Renal sympathetic nerve regulation to heating is altered in rats with heart failure

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Kenney, Michael J., Timothy I. Musch, and Mark L. Weiss. Renal sympathetic nerve regulation to heating is altered in rats with heart failure. Am J Physiol Heart Circ Physiol 280: H2868–H2875, 2001.—Heart failure (HF) alters the regulation of basal sympathetic nerve discharge (SND); however, the effect of HF on SND responses to acute stress is not well established. In the present study, renal SND responses to hyperthermia were determined in chloralose-anesthetized HF rats and in sham controls. Whole body heating (colonic temperature increased from 38 to 41°C) was used as an acute stressor because increased internal body temperature provides a potent stimulus to the sympathetic nervous system. Left ventricular end-diastolic pressure and the right ventricular wt-to-body wt ratio were increased (P < 0.05) in HF compared with sham rats. The following observations were made: 1) renal sympathoexcitatory responses to heating were significantly reduced in HF compared with sham rats, 2) renal blood flow remained unchanged from control levels during heating in HF rats but was significantly reduced in sham rats, and 3) renal SND responses to heating were significantly higher in HF rats with bilateral lesions of the hypothalamic paraventricular nucleus (PVN) compared with sham PVN-lesioned HF rats. These results demonstrate a marked attenuation in the responsiveness of renal SND to heating in HF rats and suggest that HF alters the organization of neural pathways mediating SND responses to heating.

myocardial infarction; blood flow; paraventricular nucleus; ibotenic acid

ALTERED REGULATION of basal sympathetic nerve discharge (SND) is considered a hallmark of heart failure (HF) (3, 4, 7, 31, 33). For example, norepinephrine spillover from the heart and kidney (11, 17, 32) and muscle SND are increased in human HF patients (8, 28), and renal SND has been reported to be higher in rats with HF compared with sham controls (5). In addition, arterial and cardiopulmonary mechanoreflex regulation of efferent SND is attenuated in human HF patients and in animals with HF (4, 7, 13, 45, 48, 50), and human HF patients have an attenuated and/or absent low-frequency component in efferent muscle SND (46).

Although less well established, at least three lines of evidence indicate that SND responses to acute stress are different in animals with HF and human HF patients than in control subjects. First, conscious HF rats demonstrate enhanced mean arterial pressure (MAP), heart rate (HR), and renal SND responses to air-jet stress compared with sham controls (27, 49). Second, renal sympathoexcitatory responses to noxious stimulation induced by hot-water tail immersion are higher in chloralose-anesthetized HF than in sham-operated control rats (6). Third, when compared at the same relative workload, norepinephrine, HR, and arterial blood pressure responses to exercise are attenuated in human HF patients compared with control subjects (9).

In the present study, we determined renal SND responses to hyperthermia in HF and sham-operated control rats. Based on the results of previous studies demonstrating altered sympathetic nerve regulation to acute stress in human HF patients (9, 41) and in animals with HF (6, 27, 49), we hypothesized that renal SND responses to acute heating would be different in rats with HF compared with sham rats. Whole body heating was used as an acute stressor because heat stress provides a potent stimulus to the sympathetic nervous system as demonstrated by heating-induced increases in SND in conscious humans (36) and rats (24) and in chloralose-anesthetized rats (10, 19, 20, 22). In addition, excess mortality from hyperthermia and cardiovascular disease occurs during heat waves (23, 40, 47).

