Differential responses of frequency components of renal sympathetic nerve activity to arterial pressure changes in conscious rats

Delphine Bertram, Valérie Oréa, Bruno Chapuis, Christian Barrès, and Claude Julien
Département de Physiologie et Pharmacologie Clinique, Faculté de Pharmacie, Université Claude Bernard Lyon 1, Lyon, France

Submitted 14 April 2005; accepted in final form 29 May 2005

Bertram, Delphine, Valérie Oréa, Bruno Chapuis, Christian Barrès, and Claude Julien. Differential responses of frequency components of renal sympathetic nerve activity to arterial pressure changes in conscious rats. Am J Physiol Regul Integr Comp Physiol 289: R1074–R1082, 2005. First published June 2, 2005; doi:10.1152/ajpregu.00270.2005.—The present study examined the effects of baroreceptor loading and unloading on the various frequency components of SNA. Kunitake and Kannan (21) reported that in conscious rats, the sympathetic activation induced by infusion of a single dose of sodium nitroprusside was mainly attributable to an enhancement of the cardiac-related oscillation of SNA, while there was little or no change in the amplitude of the other rhythms.

The objective of the present study was to provide a detailed description of the frequency content of multifiber SNA in rats during short-lasting, steady-state changes in AP induced by the administration of vasoactive drugs. Activity was recorded from the renal nerve, which is the most commonly used sympathetic nerve for baroreflex studies in rats (13, 26, 35). Experiments were performed on conscious animals because anesthesia has been shown to alter the discharge pattern of renal SNA ( RSNA) (7, 11). Because baroreflex-induced changes in heart rate would presumably affect the amplitude of the cardiac-related rhythm of RSNA (29), all experiments were performed under total cardiac autonomic blockade, so that changes in the amplitude of the cardiac-related rhythm truly reflected changes in the activity of its generating components.

METHODS

Animals. Experiments were performed on 10 male Sprague-Dawley rats (Charles River Laboratories, L’Arbresle, France) aged 12–14 wk. Rats were housed individually with free access to food and water and maintained on a 12:12-h light-dark cycle. On completion of the experiments, rats were euthanized with an intravenous overdose of pentobarbital sodium. All experiments were performed in accordance with the guidelines of the French Ministry of Agriculture for animal experimentation.

Surgical procedures. Rats received a single prophylactic injection of penicillin G (50 000 IU se). Under halothane anesthesia (1.5–2% in oxygen), a catheter (heat-stretched PE-10 fused to a PE-50 extension) was inserted into the abdominal aorta through the left femoral artery and was filled with a solution of polyvinylpyrrolidone (500 mg/ml) to prevent blood diffusion. For drug administration, two catheters were inserted in the left femoral vein and a third one in the right femoral vein. Arterial and venous catheters were led under the skin to exit between the scapulae. Four to 6 h later, rats were reanesthetized with pentobarbital sodium (60 mg/kg ip), and the left renal nerve was exposed via a flank incision. After careful dissection, a major branch of the intact nerve was placed on a bipolar platinum-iridium electrode and insulated with a silicone gel (604A and B; Wacker-Chemie).

The costs of publication of this article were defrayed in part by the payment of page charges. The article must therefore be hereby marked “advertisement” in accordance with 18 U.S.C. Section 1734 solely to indicate this fact.
Munich, Germany). The electrode cable was secured to back muscles and exteriorized at the same site as the catheters. The plug was protected in a small cap sewn to the skin.

**Data acquisition and experimental protocol.** Rats were allowed to recover from anesthesia overnight so that experiments were started 14–16 h after electrode implantation. AP was measured by connecting the arterial catheter to a precalibrated pressure transducer (TNE-R; Ohmeda, Bilthaven, The Netherlands) through a two-way stopcock, which allowed the continuous infusion of a 5% glucose solution (0.4 ml/h). The pressure transducer was coupled to an amplifier (model 13–4615-52; Gould, Cleveland, OH) chart recorder (model 8802; Gould). The AP signal was fed into a computer through a converter board (model AT-MIO-16; National Instruments, Austin, TX) and sampled at 500 Hz using LabVIEW 5.1 software (National Instruments). The RSNA signal was amplified (∗∗gradient, 50,000), band-pass filtered (300–3,000 Hz: Model P-511J; Grass, Quincy, MA), rectified by an analog home-made rectifier, including a low-pass filter (cut-off frequency of 150 Hz), and sampled at 5,000 Hz.

