a strain-gauge transducer.

The renal sympathetic nerve was approached retroperitoneally via a flank incision. The nerve was isolated contralaterally to the nephrectomy and placed on bipolar, Teflon-coated platinum wires with the ends bared. RSNA was recorded using a Grass high impedance probe (HIP-511) and amplified (X10K-50K) and filtered between 10 and 3K Hz with a Grass P5 series AC amplifier. The output was rectified and integrated (Coulbourn S76-01) at time constants of 50 and 600 ms. The 50-ms time constant was used to determine the 0 level of RSNA (the baroreceptor-insensitive component of RSNA, including noise) during maximal reductions in RSNA evoked by bolus injections of phenylephrine. Data obtained using the 600-ms time constant was used to construct baroreflex curves. The maximum level of RSNA was that observed during the decrease in MAP evoked by the sodium nitroprusside infusion. Baroreflex curves were obtained during intravenous infusions of phenylephrine HCl (50 μg/ml) to increase MAP and sodium nitroprusside (100 ng/ml) to decrease MAP (Fig. 1, A and B). Infusion rate was adjusted to produce changes in MAP of 1–2 mmHg/s.  

**Baroreflexes and Hypertension**

Control and renal wrap rats were prepared as described above. Either 7–10 days or 4–6 wk after induction of hypertension, anesthesia was induced with methoxyflurane inhalation, and femoral arterial and venous catheters were implanted under aseptic conditions for measurement of arterial pressure and injection of drugs, respectively. Two to three days after implantation of catheters, pulsatile arterial pressure (PAP), MAP, and HR were measured during intravenous, 100 μl, bolus injections of phenylephrine (1, 3, and 10 μg/kg), and sodium nitroprusside (5, 10, and 20 μg/kg) to raise and lower arterial pressure, respectively.

**Data analysis.** In both anesthetized and conscious rat studies, HR, RSNA, PAP, and MAP were viewed and saved for off-line analysis using a MacLab A/D system. In anesthetized rat studies, the 0 level of RSNA voltage was subtracted from all subsequent RSNA measurements. RSNA and HR values were averaged over 1-mmHg increments of MAP. Curves relating RSNA to MAP were constructed using two different approaches. In approach 1, the baseline level of RSNA was considered 100% and phenylephrine and sodium nitroprusside-induced deviations were expressed as a percentage of this baseline (22, 36). In approach 2, the resting level of RSNA was normalized between 0% (phenylephrine) and 100%, (sodium nitroprusside). Deviations from this baseline during phenylephrine and sodium nitroprusside infusions were normalized between the 0 and 100% levels of RSNA (35).

**Fig. 1.** Baroreflex curves in conscious rats. Control and renal wrap rats were prepared as described above. Either 7–10 days or 4–6 wk after induction of hypertension, anesthesia was induced with methoxyflurane inhalation, and femoral arterial and venous catheters were implanted under aseptic conditions for measurement of arterial pressure and injection of drugs, respectively. Two to three days after implantation of catheters, pulsatile arterial pressure (PAP), MAP, and HR were measured during intravenous, 100 μl, bolus injections of phenylephrine (1, 3, and 10 μg/kg), and sodium nitroprusside (5, 10, and 20 μg/kg) to raise and lower arterial pressure, respectively.

**Data analysis.** In both anesthetized and conscious rat studies, HR, RSNA, PAP, and MAP were viewed and saved for off-line analysis using a MacLab A/D system. In anesthetized rat studies, the 0 level of RSNA voltage was subtracted from all subsequent RSNA measurements. RSNA and HR values were averaged over 1-mmHg increments of MAP. Curves relating RSNA to MAP were constructed using two different approaches. In approach 1, the baseline level of RSNA was considered 100% and phenylephrine and sodium nitroprusside-induced deviations were expressed as a percentage of this baseline (22, 36). In approach 2, the resting level of RSNA was normalized between 0% (phenylephrine) and 100%, (sodium nitroprusside). Deviations from this baseline during phenylephrine and sodium nitroprusside infusions were normalized between the 0 and 100% levels of RSNA (35).