As the results reveal, renal SND responses to heating are markedly attenuated in HF rats. To determine the factors responsible for and the functional significance of the diminished renal SND response to heating in HF rats, we completed experiments to address three questions. First, does HF impair the ability of sympathetic neural circuits to respond to other stressors such as a short bout of asphyxia and acute hypothermia? Second, does renal blood flow remain constant during hyperthermia in HF but not sham HF rats? Third, are...
forebrain neural circuits involved in suppressing SND responses to heat stress in HF rats? Because forebrain neurons contribute to alterations in the regulation of basal SND in the HF state (37, 38), we hypothesized that hypothalamic nuclei might play a key role in mediating SND responses to heating in HF rats. In the present study, we determined renal SND responses to heat stress in HF rats with ibotenic acid-induced lesions of the paraventricular nucleus of the hypothalamus (PVN), in HF rats with sham PVN lesions, and in sham HF rats with PVN lesions. We chose to study the role of the PVN in suppressing renal SND responses to heat stress in HF rats because, as noted by Sun (42), the role of the PVN in cardiovascular and autonomic regulation can be altered depending on the experimental conditions and the types of neurons activated. We hypothesized that HF might be a physiological (experimental) condition that influences the contribution of this nucleus to SND regulation.

METHODS

The surgical procedures and experimental protocols used were approved by the Institutional Animal Care and Use Committee.

HF induced by myocardial infarction. Male Sprague-Dawley rats were anesthetized (using 3% halothane), intubated, and ventilated. After a left side thoracotomy, the heart was exteriorized, and the left coronary artery was ligated between the pulmonary artery and the left atrium to create a large myocardial infarction in the HF rats (35). In the sham rats, the same surgical procedures were completed but the coronary artery was not ligated; the thoracotomy was closed using surgical suture. The creation of a large myocardial infarction was confirmed from electrocardiogram recordings obtained 1 and 7 days after surgery (44). Topically administered analgesic agents were applied to the incision site. Penicillin G (10,000 units im) was given in the biceps femoris muscle (PVN), in HF rats with sham PVN lesions, and in sham HF rats with PVN lesions. We chose to study the role of the PVN in suppressing renal SND responses to heat stress in HF rats because, as noted by Sun (42), the role of the PVN in cardiovascular and autonomic regulation can be altered depending on the experimental conditions and the types of neurons activated. We hypothesized that HF might be a physiological (experimental) condition that influences the contribution of this nucleus to SND regulation.

METHODS

The surgical procedures and experimental protocols used were approved by the Institutional Animal Care and Use Committee.

HF induced by myocardial infarction. Male Sprague-Dawley rats were anesthetized (using Brevital, 50–60 mg/kg ip; then α-chloralose, 50 mg/kg iv initial dose), artificially ventilated, and paralyzed with gallamine triethiodide (5–10 mg/kg iv initial dose). Body weights were not different in HF (470 ± 13 g) and sham (451 ± 16 g) rats. Catheters were placed in the femoral vein for the administration of drugs including maintenance doses of α-chloralose (35 mg·kg⁻¹·h⁻¹), methohexital sodium (10–20 mg/kg administered during surgical interventions), and gallamine triethiodide (10–15 mg·kg⁻¹·h⁻¹). End-tidal CO₂ was kept near 4.5% by adjusting the frequency of respiration. Colonic temperature (Tc) was measured with a thermistor probe inserted −5–6 cm into the colon and was kept at 38.0°C during surgery by a temperature-controlled table. Femoral arterial blood pressure and HR were recorded using standard procedures.

Neural recordings. Activity was recorded biphasically with a platinum bipolar electrode after capacity-coupled preamplification (band pass, 30–3,000 Hz) from the central end of cut renal sympathetic nerves. The left renal nerve was isolated retroperitoneally. The nerve-electrode preparation was covered with a silicone gel. The sympathetic nerve potentials were full-wave rectified and integrated (time constant of 10 ms). Renal SND was quantified after integration as volts × seconds and corrected for background noise after ganglionic blockade (with 15 mg/kg trimethaphan camsylate).