To prevent the effect of drug-induced changes in heart rate on the amplitude of the cardiac-related oscillation of RSNA, experiments were performed under total cardiac autonomic blockade, which has little or no effect on AP and its variability in conscious rats (6). Blockade was achieved by the combined intravenous administration of atropine methyl nitrate and atenolol (2 mg/kg each as a bolus injection, followed by the continuous infusion of 2 mg·kg⁻¹·h⁻¹). With this treatment, reflex changes in heart rate never exceeded 15 bpm. The experiment consisted of the alternate intravenous infusion of phenylephrine and sodium nitroprusside with the objective of obtaining a sequence of randomly chosen increases and decreases in AP. Venous catheters were filled with solutions of phenylephrine and sodium nitroprusside at concentrations of 25 and 500 µg/ml, respectively. The infusion rate was adjusted until the targeted change in AP was reached. In the case of phenylephrine, infusion rates ranged from 8.3 to 33.3 µl/min, which yielded doses ranging from 0.63 to 2.5 µg·kg⁻¹·min⁻¹ for a 330-g rat. In the case of sodium nitroprusside, infusion rates ranged from 3.3 to 41.7 µl/min, which yielded doses ranging from 5 to 63 µg·kg⁻¹·min⁻¹. Infusions were initiated when the rat was awake, in a resting state, and were continued until a stable AP change lasting at least 131 s was obtained. If for any reason, such a change could not be obtained after 8 min, the infusion was stopped. Usually, infusions lasted 4–5 min. The recovery period between consecutive infusions lasted at least 5 min.

In 5 of 10 rats, the ganglionic blocker chlorisondamine was administered (2.5 mg/kg iv) to determine the background noise of RSNA. Activity measured under ganglionic blockade incorporated possible movement artifacts and, as the nerve was not cut distal to the electrode, afferent renal nerve activity, if present. On completion of the experiments, the rats received an intravenous lethal dose of pentobarbital sodium, and RSNA was recorded for an additional 15 to 20-min period to estimate the background noise without any contamination of biological origin.

**Spectral analysis.** AP and RSNA time series were filtered at 100 Hz using a finite-impulse response digital filter. The RSNA signal was then resampled at 500 Hz. From each test period (during drug infusion) and whenever possible, a 131-s period during which AP showed a steady change was selected. Another 131-s period was taken from each baseline period preceding the start of a drug infusion. These 131-s periods were split into seven data segments of 16,384 points (32.8 s) overlapping by half. For each data set, power spectral density was calculated using a fast Fourier transform (FFT) algorithm after linear detrending and application of a Hanning window (4). The spectra obtained for the seven data sets were then averaged. The frequency resolution was 0.0305 Hz. The low (LF, 0.030–0.244 Hz), mid (MF, 0.275–0.763 Hz), respiratory (0.794–2.5 Hz), high (HF, 2.53–25 Hz)-frequency and total (0.03–25 Hz) powers were calculated by integration. Spectral power at the frequency of the heart beat was calculated as the area under the peak at peak frequency ± 0.25 Hz.

Cross-spectral techniques using a FFT algorithm were used to calculate the magnitude squared coherence function between AP and RSNA (18). The significance threshold (P < 0.05) for coherence was 0.486 (2).

**Statistics.** Values are expressed as means ± SE. For the purpose of presenting group-average values, changes in RSNA mean level and spectral powers were expressed as percent changes from baseline. Actual changes in AP and corresponding RSNA variables were averaged within 5- to 10-mmHg AP intervals centered on each targeted AP change (see RESULTS). However, absolute values were considered for performing paired comparisons (test period vs. baseline period) by the Wilcoxon signed rank test.

Equations of four-parameter sigmoid and Gaussian curves were fitted to group-average data pairs using an iterative least-squares procedure (SigmaPlot 2000; SPSS, Chicago, IL).