**Fig. 1.** Baroreflex curves in a 4 wk HT rat. A, B: changes in (from top to bottom) pulsatile arterial pressure (PAP) and mean arterial pressures (MAP; mmHg), heart rate (HR) in beats per minute (rpm), integrated RSNA (time constant = 600 ms) during phenylephrine (A) and nitroprusside (B) infusions. C, D: curves obtained using logistic fit (solid line) drawn through the binned data (circles) for RSNA normalized between 0 and 100% (C) and HR (D) as a function of MAP.
In experiments with anesthetized rats, RSNA vs. MAP curves obtained using both approaches and HR-MAP curves were fit as previously described (22, 28, 35, 36) using a sigmoid logistic function of equation: RSNA = P4 + P1/[1 + exp(P2(MAP - P3))], where P1 is the range of RSNA, P2 is a coefficient that describes gain as a function of MAP, P3 is the MAP at the midrange of the curve, and P4 is the minimum value of RSNA. The numbers of animals in various groups are not equal because in some experiments in which RSNA could not be recorded, it was still possible to obtain HR reflex curves, and in some animals, HR curves were not adequately described by the sigmoidal function. HR-MAP curves obtained from conscious rats were fit using linear regression. Statistical significance was determined using one-way ANOVA with Student-Newman-Keuls used for post hoc comparisons. All values are expressed as means (SD), and significance was accepted at P < 0.05.

RESULTS

Anesthetized Rat Studies

RSNA expressed as a percentage of baseline. MAP was greater in both HT groups compared with NT rats (P < 0.001). NT rats had a lower MAP (118 mmHg, SD 6, n = 9) than 1 wk HT (132 mmHg, SD 11, n = 7; P = 0.011) and 4 wk HT (135 mmHg, SD 12, n = 9; P = 0.004) rats. There was no difference in resting HRs (NT 373 bpm, SD 36; 1 wk HT 383 bpm, SD 34; 4 wk HT 411 bpm, SD 27, P = 0.057).

Baseline RSNA was considered 100%, and changes in RSNA referenced to this baseline as described in the METHODS. Table 1 contains the averaged curve fit parameters. Curves drawn using the averaged parameters are illustrated in Fig. 2A. There was a significant shift in P3, the midpoint of the curve, comparing NT to both 1 wk (P = 0.037) and 4 wk (P = 0.025) rats. All other parameters were the same comparing NT to 1- and 4-wk HT rats. The relationship between the P2, the gain coefficient, and MAP is illustrated in Fig. 2C. There were no differences in any parameters comparing 1 wk to 4 wk HT rats.

RSNA normalized between 0 and 100%. These are the same rats as in the preceding section; therefore, the basal levels of MAP and HR are the same. RSNA was normalized and expressed as a percentage between 0 and 100% as described in METHODS. Resting RSNA was 63% (SD 12) of the 100% value in NT rats, 69% (SD 16) in 1 wk HT and 67% (SD 15) in 4 wk HT rats. There was no difference between these values (P = 0.692).

Table 2 contains the averaged curve fit parameters. Curves drawn using the averaged parameters are illustrated in Fig. 2B. There was a significant shift in P3 comparing NT to both 1 wk (P = 0.027) and 4 wk (P = 0.025) rats. All other parameters were the same comparing NT to 1 and 4 wk HT rats. The relationship between the P2, the gain coefficient, and MAP is illustrated in Fig. 2D. There were no differences in any parameters comparing 1 wk to 4 wk HT rats.

Heart rate. MAP was greater in both HT groups compared with NT rats (P < 0.001). NT rats had a lower MAP (118 mmHg, SD 9, n = 10) than 1 wk HT (131 mmHg, SD 4, n = 5; P = 0.017) and 4 wk HT (141 mmHg, SD 11, n = 8; P < 0.001) rats. There were no differences in resting HRs (NT 401 bpm, SD 32; 1 wk HT 399 bpm, SD 36; 4 wk HT 397 bpm, SD 34; P = 0.969).

Table 3 contains the averaged curve fit parameters for baroreflex regulation of HR in anesthetized rats. Curves drawn using the averaged parameters are illustrated in Fig. 3A. There was a significant shift in P3 comparing NT to both 1 wk (P = 0.049) and 4 wk (P = 0.009) HT rats. In contrast to the RSNA curves, P2 was significantly greater in NT compared with 1 wk (P = 0.007) and 4 wk (P = 0.002) HT rats. In addition, the Gmax of the relationship was greater in NT compared with 1 wk (P = 0.009) and 4 wk (P = 0.001) HT rats. There were no differences in any parameters comparing 1 wk to 4 wk HT rats. The relationship between the P2, the gain coefficient, and MAP is illustrated in Fig. 3B.