Determination of left-ventricular dysfunction and HF. Before the experimental protocols were initiated, left ventricular (LV) dysfunction was documented in each myocardial infarcted rat by the measurement of LV end-diastolic pressure (LVEDP). In the anesthetized state (see Animal preparation) and after a small incision was made on the ventral surface of the rat neck, a 2-Fr microMillar pressure transducer catheter was inserted into the right carotid artery and threaded into the left ventricle for measurement of LVEDP. LV systolic and diastolic pressures were measured and recorded while the rat breathed spontaneously. The micromanometer was removed from the left ventricle and placed in the aortic arch, where arterial systolic and diastolic pressures were measured and recorded, and was then removed from the animal. The wound was closed with silk suture.

At the end of each experimental protocol, rats were euthanized with an overdose of methohexital sodium (150 mg/kg iv). The heart was removed, the right ventricle was surgically separated from the left ventricle and septum, and both tissues were weighed. The left ventricle was examined for scar tissue on the LV free wall for documentation that a large myocardial infarction had been produced in the HF animal. For each experimental protocol, rats were considered to have a significant degree of LV dysfunction and HF when LVEDP and the right ventricular weight-to-body weight (RV/BW) ratio were significantly increased compared with nonfarcted sham rats (29).

Renal blood flow determination. Catheters were placed in the right carotid artery and the femoral artery. The right carotid artery catheter was advanced toward the heart and secured in a position just inside the aortic arch. The femoral artery catheter was advanced toward the descending aorta and secured in place. The carotid catheter was connected to a pressure transducer, and the femoral artery catheter was connected to a 5-ml glass syringe placed in a Harvard withdrawal pump. For each blood flow determination, blood withdrawal from the femoral artery catheter was initiated at a rate of 0.25 ml/min. At the same time, arterial blood pressure was recorded from the carotid artery catheter. After 30 s of blood withdrawal, the carotid artery catheter was disconnected from the pressure transducer, and radioactive microspheres (∼6–7 × 10⁵ in number) were injected into the aortic arch. Labeled microspheres were 15 ± 3 µm in diameter. The microspheres were suspended in normal saline containing 0.01% Tween 80 with a specific activity ranging from 7–15 mCi/g. Before each injection, the microspheres were thoroughly mixed and agitated by sonication to prevent clumping. Microspheres were injected into the ascending aorta in a volume of ~0.10 ml, and the different radioactive labels were used in random order. At the end of each experiment, the rat was killed with an overdose (150 mg/kg iv) of methohexital sodium. The placement of each catheter was verified by anatomical dissection. The kidneys were removed, blotted, weighed, and placed immediately into counting vials. The radioactivity of renal tissue was determined on a Packard Cobra II Auto-Gamma Spectrometer set to record the peak energy activity of each isotope for 5 min. Recordings were then analyzed by computer, taking into account the cross-talk fraction between the different isotopes.

Renal blood flow was calculated by the reference sample method (16) and expressed as milliliters per minute per gram of tissue. Adequate mixing of the microspheres was verified for each injection by demonstrating a <15% difference in blood flows to the right and left kidneys. Blood flow results were normalized to MAP and expressed as conductance (in
with ibotenic acid-induced lesions of the PVN (ibotenic acid-induced lesions of the PVN and in sham HF rats protocol as described above) on renal blood flow in HF (n = 5).

PVN lesions. Lesions were completed using procedures described by Herman and Wiegand (12). Rats were randomly selected for a hypothalamic or sham lesion, anesthetized with 3% halothane, and given prophylactic antibiotic (Polyflex, 2,500 units sc). The skull was leveled between the bregma and lambda sutures and burr holes were made in the skull to permit a micropipette (which was glued to the tip of a Hamilton microsyringe) to be lowered into the PVN (stereotaxic coordinates: 1.8 mm caudal to bregma; 0.8 mm lateral to midline; and 7.7 mm ventral to the surface of the brain) (39). Bilateral lesions were made by injecting 100 nl of ibotenic acid (5 µg/µl in sterile phosphate-buffered saline) into the PVN. The sham lesioned animals received sterile vehicle-solution injections. After injection of ibotenic acid or vehicle, the micropipette was left in place for an additional 3–5 min before it was slowly withdrawn to minimize the spread of the injectate up the cannula tract. Sterile bone wax was placed in the burr holes before the scalp incision was closed with wound clips. After surgery, the rats were given 7–10 days to recover.

