Dynamic interactions between arterial pressure and sympathetic nerve activity: role of arterial baroreceptors

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Julien, Claude, Bruno Chapuis, Yong Cheng, and Christian Barrès. Dynamic interactions between arterial pressure and sympathetic nerve activity: role of arterial baroreceptors. Am J Physiol Regul Integr Comp Physiol 285: R834–R841, 2003.—The role of arterial baroreceptors in controlling arterial pressure (AP) variability through changes in sympathetic nerve activity was examined in conscious rats. AP and renal sympathetic nerve activity (RSNA) were measured continuously during 1-h periods in freely behaving rats that had been subjected to sinoaortic baroreceptor denervation (SAD) or a sham operation 2 wk before study (n = 10 in each group). Past Fourier transform analysis revealed that chronic SAD did not alter high-frequency (0.75–5 Hz) respiratory-related oscillations of mean AP (MAP) and RSNA, decreased by ∼50% spectral power of both variables in the midfrequency band (MF, 0.27–0.74 Hz) containing the so-called Mayer waves, and induced an eightfold increase in MAP power without altering RSNA power in the low-frequency band (0.005–0.27 Hz). In both groups of rats, coherence between RSNA and MAP was maximal in the MF band and was usually weak at lower frequencies. In SAD rats, the transfer function from RSNA to MAP showed the characteristics of a second-order low-pass filter containing a fixed time delay (∼0.5 s). These results indicate that arterial baroreceptors are not involved in production of respiratory-related oscillations of RSNA but play a major role in the genesis of synchronous oscillations of MAP and RSNA at the frequency of Mayer waves. The weak coupling between slow fluctuations of RSNA and MAP in sham-operated and SAD rats points to the interference of noise sources unrelated to RSNA affecting MAP and of noise sources unrelated to MAP affecting RSNA.

Mayer waves; renal sympathetic nerve activity; sinoaortic baroreceptor denervation; spectral analysis; transfer function

ARTERIAL PRESSURE (AP) recordings in conscious sympatheticallydenervated rats have suggested that the baroreflex control of sympathetic nerve activity (SNA) plays a major role in minimizing slow (<0.1 Hz) AP fluctuations (19). Accordingly, cross-correlation analysis in the time domain was used to show that renal SNA (RSNA) and AP are negatively correlated ∼90% of the time in conscious baroreceptor-intact rats and much less frequently in SAD rats (1). However, it could not be excluded that this inverse relation might, at least partly, be explained by the prominent, reciprocal oscillations of RSNA and AP that occur spontaneously at the frequency of 0.4 Hz in rats (4, 7). Surprisingly, with the use of cross-spectral techniques, little, if any, coherence between low-frequency AP and RSNA fluctuations was reported in the conscious rat (8, 9). This observation suggested that the dynamic relations between slow RSNA and AP fluctuations cannot be explained solely on the basis of simple baroreflex patterns.

An obvious experimental approach to the question of the involvement of the baroreceptor reflex in the coupling (or the lack of coupling) between AP and RSNA would be to evaluate the effects of arterial baroreceptor denervation on RSNA and AP variabilities. This has been done in anesthetized rats (12), i.e., in the absence of behavioral influences that make a major contribution to RSNA and AP variabilities (7, 27). To our knowledge, frequency domain analysis of RSNA variability in conscious SAD rats has been performed on one occasion (23). In this study, spectra were calculated over 20-s periods, which precluded the analysis of <0.1-Hz fluctuations.

The main objective of the present study was to describe the effects of arterial baroreceptor denervation on spontaneous fluctuations of RSNA in conscious rats, as well as on the coupling between these fluctuations and those of AP. The renal circulation receives a large fraction of cardiac output, and thus changes in RSNA can affect AP through changes in renal vascular resistance (3, 13, 16, 26). Therefore, the study provided the opportunity to characterize the feedforward link between RSNA and AP under open-loop conditions by modeling the transfer function between these variables in SAD rats.

METHODS

Experiments were performed on male 10- to 12-wk-old Sprague-Dawley rats (Charles River Laboratories, L’Arbresle, France). Animals were housed individually with free access to food and water and maintained on a 12:12-h light-dark cycle. At the end of the experiments, the rats were killed with an intravenous overdose of pentobarbital sodium. All experiments were

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performed in accordance with the guidelines of the French Ministry of Agriculture for animal experimentation.