**RESULTS**

**Basal characteristics.** Basal values of AP and HR (under cardiac autonomic blockade) were 112 ± 4 mmHg and 360 ± 8 bpm, respectively. Spectral analysis revealed the presence of four rhythmic components in the RSNA signal (Fig. 1A): in the MF band at ~0.4 Hz, which corresponds to the frequency of Mayer waves (7); in the respiratory band at ~1.5 Hz, which corresponds to the frequency of respiratory movements in conscious rats (30); in the HF band at ~6 and 12 Hz, which corresponds to the frequency of the heart beat and of its first harmonic. Corresponding peaks were observed in the AP spectra (Fig. 1B), as well as in the coherence function computed between AP and RSNA (Fig. 1C). However, spectral analysis of AP also revealed the presence of peaks at several harmonics of heart rate that were not observed in the RSNA spectra nor in the coherence spectra.

The background noise level of RSNA measured after chlorisondamine administration (n = 5 rats) was 0.29 ± 0.04 µV, which was not significantly different (Wilcoxon signed rank test, P = 0.1025) from the postmortem RSNA value (0.28 ± 0.03 µV) measured in the same animals. This result indicates that afferent renal nerve activity and movement-related artifacts did not make a significant contribution to RSNA measured under our experimental conditions. In the 10 rats of the study, spectral analysis was applied to a 131-s period of postmortem RSNA. It was observed that fluctuations in the background noise amounted to 3.9 ± 1.8%, 1.6 ± 0.6%, 1.4 ± 0.5%, and 2.7 ± 0.9% of the LF, MF, respiratory, and HF powers of RSNA recorded under baseline conditions.

**Effect of drug-induced changes in AP on RSNA spectral powers.** Phenylephrine-induced increases in AP and nitroprusside-induced decreases in AP were accompanied by significant, opposite changes in the mean level of RSNA (Fig. 2) and in the total power of RSNA (Fig. 3A). The relationship between changes in AP and changes in both indices of RSNA could be characterized by a four-parameter sigmoid equation. Considering either index, it was found that basal AP lay slightly above the zero baseline, it was found that basal AP lay slightly above the zero baseline, so that it was close to the lower plateau of the sigmoid. Changes in LF, respiratory, and HF powers of RSNA (Fig. 3, B, D, and E) also showed sigmoid relationships with AP changes. In the case of changes in MF power (Fig. 3C), there was a clear reversal of the nitroprusside effects for the two largest AP decreases. In this case, the baroreflex relationship was best characterized by the equation of a Gaussian curve.
that reached its maximum 21 mmHg below basal AP. Even more obviously, the relationship between changes in AP and changes in cardiac-related RSNA power showed a bell curve shape (Fig. 3F). Its maximum was observed 22 mmHg below basal AP.

Effect of drug-induced changes in AP on the percentage of total RSNA power in selected frequency bands. Under baseline conditions, RSNA spectral powers in the LF, MF, respiratory, and HF bands accounted for 3.2\(^\pm\)0.2%, 10.4\(^\pm\)0.6%, 17.7\(^\pm\)0.7%, and 68.7\(^\pm\)1.3% of the total power, respectively. RSNA spectral power at the heart rate (\(0.25\) Hz) accounted for 11.1\(^\pm\)0.6% of power in the HF band. Drug-induced changes in AP did not consistently alter the predominant contribution of respiratory and HF powers to total RSNA power (Table 1).

Linear modeling of the generation of the cardiac-related RSNA rhythm. It was examined whether a simple linear model could predict the biphasic response of the cardiac-related RSNA rhythm to AP decreases resulting in the characteristic bell curve shown in Fig. 3F. An open-loop model of the baroreceptor reflex was implemented using LabVIEW 5.1. The input in the model was a theoretical baroreceptor activity (BA) that varied from 0 to 1 depending on whether AP was below (BA = 0) or above (BA = 1) a threshold value. Under this condition, the percentage of the cardiac cycle during which

\[
\begin{align*}
\Delta \text{mean AP} (\text{mmHg}) & \\
\text{AP} (\text{mmHg}^3/\text{Hz}) & \\
\text{Coherence} & \\
\end{align*}
\]