Brain histology. At the end of each experiment involving PVN- or sham lesioned rats, the anesthetized rats received an overdose (150 mg/kg iv) of methohexital sodium and were transcardially perfused first with 0.15 M NaCl (containing 3 IU/ml heparin) to rinse out blood and then with a fixative solution consisting of 10% buffered neutral formalin (pH 7.4). The brain was removed and stored in fixative for 3 h and was then transferred to a cryoprotectant solution containing 20% sucrose. The brain was frozen-sectioned in the coronal plane using a microtome (40 µm thickness). To reconstruct the lesioned areas, serial sections through the hypothalamus were mounted on slides, Nissl stained, and examined with light microscopy. The extent of each excitotoxic lesion was determined by the loss of neurons and the infiltration of glia into the injection site (12). To be included in the data analysis, the injection sites needed to be placed within 200 µm of the center of the PVN and produce damage to the dorsal parvocellular subdivision.

Experimental protocols. After instrumentation and isolation of the renal sympathetic nerve, rats were allowed to stabilize for 30–60 min before beginning each experimental protocol. Three protocols were completed. Protocol 1 determined the effect of hyperthermia and hypothermia on renal SND. Hyperthermia was produced in HF (n = 12) and sham (n = 10) rats by increasing Tc at a rate of −0.1°C/min from 38 to 41°C using a heat lamp (19, 20, 22). Hypothermia was produced in HF (n = 5) and sham (n = 4) rats by decreasing Tc at a rate of −0.1–0.2°C/min from 38 to 31°C using externally cooled water that was circulated through a perfusion pad (21). MAP, HR, and renal SND were recorded continuously during progressive increases and decreases in Tc. Protocol 2 determined the effect of increased Tc (same heating protocol as described above) on renal blood flow in HF (n = 6) and sham (n = 6) rats. Protocol 3 determined MAP, HR, and renal SND responses to heating (same heating protocol as described above) in HF rats with (n = 6) or without (n = 5) ibotenic acid-induced lesions of the PVN and in sham HF rats with ibotenic acid-induced lesions of the PVN (n = 5).

Statistical analysis. Control values of SND were taken as 100%. Where appropriate, results between HF and sham control rats were compared using unpaired t-tests with P < 0.05 indicating statistical significance. Otherwise, results from heating experiments were analyzed using ANOVA techniques with a repeated-measures design. Statistical simple effects provided comparisons between HF and sham control rats at each specific Tc during heating. The significance of ANOVA main effects and simple effects at both the P < 0.05 and P < 0.10 levels were identified; the latter significance criterion allowed us to examine the results under conditions in which the probability of making a type II error (accepting the null hypothesis when it is false) is reduced (14). This reduction in type II error probability is associated with an increase in statistical power (14). For descriptive purposes, all results are presented as means ± SE.

RESULTS

Protocol 1: renal SND responses to heating and cooling in HF and sham rats. Mean LVEDP (HF, 18 ± 2 mmHg; sham, 3 ± 1 mmHg) and RV/BW ratio (HF, 0.78 ± 0.07; sham, 0.57 ± 0.03) were significantly higher in HF compared with sham rats. Figure 1A shows representative responses of renal SND to heating from 38 to 41°C. Note that SND was elevated during heating in the sham but not in the HF rats. Figure 1B summarizes the data from 12 HF and 10 sham rats to progressive increases in Tc. Whereas there was a progressive and significant increase in renal SND during heating in sham rats, renal SND was increased significantly only at the highest level of Tc in HF rats. Renal SND was significantly higher in sham compared with HF rats at Tc values of 39, 40, 40.5, and 41°C. As shown in Table 1, heating-induced increases in MAP were similar in the two groups of rats, but increases in HR were significantly greater in sham than in HF rats at 40 and 40.5°C.