SAD. SAD was performed as previously described (33). Rats were anesthetized with a mixture of acepromazine maleate (12 mg/kg ip) and ketamine hydrochloride (120 mg/kg ip). Aortic baroreceptor denervation was achieved by bilaterally removing the superior cervical ganglia and sectioning the superior laryngeal nerves and aortic depressor nerves. Carotid baroreceptor denervation was accomplished by stripping all fibers from the carotid bifurcations and applying 10% phenol (in 95% ethanol). Sham surgery consisted of a midline neck incision and bilateral retraction of the sternothyroid muscles. Animals were studied 14 days after denervation or sham surgery.

Measurement of AP. Under halothane anesthesia (1.5–2% in oxygen), femoral arterial and venous polyethylene catheters were inserted into the lower abdominal aorta and the inferior vena cava for AP measurement and drug administration, respectively. Both catheters were tunneled subcutaneously and exteriorized between the scapulae. AP was measured by connection of the arterial catheter to a precalibrated pressure transducer (Statham P23 ID, Gould, Cleveland, OH) coupled to an amplifier (model 13-4615-52, Gould)-chart recorder (model 8802, Gould).

Measurement of RSNA. RSNA was measured using a previously described technique (1). Briefly, under pentobarbital sodium anesthesia (60 mg/kg ip), the left renal nerve was exposed via a flank incision. After careful isolation, a major branch of the renal nerve was placed on a bipolar platinum-iridium electrode and insulated with a silicone gel (Wacker Chemie, Munich, Germany). The electrical signal from the nerve was amplified (50,000 times), band-pass filtered (300–3,000 Hz; model P-511J, Grass, Quincy, MA), and rectified (analog home-made rectifier including a low-pass filter with a cutoff frequency of 5 Hz). The rectified RSNA was then simultaneously recorded with the AP signal on the chart recorder.

Experimental protocol. Twelve days after baroreceptor denervation or sham surgery, the arterial and venous catheters were implanted. One day later, the renal electrode was positioned, and the rats were then allowed 12–14 h for recovery from anesthesia before the experiments were started.

On the day of the study, i.e., 14 days after denervation, while the rats were unrestrained, AP and RSNA were simultaneously and continuously recorded for ≥3 h. Then the sensitivity of the baroreceptor reflex was evaluated using intravenous injections of phenylephrine hydrochloride (1.5 μg/kg; Sigma Chemical, St. Louis, MO) and sodium nitroprusside (8 μg/kg; Sigma Chemical). Finally, at the end of the experiment, the background noise level of RSNA was measured as the residual electrical activity obtained after administration of the short-acting ganglionic blocker trimethaphan camsylate (10 mg/kg iv; Hoffmann-LaRoche, Basel, Switzerland).

Data acquisition and analysis. With the use of a personal computer with an analog-to-digital converter (model ATMIO-16, National Instruments, Austin, TX) and LabVIEW 5.0 software (National Instruments), the AP and RSNA data were sampled at 500 Hz and stored on CD-ROM.

From the total recording, one continuous 60-min period free of artifacts was selected for further analysis. Offline processing of data was performed on a workstation (Sparc1, Sun Microsystems, Mountain View, CA). For each cardiac cycle, the computer calculated mean AP (MAP) and heart rate (HR). Beat-to-beat time series of MAP were then resampled at 10 Hz after linear interpolation. RSNA data were averaged over consecutive 100-ms periods, the background noise was subtracted, and all values were normalized by the mean value calculated over the 1-h period. For MAP and RSNA, the 10-Hz time series were segmented into 34 data sets of 2,048 points (204.8 s) overlapping by one-half. For each data set, power spectral density was calculated using a fast Fourier transform algorithm after linear trend removal and application of a Hanning window (10). The spectra obtained for the different data sets were averaged. The frequency resolution was 0.005 Hz, and the upper frequency limit was 5 Hz. Spectral powers were calculated by integration within three frequency bands: a low-frequency (LF) band, extending from 0.005 to 0.269 Hz, a midfrequency (MF) band, extending from 0.273 to 0.742 Hz, and a high-frequency (HF) band, extending from 0.747 to 5 Hz.

The coherence function between RSNA and MAP was assessed by cross-spectral analysis as previously described (10). Coherence values exceeding 0.2 indicate a statistically (P < 0.01) reliable linear relation between fluctuations of the two signals (22). In addition, cross-spectral analysis was used to calculate the gain and phase of the transfer function (4, 5) from RSNA to MAP. In each SAD rat, gain and phase functions were subjected to linear modeling analysis (see results).

The baroreceptor reflex sensitivity was estimated as the ratio of the peak change in HR (beats/min) or RSNA (percent change from predrug value) to the peak change in MAP (mmHg) after phenylephrine and nitroprusside administrations.

Statistics. Values are means ± SE. Statistical comparisons between sham-operated and SAD rats were performed using the nonparametric Mann-Whitney U test.