Fig. 1. Example of spectral analysis of renal sympathetic nerve activity (RSNA) and arterial pressure (AP). Power spectra of RSNA (A) and AP (B), and coherence function (C) were computed from a 131-s recording (segmented into 33-s periods) in one conscious rat during the infusion of sodium nitroprusside (5 \(\mu\)g·kg\(^{-1}\)·min\(^{-1}\)). The y-scale was chosen to emphasize peaks of low amplitude. Thus numbers in parentheses indicate the maximum value reached by peaks of larger amplitude. The vertical dashed lines delimit the frequency bands of interest, namely the low (LF, 0.030–0.244 Hz), mid (MF, 0.275–0.763 Hz), respiratory (Resp, 0.794–2.5 Hz) and high (HF, 2.53–25 Hz)-frequency bands. In the coherence spectrum, the horizontal dashed line shows the significance threshold (\(P < 0.05\)).

Fig. 2. Baroreflex curve relating changes in the mean level of RSNA to changes in mean AP. Graphs show group-average values (±SE) for 10 rats. Numbers in parentheses are the number of observations for each targeted AP change (from −10 to −40 mmHg during sodium nitroprusside infusions and from 5 to 30 mmHg during phenylephrine infusions). Note that actual changes in AP are shown but that the symbol size exceeds the error bars. Changes in RSNA level are expressed as percent changes from baseline. Postmortem values were subtracted from RSNA data before calculating percentage changes. Equation of a 4-parameter sigmoid curve (forced through 0,0 coordinates) was fitted to group-average data pairs. Results of the fitting are given in the upper right hand corner of the graph. \(\rho^2\), coefficient of determination; a, full range of RSNA variation; b, slope coefficient; \(x_0\), AP change at the midrange of the curve; \(y_0\), lower plateau. *\(P < 0.05\) vs. baseline condition.
Fig. 3. Baroreflex relationships for frequency-domain indices of RSNA. Graphs show group-average values (±SE) for 10 rats. Equations of 4-parameter sigmoid ($A, B, D, E$) or Gaussian ($C, F$) curves (forced through 0,0 coordinates) were fitted to group-average data pairs. Results of curve fittings are given in the upper right hand corner of each graph. Other details are as in Fig. 2 except that $b$ is a curvature coefficient in the case of the Gaussian equation. *$P < 0.05$ vs. baseline condition.
Table 1. Effect of drug-induced changes in AP on the relative contribution of different frequency components to total spectral power of RSNA in conscious rats

<table>
<thead>
<tr>
<th>BA, Drug-Induced Change in AP, mmHg</th>
<th>LF</th>
<th>MF</th>
<th>Resp</th>
<th>HF</th>
<th>CR, % of HF power</th>
</tr>
</thead>
<tbody>
<tr>
<td>% of Total Spectral Power</td>
<td>38.8±0.7</td>
<td>30.7±0.6</td>
<td>23.7±0.2</td>
<td>20.4±0.5</td>
<td>15.5±0.4</td>
</tr>
<tr>
<td>(n = 6)</td>
<td>(n = 8)</td>
<td>(n = 7)</td>
<td>(n = 5)</td>
<td>(n = 8)</td>
<td>(n = 10)</td>
</tr>
<tr>
<td>LF 1.2±0.2*</td>
<td>1.4±0.6</td>
<td>1.1±0.5*</td>
<td>1.1±0.1*</td>
<td>1.3±0.2*</td>
<td>1.6±0.4</td>
</tr>
<tr>
<td>MF 5.2±1.0*</td>
<td>5.0±0.6*</td>
<td>7.8±2.1</td>
<td>10.7±3.1</td>
<td>9.0±1.2</td>
<td>11.1±1.7</td>
</tr>
<tr>
<td>Resp 23±2</td>
<td>21±1*</td>
<td>19±2</td>
<td>18±2</td>
<td>17±1</td>
<td>17±1</td>
</tr>
<tr>
<td>HF 71±2</td>
<td>73±1*</td>
<td>72±2</td>
<td>71±1</td>
<td>73±1</td>
<td>70±2</td>
</tr>
<tr>
<td>CR, % of HF power</td>
<td>6.5±0.6*</td>
<td>10.4±1.1</td>
<td>11.6±1.4</td>
<td>10.0±0.8</td>
<td>12.5±1.1</td>
</tr>
</tbody>
</table>

Values are presented as means ± SE; n = no. of observations; *P < 0.05 compared with baseline condition (column 0). LF, low frequency; MF, mid-frequency; Resp, respiratory; HF, high frequency; CR, cardiac-related (in bold).