Renal SND responses to a short bout of asphyxia (10–20 s) was determined after Tc had been increased to 41°C in five HF and five sham rats. Asphyxia significantly increased renal SND in sham (415 ± 51%) and HF (249 ± 78%) rats, demonstrating that the attenuated renal SND responses to heating in HF rats were not the result of a ceiling effect.

Figure 2 summarizes the data from five HF and four sham rats to progressive decreases in Tc. Hypothermia reduced renal SND in HF and sham rats. Importantly, decreases were similar between groups at each level of Tc. Hypothermia-induced increases in MAP (HF, 38 to 31°C, 31 ± 9 mmHg; sham, 38 to 31°C, 41 ± 9 mmHg) and decreases in HR (HF, 38 to 31°C, 34 ± 8 beats/min; sham, 38 to 31°C, 30 ± 16 beats/min) were similar in HF and sham rats.

Protocol 2: renal blood flow responses to heating in HF and sham rats. Mean LVEDP (HF, 25 ± 2 mmHg; sham, 8 ± 3 mmHg) and RV/BW ratio (HF, 0.86 ± 0.14; sham, 0.49 ± 0.01) were significantly higher in HF compared with sham rats. Figure 3 summarizes renal blood flow responses to increases in Tc in HF and sham rats. As shown in Fig. 3A, renal blood flow was significantly reduced in sham rats when Tc was increased from 38°C (open bars) to 41°C (hatched bars). In con-
trast, renal blood flow remained unchanged after this maneuver in HF rats. Heating-induced increases in MAP from 38 to 41°C were significantly greater in sham (36 ± 7 mmHg) compared with HF (13 ± 6 mmHg) rats. Because of increases in MAP, renal blood flow was normalized to MAP and expressed as renal conductance (see METHODS). As shown in Fig. 3B, renal conductance was reduced in sham and HF rats when Tc was increased to 41°C; however, the magnitude of the response was significantly less in HF (−19 ± 10%) compared with sham (−51 ± 14%) rats.

Protocol 3: MAP, HR, and renal SND responses to heating in PVN-lesioned HF and sham HF rats and in sham PVN-lesioned HF rats. Renal SND responses to heating were analyzed in HF rats with sham PVN lesions (LVEDP, 21 ± 2 mmHg; RV/BW ratio, 0.76 ± 0.08), HF rats with PVN lesions (LVEDP, 24 ± 3 mmHg; RV/BW ratio, 0.75 ± 0.12), and sham HF rats with PVN lesions (LVEDP, 6 ± 1 mmHg; RV/BW ratio, 0.66 ± 0.01). As previously reported (12), we found that injection of 0.5 μg of ibotenic acid into the PVN selectively damaged the parvocellular neurons and left the magnocellular neurons intact. The boundary of an ibotenic acid injection from a representative HF rat, as indicated by the halo of invading glia, is shown in Fig. 4. The anatomic extent of PVN lesions was similar in HF and sham HF rats. Functionally, all PVN ibotenic acid injections were identical in their physiological effect.

Figure 5A shows representative responses of renal SND to heating from three experiments: a HF rat with a sham PVN lesion, a HF rat with a PVN lesion, and a sham HF rat with a PVN lesion. Note that SND was elevated in the PVN-lesioned HF and sham HF rats but not in the HF rat with a sham PVN lesion. Figure 5B summarizes renal SND responses to heating in these three groups. Renal SND was progressively increased during heating in PVN-lesioned HF rats and sham HF rats with PVN lesions but was only modestly increased during heating in HF rats with sham PVN lesions.