Conscious rat studies. The range of HR, the P1 value, was small in the anesthetized, paralyzed rat (22). Therefore, curves relating MAP and HR were generated in conscious NT rats (n = 5) and HT rats after 1 wk (n = 4) and 4 wk (n = 5) of hypertension. MAP was greater in both HT groups compared with NT rats (NT 102 mmHg, SD 6; 1 wk HT 131 mmHg, SD 10; 4 wk HT 151 mmHg, SD 22; P < 0.001), and there was no difference in resting HR (NT 362 bpm, SD 13; 1 wk HT 352 bpm, SD 36; 4 wk HT 366 bpm, SD 31; P = 0.750). Fig. 4 illustrates the slope of the regression line drawn through the mean points was reduced in both 1 wk and 4 wk HT rats, compared with NT rats. The mean values of slope for regression fits of the individual curves in the NT group was −2.31 bpm/mmHg (SD 0.66) with a mean r² of 0.971 (SD 0.024). In the 1-wk HT group, the mean slope was −1.30 bpm/mmHg (SD 0.38) (P = 0.031 vs. NT rats) with a mean r² of 0.975 (SD 0.012). In 4-wk HT rats the mean slope was −1.33 bpm/mmHg (SD 0.22) (P = 0.014 vs. NT rats) with a r² of 0.966 (SD 0.020). There was no difference in the slope of the regression line comparing 1 wk and 4 wk HT rats (P = .885).

Table 1. Curve fit parameters for baroreflex regulation of RSNA in anesthetized rats, where RSNA is calculated as a percentage of baseline

<table>
<thead>
<tr>
<th></th>
<th>r²</th>
<th>P1 (mmHg)</th>
<th>P2 (gain coefficient)</th>
<th>P3 (mmHg)</th>
<th>P4 (mmHg)</th>
<th>Gmax, % RSNA/mmHg</th>
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<tbody>
<tr>
<td>NT (n = 9)</td>
<td>0.98±0.03</td>
<td>157±51</td>
<td>0.06±0.03</td>
<td>123±12</td>
<td>3±6</td>
<td>−2.27±0.93</td>
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<td>1 wk HT (n = 7)</td>
<td>0.95±0.05</td>
<td>172±37</td>
<td>0.06±0.03</td>
<td>138±13</td>
<td>2±3</td>
<td>−2.46±0.90</td>
</tr>
<tr>
<td>4 wk HT (n = 9)</td>
<td>0.96±0.03</td>
<td>168±45</td>
<td>0.05±0.03</td>
<td>141±15</td>
<td>9±15</td>
<td>−2.14±0.54</td>
</tr>
<tr>
<td>One-way ANOVA (P)</td>
<td>0.786</td>
<td>0.967</td>
<td>0.022</td>
<td>0.305</td>
<td>0.733</td>
<td></td>
</tr>
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</table>

Values are presented as means ± SD. Arrows indicate significant differences between groups. RSNA, renal sympathetic nerve activity; r², correlation coefficient; P1, range of RSNA; P2, coefficient that describes gain as a function of MAP; P3, MAP at the midrange of the curve; P4, minimum value of RSNA; Gmax, maximal gain.
DISCUSSION

Surgically induced models of renal dysfunction are useful models for the study of hypertension. A major advantage of these models is that they are not genetically different before the induction of hypertension; therefore, sham-operated animals provide genetically identical control groups. Both one-kidney, renal wrap (Grollman) hypertension and one-kidney, renal artery clip (Goldblatt) hypertension are associated with indices of elevated sympathetic outflow [e.g., enhanced responses to ganglionic blockade (20, 24, 33, 39) with normal vascular responses to vasoconstrictors (24); enhanced plasma levels of norepinephrine (24, 39)]. Renal wrap hypertension is sodium-dependent. Sodium-depleted rats do not develop hypertension following renal wrapping (20), and rigid sodium restriction reverses established renal wrap hypertension (15). Similar to renal artery clip hypertension, renal wrap hypertension depends upon activation of the renin-angiotensin system because blockade of ANG II receptors with losartan (37) or ZD7155 (J. R. Haywood, unpublished observation) lowers MAP in renal wrap HT rats. Thus the renal wrap model of hypertension could provide insights into the etiology of and consequences of hypertension in humans with renal dysfunction.