BA = 1 (duty cycle) was a linear function of mean AP. BA was translated into RSNA by using parameters of the transfer function (H) relating RSNA to aortic depressor nerve stimulation that had been determined in a previous study (29). The transfer function combined a static gain (K, arbitrarily set to 1), a derivative gain (defined by its corner frequency, fc = 0.1577 Hz), a second-order low-pass filter (defined by its natural frequency, fn = 1.12 Hz, and its damping coefficient, λ = 1.71) and a fixed time delay (T = 0.101 s):

\[
H(jf) = K \frac{1 + j(f f c)}{1 + 2\lambda f f c (j f f c) + (f f c)^2} \exp(-2\pi T j f)
\]

where j and f are the imaginary operator and frequency (Hz), respectively.

The amplitude of the cardiac-related rhythm of RSNA was computed at the frequency of the heart beat that was set at 6 Hz in the model. Increasing mean AP increased the duty cycle for baroreceptor activity, which resulted in I) a biphasic change in the amplitude of the rhythmic component of RSNA at the frequency of the heart beat, and 2) a progressive decrease in the mean level of RSNA (Fig. 4). When plotted as a function of the duty cycle for baroreceptor activity, the amplitude of the cardiac-related RSNA rhythm exhibited a bell curve shape, at least in the 10–90% range (Fig. 5).

DISCUSSION

The present study indicates that most of the baroreflex-induced changes in RSNA are mediated by changes in the amplitude of fast, irregular fluctuations, and to a lesser extent, by changes in the amplitude of an oscillation occurring at or near the respiratory frequency. The amplitude of the oscillation associated with Mayer waves and that of the pulse-synchronous oscillation show a biphasic response to AP decreases, that is, amplification during moderate decreases and a reversal during the largest decreases, which results in a bell-curve shape. Regarding the cardiac-related rhythm, this particular behavior is easily explained on the basis of a simple linear model translating baroreceptor activity into RSNA.

Methodological aspects. Data were collected shortly after electrode implantation surgery, which could be viewed as a limitation of the study. In rabbits, it has been shown that the postsurgical phase is associated with high levels of RSNA (3). It is of note, however, that the RSNA-AP relationships observed in the present study were similar to those reported in conscious rats that had been instrumented 3 days before study (26). In particular, the location of basal AP on the sympathetic baroreflex curve in the quiet awake rats of the present study was quite comparable to that observed during sleep states in rats of the quoted study, that is, a few mmHg above AP at midrange. On the contrary, during grooming-induced sympathetic activation, the steady-state level of AP was located below AP at midrange (26).

A possible limitation of the study concerns the use of atropine methyl nitrate to antagonize the effects of reflex changes in vagal activity on heart rate. Cholinergic muscarinic receptor activation has been shown to trigger norepinephrine release from rat sympathetic neurons in culture (22) and has been suggested to mediate neurotransmission in the renal ganglia of urethane-anesthetized, chlorisondamine-treated rabbits (20). In pilot experiments performed on conscious rats, we were unable to reproduce the results of the latter study. Specifically, administration of atropine methyl nitrate (2 mg/kg iv) did not induce any significant change in the RSNA of conscious rats pretreated with chlorisondamine (2.5 mg/kg iv). We, therefore, suggest that, at least under our experimental conditions, the muscarinic component plays little if any role in modulating neurotransmission in renal ganglia.