Table 1. MAP and HR values recorded before (38°C) and during (39–41°C) heating in HF and sham HF rats

<table>
<thead>
<tr>
<th>Colonic Temperature</th>
<th>MAP, mmHg</th>
<th>HR, beats/min</th>
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<tbody>
<tr>
<td></td>
<td>38°C</td>
<td>39°C</td>
</tr>
<tr>
<td>HF</td>
<td>134 ± 3</td>
<td>130 ± 5</td>
</tr>
<tr>
<td>Sham</td>
<td>136 ± 6</td>
<td>137 ± 5</td>
</tr>
<tr>
<td>HF</td>
<td>383 ± 8</td>
<td>394 ± 10</td>
</tr>
<tr>
<td>Sham</td>
<td>400 ± 9</td>
<td>441 ± 10*</td>
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Values are means ± SE. MAP, mean arterial pressure; HR, heart rate; HF, heart failure. *Significantly different from 38°C at P < 0.05; †significantly different from HF at P < 0.05.
lesions. Renal SND responses to heating were significantly greater at 40.5 and 41°C in PVN-lesioned HF rats and sham HF rats with PVN lesions than in HF rats with sham PVN lesions. Renal SND responses to heating were not different between PVN-lesioned HF rats and sham HF rats with PVN lesions. As shown in Table 2, control levels of MAP and HR were similar in

Fig. 2. Changes in renal SND during progressive reductions in Tc from 38 to 31°C in HF and sham rats.

Fig. 3. Renal measurements for sham and HF rats during control (Tc, 38°C; open bars) and after heating (Tc, 41°C; hatched bars). A: renal blood flow. B: renal conductance. *Significantly different from control, \( P < 0.05 \). ns, Not significant.

Fig. 4. Anatomic boundary from a representative experiment of an ibotenic acid-induced lesion in the paraventricular nucleus (PVN) of a HF rat. Ibotenic acid was stereotaxically injected bilaterally into the PVN. MeA, medial nucleus of the amygdala; 3v, third cerebroventricle; fx, fornix; RCh, retrochiasmatic area; ic, internal capsule; CA3, field CA3 of hippocampus; fi, fibria of fornix; ot, optic tract; cc, corpus callosum.

Fig. 5. A: traces of integrated renal SND bursts from three experiments recorded during control (Tc, 38°C) and after heating (Tc, 41°C). Horizontal calibration is 500 ms. Amplifier settings were the same for the nerves in each experiment. B: changes in renal SND during increases in Tc from 38 to 41°C. *Significantly different from 38°C, \( P < 0.05 \). †HF with PVN lesion significantly different from HF with sham PVN lesion, \( P < 0.05 \). ‡Sham HF with PVN lesion significantly different from HF with sham PVN lesion, \( P < 0.05 \).
HF rats with sham PVN lesions, HF rats with PVN lesions, and sham HF rats with PVN lesions. MAP and HR were significantly increased from control during heating in each of these groups.

**DISCUSSION**

We present three new findings concerning sympathetic nerve regulation during heat stress in chloralose-anesthetized HF rats. First, unlike sham rats that show a progressive increase in renal SND during heating from 38 to 41°C, renal SND in HF rats remained essentially unchanged until the highest Tc, which demonstrates an attenuation in the responsiveness of sympathetic nerve regulation during heat stress in chloralose-anesthetized HF rats. Second, anesthesia may influence SND responses to heating. Although this cannot be discounted, several factors argue against this possibility. Chloralose anesthesia is widely used in studies concerned with autonomic regulation and to sympathetic preganglionic neurons of the intermediolateral cell column (30, 34, 43). Our lesion data suggest that damage to the parvocellular neurons of the PVN is likely responsible for the altered SND responses to heating in HF rats. Important relative to the current study, both the dorsal and medial parvocellular subdivisions of the PVN project to brain stem regions involved in autonomic regulation and to sympathetic preganglionic neurons of the intermediolateral cell column (30, 34, 43). The magnocellular neurons produce the hormones vasopressin and oxytocin and project to the posterior pituitary (30, 34, 43). Portions of the PVN parvocellular neurons control anterior pituitary function, whereas other parvocellular neurons such as those in the dorsal parvocellular subdivisions are involved with central autonomic regulation (30, 34, 43). Important relative to the current study, the PVN of the hypothalamus is involved in suppressing renal SND responses to heating in HF rats. There are at least two limitations to the present study. First, because it is widely accepted that the sympathetic nervous system is capable of producing nonuniform changes in peripheral SND to selectively control different regional circulations (2, 15, 18, 21), the current results are applicable to renal SND only. Second, anesthesia may influence SND responses to heating. Although this cannot be discounted, several factors argue against this possibility. Chloralose anesthesia is widely used in studies concerned with autonomic and cardiovascular regulation, and heating pro-