![Baroreflex curves relating MAP to RSNA as a percentage of baseline (A) and MAP to RSNA normalized between 0 and 100% (B) in normotensive (●), 1 wk HT (○) and 4 wk HT (□) anesthetized rats. Curves were generated from the mean values of the curve fit parameters (Tables 1 and 2) for each group. Gray-shaded symbols on curves denote resting level of MAP in each group. C, D: calculated gain vs. MAP using same symbols as above.](http://ajpregu.physiology.org/)

![Table 2. Curve fit parameters for baroreflex regulation of RSNA in anesthetized rats, where RSNA normalized between 0 and 100%](http://ajpregu.physiology.org/)

<table>
<thead>
<tr>
<th></th>
<th>r^2</th>
<th>P1, mmHg</th>
<th>P2 (gain coefficient)</th>
<th>P3, mmHg</th>
<th>P4, mmHg</th>
<th>Gmax, % RSNA/mmHg</th>
</tr>
</thead>
<tbody>
<tr>
<td>NT (n = 9)</td>
<td>0.96±0.03</td>
<td>100±3</td>
<td>0.12±0.03</td>
<td>122±12</td>
<td>1±3</td>
<td>−3.11±0.93</td>
</tr>
<tr>
<td>1 week HT (n = 7)</td>
<td>0.97±0.05</td>
<td>98±5</td>
<td>0.14±0.03</td>
<td>138±13</td>
<td>1±3</td>
<td>−3.26±0.95</td>
</tr>
<tr>
<td>4 week HT (n = 9)</td>
<td>0.95±0.03</td>
<td>98±3</td>
<td>0.11±0.03</td>
<td>140±15</td>
<td>1±3</td>
<td>−2.70±0.81</td>
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</table>

Values are presented as means ± SD. Arrows indicate significant differences between groups.
The results of this study show that the sensitivity of baroreflex regulation of RSNA, as described by the gain coefficient (P2) and the Gmax, is unchanged in HT rats with the midpoint of the MAP-RSNA relationship shifted to the right and centered near the new HT level of MAP. At the same time, baroreflex regulation of HR is attenuated in HT rats. The attenuated HR baroreflex in anesthetized rats is not due to the anesthetic, as the same result was found when examined in conscious rats. The changes in baroreflex function are evident within 1 wk of hypertension and persist, with no apparent further alterations, when studied after 4 – 6 wk of hypertension.

One explanation for this dissociation between baroreflex regulation of RSNA and HR in HT rats could be that our analysis of RSNA is based upon recording from the sympathetic nerves innervating the kidney, while HR is a direct measure of the end-organ response. However, our finding of dissociation between baroreflex regulation of RSNA and HR in HT rats is consistent with previous studies in a rabbit model of renal hypertension (17). These authors found that in HT rabbits baroreflex regulation of hindlimb vascular resistance and lumbar SNA was normal and baroreflex regulation of HR was attenuated. Blunted baroreflex regulation of HR in a rat model of renovascular hypertension has also been reported (34); however, sympathetic nerve discharge was not studied. The normal gain of baroreflex regulation of renal and lumbar sympathetic outflows suggests normal regulation of vasomotor tone, albeit around a presumed higher baseline level as discussed below. The reduced gain of the baroreflex regulation of heart rate suggests a blunting of the ability of heart rate to respond to perturbations in blood pressure. This might protect the heart from marked increases and decreases in rate as hypertensive damage to the myocardium progresses.

The dissociation of baroreflex regulation of RSNA and HR is likely the result of alterations within the central pathways regulating RSNA and HR. These alterations could occur during the medullary processing of the baroreceptor afferent input (32) and could be the result of changes at the level of the medullary neurons (31). Alternatively, the alterations in reflex function could be the result of changes in the descending modulation of the medullary neurons in the baroreflex circuit. For example, the paraventricular nucleus plays a critical role in the etiology and maintenance of renal role wrap hypertension (19, 23, 30) and the paraventricular nucleus has been shown to

Table 3. Curve fit parameters for baroreflex regulation of HR in anesthetized rats

<table>
<thead>
<tr>
<th></th>
<th>r²</th>
<th>P1, mmHg</th>
<th>P2 (gain coefficient)</th>
<th>P3, mmHg</th>
<th>P4, mmHg</th>
<th>Gmax, %HR/mmHg</th>
</tr>
</thead>
<tbody>
<tr>
<td>NT (n = 10)</td>
<td>0.96±0.03</td>
<td>59±22</td>
<td>0.29±0.13</td>
<td>121±10</td>
<td>360±41</td>
<td>-4.28±1.93</td>
</tr>
<tr>
<td>1 wk HT (n = 5)</td>
<td>0.98±0.02</td>
<td>60±18</td>
<td>0.12±0.04</td>
<td>139±9</td>
<td>362±18</td>
<td>-1.80±0.52</td>
</tr>
<tr>
<td>4 wk HT (n = 8)</td>
<td>0.96±0.03</td>
<td>57±14</td>
<td>0.13±0.03</td>
<td>146±23</td>
<td>359±40</td>
<td>-1.82±0.62</td>
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<tr>
<td>One-way ANOVA (P)</td>
<td>0.956</td>
<td>0.001</td>
<td>0.009</td>
<td>.990</td>
<td>0.005</td>
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</table>

Values are presented as means ± SD. Arrows indicate significant differences between groups.