Finally, it should be mentioned that sodium nitroprusside is converted to cyanide, which could activate the arterial chemoreceptor reflex, thereby contributing to the sympathetic activation observed during sodium nitroprusside infusion, especially at the largest doses. Chemoreceptor activation also induces tachypnea in conscious rats (12). However, the infusion of sodium nitroprusside (50 µg·kg⁻¹·min⁻¹ iv) in conscious rats has been reported not to alter breathing frequency over a 20-min timescale (36). In the present study, it was observed that whenever a single, well-defined peak was present in the respiratory band of AP spectra (in 5 of 10 rats), infusion of sodium nitroprusside at the largest dose did not change its frequency (1.62 ± 0.13 vs. 1.55 ± 0.11 Hz before and during infusion, respectively). In the same animals, power in the respiratory band was not significantly altered by nitroprusside infusion (0.56 ± 0.10 vs. 0.49 ± 0.13 mmHg² before and during infusion, respectively). These observations make it quite unlikely that cyanide accumulation and consequent chemoreceptor activation had occurred during nitroprusside infusions.

Baroreflex relationships for total power and LF rhythms of RSNA. The baroreflex curve for the mean RSNA level showed the classical sigmoid shape. The 300% range of RSNA...
variations observed during short-lasting, steady-state changes in AP is comparable to that previously reported in conscious rats during either slow ramp increases and decreases in AP (31) or faster AP changes induced by the rapid infusion of phenyl-ephrine and sodium nitroprusside (11). The relationship between AP and RSNA total power could also be approximated by a sigmoid curve. The range of RSNA variations was somewhat larger in this case, which could be expected as the total power relates directly to the variance of the signal, that is, to the squared amplitude of fluctuations. An important finding is that control, resting AP was located 5–6 mmHg above AP at midrange, considering either mean RSNA level or RSNA total power. Overall, these observations indicate that the mean level and the total power basically provide the same information regarding the baroreflex control of RSNA (33).

Total power was split into four frequency components. In our experimental conditions, the LF component accounted for only 3% of the total power. This is not surprising because the LF component consists of fluctuations lasting from 4 to 32 s, which are usually associated with the performance of natural behaviors (9, 18). In rats, natural behaviors have been shown to increase RSNA (37) and to alter the AP-RSNA baroreflex curve (26). For these reasons, recordings used for spectral analysis were taken from periods during which rats
were as quiet as possible and thus did not show much LF variability.

The RSNA oscillation at Mayer wave’s frequency. The amplitude of the RSNA oscillation at Mayer wave’s frequency consistently decreased during phenylephrine-induced increases in AP and increased during mild to moderate nitroprusside-induced decreases in AP. This is similar to what has been shown for muscle SNA in healthy human subjects (28). However, when AP was further decreased, there was an almost complete reversal of the amplification of the RSNA oscillation. The mechanism of this biphasic response is unclear. By modeling AP and RSNA variabilities recorded in conscious sinoaortic baroreceptor denervated rats, we could recently propose that Mayer waves and accompanying RSNA oscillations are transient oscillatory responses to slow hemodynamic perturbations (9). Their frequency then depends on the resonance frequency of the baroreflex loop (5), and their amplitude depends both on the strength of the triggering perturbations and on the sensitivity of the baroreceptor reflex. In the present study, there is no indication that slow hemodynamic perturbations were altered during drug-induced changes in AP, as the LF component of AP variability did not consistently differ from baseline conditions (data not shown). It is therefore likely that changes in the amplitude of MF oscillations of RSNA reflect changes in baroreflex sensitivity. Baroreflex sensitivity refers to the open-loop gain from baroreceptor pressure to systemic AP, which combines the gain of the central arc (from baroreceptor pressure to RSNA) and the gain of the peripheral arc (from RSNA to AP). Although changes in either component cannot be assessed from the present study, it could be speculated that changes in the gain of the peripheral arc (i.e., vascular reactivity) might explain at least part of the observed changes in the amplitude of the RSNA oscillation. In particular, it is likely that during phenylephrine-induced vasoconstriction, vascular responses to superimposed SNA would be reduced. On the other hand, vascular reactivity during strong relaxation induced by a nitric oxide donor is also likely to be reduced, which would explain the reversal of the nitroprusside effects during the largest AP decreases.