<table>
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<tr>
<th>Colonic Temperature</th>
<th>38°C</th>
<th>39°C</th>
<th>40°C</th>
<th>40.5°C</th>
<th>41°C</th>
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<tr>
<td><strong>MAP, mmHg</strong></td>
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<td>HF, sham PVN lesion</td>
<td>118 ± 8</td>
<td>115 ± 10</td>
<td>130 ± 10*</td>
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<td>126 ± 9*</td>
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<td>391 ± 16</td>
<td>409 ± 13*</td>
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<td>Sham HF, PVN lesion</td>
<td>387 ± 12</td>
<td>422 ± 14</td>
<td>454 ± 19</td>
<td>481 ± 22*</td>
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Values are means ± SE. PVN, paraventricular nucleus. *Significantly different from 38°C at P < 0.05; †significantly different from HF, PVN lesion at P < 0.05.
vides a potent stimulus to efferent sympathetic nerve outflow in conscious humans (36), conscious rats (24), and noninfarcted, chloralose-anesthetized rats (10, 19, 20, 22, and the current study). In addition, the circulatory responses to heating are quite similar in conscious and chloralose-anesthetized rats (25). Moreover, the current results strongly support the hypothesis that the pathophysiological state of HF and not anesthesia plays an important role in mediating the observed responses. For example, renal SND responses to hyperthermia but not hypothermia were different in chloralose-anesthetized HF and sham HF rats, and renal sympathoexcitatory responses to heating were observed in chloralose-anesthetized, PVN-lesioned HF, and sham HF rats but not in chloralose-anesthetized HF rats with sham PVN lesions. Finally, physiological responses to changes in Tc can be altered by behavioral modifications. For example, conscious animals use locomotion as a behavioral strategy to limit heat gain or facilitate heat loss (1). With this in mind, we have chosen in the current and previous studies (19, 20, 22) to characterize SND responses to heating in chloralose-anesthetized rats, thereby removing the behavioral component.

**Perspectives.** Changing the level of activity in peripheral sympathetic nerves is a primary strategy used by mammals to respond to acute physical stress. The direction of change depends on the specific experimental stimulus and on the peripheral nerve from which activity is being recorded. Important relative to the current study, increasing the level of peripheral SND is an important way that mammals respond to acute heating. Hyperthermia-induced sympathoexcitation, including substantial increases in renal SND, is likely essential for providing increased blood flow distribution for heat dissipation while maintaining arterial blood pressure (i.e., vital organ perfusion pressure). The present results demonstrate a marked attenuation in the responsiveness of renal SND to heating in HF rats and suggest that HF alters the organization of pathways mediating SND responses to heating. As stated previously, it is widely accepted that in response to acute stress the sympathetic nervous system is capable of selectively controlling the level of activity and the frequency components of SND to different regional circulations (2, 15, 18, 21). The current results suggest another level of selectivity, that is, pathophysiological states may selectively alter the functional organization and regulatory strategies employed by sympathetic neural circuits to respond to acute stress.

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**REFERENCES**

HEART FAILURE ALTERS SYMPATHETIC RESPONSES TO HEATING