Fig. 3. Baroreflex curves relating MAP to HR (A) in anesthetized normotensive (●), 1 wk HT (○) and 4 wk HT (□). Curves were generated from the mean values of the curve fit parameters (Table 3) for each group. Grey filled symbols denote resting level of MAP in each group. B: calculated gain vs. MAP using same symbols as above.

Fig. 4. Baroreflex curves relating MAP to HR in conscious normotensive (●), 1 wk HT (open circles), and 4 wk HT (□). Symbols denote means ± SD. Regression lines are drawn through the points. Grey filled symbols denote resting level of MAP in each group.
modulate the integration of baroreceptor afferent inputs within the medulla (1, 10, 26).

**Absolute level of RSNA.** Comparisons of absolute levels of sympathetic discharge between groups of animals are not valid (35, 36). The present analytical procedure normalizes RSNA to a maximum and minimum for each rat and cannot discern alterations in absolute levels of RSNA. Many indirect indices suggest elevated levels of SNA in this and other models of hypertension as previously discussed. More specifically, evidence indicates increased RSNA in human and animal hypertension (see Ref. 7 for a review). Surprisingly, the first direct recordings of RSNA for extended time periods, so that RSNA could be measured before and after the development of hypertension in the same animal, found that during ANG II infusions there was a sustained reduction in RSNA (5), leading the authors to suggest that ANG II-dependent hypertension does not require an increase in the absolute level of RSNA but, rather, an increase in sympathetic outflow relative to the increased MAP (4). The finding of reduced RSNA during chronic ANG II infusions has been subsequently verified (2). However, these findings may be specific for RSNA in ANG II infusion models of hypertension, reflecting reflex and/or direct effects on renal blood flow and/or sodium reabsorption. The neurohumoral response during hypertension is possibly fundamentally different if the renin-angiotensin system is activated (13, 18, 41). Although electrical stimulation of afferent fibers is not directly analogous to natural stimulation of the arterial baroreflex (3, 4, 17, 21). This indicates that some component(s) of the reflex adapts, or “resets,” to the higher prevailing MAP; otherwise RSNA and HR would remain depressed at the lower, plateau level, as in the NT during acute increases in MAP. Resetting enables baroreflex responses to both increase and decrease in MAP.

The above discussion assumes a passive role of the baroreflex in the response to hypertension. It has been suggested that baroreflex resetting is an active process necessary for maintaining SNA in hypertension (4); otherwise, RSNA and HR would remain depressed at the lower, plateau level, as in the NT rat during acute increases in MAP. Baroreflex resetting likely reflects some mixture of receptor resetting (25, 29, 40), and alterations in the central nervous system (CNS; 11, 19, 30, 31, 33, 42), including descending modulation of medullary neurons integrating baroreceptor afferent inputs (1, 10, 26). A lack of resetting of the MAP-RSNA relationship has been reported in ANG II-infused HT rabbits (2), so that at resting levels of MAP, further inhibition of RSNA is not possible. This contrasts with previous studies in ANG II-infused HT rabbits where resetting of the MAP-RSNA curve was observed (4). Clearly, in our (Fig. 1) and other studies (3, 4, 17, 21), baroreflex inhibition of RSNA can be evoked in chronic hypertension.

Baroreflex regulation of RSNA remains unchanged in hypertension; however, electrical activation of aortic nerve afferents results in reduced depressor responses in this model of hypertension (16, 38, 42) and spontaneously hypertensive rats (13, 18, 41). Although electrical stimulation of afferent fibers is not directly analogous to natural stimulation of the arterial baroreceptors, electrical stimulation of baroreceptor afferent fibers reveals an attenuated reflex function that is not apparent when one naturally activates the arterial baroreceptors by increasing arterial pressure. To this end, a recent report indicates that baroreflex regulation of hypertension remains depressed after normalization of MAP and the return of baroreceptor discharge to the normal, pre-HT level (12). Electrical stimulation of baroreceptor afferents could reveal altered CNS integration as a result of and in adaptation to increased peripheral baroreceptor afferent inputs (32).

**GRANTS**

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REFERENCES