Respiration-linked oscillation of RSNA. In rats, the prevailing view is that the respiratory rhythm of SNA is due to a central coupling of respiratory and sympathetic neurons with some modulation by the baroreceptor reflex (15). In conscious sinoaortic baroreceptor-denervated rats, it has been reported that a respiratory oscillation of RSNA only occurs sporadically (21). However, we have recently shown that in these animals, RSNA spectral power in the respiratory band is unchanged (18). In the present study, the RSNA oscillation present in the respiratory band was strongly coherent with a corresponding oscillation of AP. It is quite unlikely, however, that the respiration-linked oscillation of AP directly caused the RSNA oscillation because the former was usually of very small amplitude (see Fig. 1). Whatever the mechanism of its generation, this rhythm accounted for \( \sim 18\% \) of total RSNA power under baseline conditions and was highly responsive to changes in AP so that it contributed significantly to baroreflex-induced changes in RSNA total power.

The HF Rhythms of RSNA. One major finding of this study is that HF rhythms (faster than respiration) make up about 70% of the total power. Apart from the cardiac-related oscillation (see below) and its first harmonic, HF power did not show any clear periodicity. Surprisingly, in the literature, HF power is either not mentioned or referred to as “background power” (39). Spectral analysis of postmortem RSNA revealed that HF power was not the result of measurement noise and was therefore produced by fast, irregular fluctuations of biological origin. Although the mechanisms leading to the production of fast SNA rhythms are still poorly understood (24), the present study reveals that these rhythms are strongly modulated by baroreceptor input. This is important from a functional point of view because fluctuations of SNA at frequencies above 1 Hz are responsible for the generation and modulation of sympathetic vasoconstrictor tone (4, 17, 32).

Cardiac-related RSNA rhythm. Because it is prominent in the recordings from sympathetic nerves of all mammalian species studied so far, the pulse-synchronous SNA oscillation is generally regarded as the fundamental bursting pattern of sympathetic nerves involved in the reflex control of the circulation (25). Regarding the renal vascular bed, it has been shown that arterial baroreceptor denervation abolishes the cardiac-related rhythm of RSNA in both anesthetized (29) and conscious (21) rats, which points to the baroreflex origin of this rhythm. Two mechanisms have been proposed to explain the genesis of the cardiac-related SNA oscillation: periodic inhibition of randomly generated activity or entrainment of a central oscillator by pulse-synchronous baroreceptor activity (1). In the present study, we could show that the amplitude of the cardiac-related RSNA oscillation was decreased by phenylephrine-induced increases in AP and increased by nitroprusside-induced decreases in AP down to \( \sim 20 \) mmHg below control values. The latter observation is in agreement with a study reporting the effect of a single dose of sodium nitroprusside on the RSNA of conscious rats (21). However, for larger AP decreases, there was a progressive reversal of the amplification of the RSNA rhythm. This biphasic change was not secondary to drug-induced changes in the pulse pressure (data not shown). We therefore designed a simple linear model of the
baroreceptor reflex in the open-loop configuration. In this model, it was assumed that the reflex inhibits a steady level of centrally generated activity. With the additional assumption that baroreceptor activity occurs above a threshold AP (8, 14), the model predicted the bell curve shape of the relationship between AP (or baroreceptor activity) and the amplitude of the cardiac-related RSNA oscillation. It is worth noting that baroreceptor activity has been reported to occur preferentially between AP (or baroreceptor activity) and the amplitude of the RSNA variation. In a study performed on anesthetized cats, it was reported that phenylephrine enhanced the cardiac-related oscillation of cardiac SNA (39). We suggest that in this study, anesthesia might have moved the resting AP along the baroreflex curve below the pressure at which maximal enhancement of the cardiac-related rhythm occurs. Baroreflex studies in rats anesthetized with pentobarbital sodium (16) or Inactin (35), indeed, suggest that anesthesia induces a leftward shift of resting AP on the baroreflex curve.

Conclusions and Perspectives

The cardiac-related power of RSNA accounts for ~10% of HF power and its contribution to overall RSNA decreases at the highest levels of baroreflex-induced sympathetic activation. We, therefore, suggest that this rhythm is not mandatory for the production of sympathetic vasoconstrictor tone. This hypothesis is supported by the simple observation that sympathetic tone in conscious sinoaortic baroreceptor denervated rats is either normal or increased (38), although in the absence of a pulse-synchronous SNA rhythm (21). It remains to be determined whether cardiac-related SNA oscillations are merely a byproduct of normal baroreflex operation or have a specific function.

REFERENCES