RESULTS

Ten sham-operated and 10 SAD rats were studied. On the day of the recording session, their body weights were comparable (335 ± 5 and 324 ± 9 g in sham-operated and SAD rats, respectively).

Baroreflex sensitivities, mean levels, and overall variabilities of MAP, HR, and RSNA. As indicated in Table 1, SAD markedly reduced the reflex HR and RSNA responses to phenylephrine-induced increases in MAP and nitroprusside-induced decreases in MAP. The 1-h mean levels of MAP and HR did not differ significantly between sham-operated and SAD rats. After denervation, the overall variabilities (variation coefficients) of MAP and HR were increased and decreased, respectively, whereas the RSNA variability was not significantly altered (Table 1). The cardiovascular consequences of baroreceptor denervation, especially the exaggerated MAP variability, are illustrated in Fig. 1.

Spectral analysis of MAP and RSNA time series. For each group of rats, the 1-h average spectra of MAP and RSNA and the corresponding coherence function are shown in Fig. 2. In the HF band containing respiratory fluctuations (30), peaks were observed in the MAP and RSNA spectra from sham-operated and SAD rats. For both variables, spectral power in the HF band was not altered after denervation (Table 2) and maximum coherence did not differ between sham-operated (0.55 ± 0.02 at 1.54 ± 0.09 Hz) and SAD (0.60 ± 0.04 at 1.46 ± 0.07 Hz) rats. In sham-operated rats, spectral peaks for
MAP and RSNA were also present in the MF band (Fig. 2). Coherence between RSNA and MAP reached a maximum (0.89 ± 0.03 at 0.42 ± 0.01 Hz) at 0.42 ± 0.01 Hz. After SAD, MF spectral power was reduced by 50% for MAP and RSNA (Table 2) and residual power in the band was not organized with a clear periodicity (Fig. 2). Maximum coherence between RSNA and MAP (0.69 ± 0.06 at 0.39 ± 0.02 Hz) was significantly (P < 0.001) decreased compared with sham-operated rats in the MF band. These effects of baroreceptor denervation on Mayer waves and corresponding RSNA oscillations are illustrated in Fig. 3. Finally, SAD induced a large increase in the LF component of MAP variability, especially below 0.1 Hz, without altering the corresponding LF component of RSNA variability (Fig. 2, Table 2). In both groups of rats, coherence was usually weak in the LF band. Average coherence calculated below 0.1 Hz did not differ statistically between sham-operated (0.21 ± 0.02) and SAD (0.27 ± 0.04) rats.

Transfer function analysis and modeling. In sham-operated and SAD rats, the transfer function from RSNA to MAP was studied up to 1 Hz, inasmuch as previous studies indicated that SNA fluctuations are not translated into MAP fluctuations at frequencies beyond 1 Hz (18, 25, 32). In both groups of rats, gain values declined with increasing frequency, especially beyond 0.1 Hz (Fig. 4A). Below 0.1 Hz, gain values were significantly (P < 0.001) higher in SAD than in sham-operated rats (0.243 ± 0.036 vs. 0.063 ± 0.004 mmHg/NU, where NU is normalized units). At higher frequencies, the gain functions were similar in both groups of rats. In particular, the gain values measured at the peak coherence frequency were almost identical in sham-operated (0.045 ± 0.004 mmHg/NU at 0.42 ±...

Table 1. Baroreflex sensitivities, mean levels, and overall variabilities of MAP, HR, and RSNA in conscious sham-operated and SAD rats

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<tr>
<td>Cardiac BRS, beats·min⁻¹·mmHg⁻¹</td>
<td>−2.09 ± 0.24</td>
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<td>Phenylephrine</td>
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<tr>
<td>Sympathetic BRS, %/mmHg</td>
<td>−6.26 ± 0.70</td>
<td>−1.43 ± 0.14†</td>
</tr>
<tr>
<td>MAP Mean, mmHg</td>
<td>110 ± 1</td>
<td>108 ± 3</td>
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<tr>
<td>VC, %</td>
<td>5.0 ± 0.4</td>
<td>12.9 ± 1.1†</td>
</tr>
<tr>
<td>HR Mean, beats/min</td>
<td>412 ± 11</td>
<td>431 ± 13</td>
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<tr>
<td>VC, %</td>
<td>6.4 ± 0.6</td>
<td>4.0 ± 0.3*</td>
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<tr>
<td>RSNA Mean, µV</td>
<td>1.37 ± 0.15</td>
<td>1.96 ± 0.22</td>
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<td>VC, %</td>
<td>80 ± 6</td>
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Values are means ± SE; n = 10 in each group. BRS, baroreflex sensitivity; MAP, mean arterial pressure; HR, heart rate; RSNA, renal sympathetic nerve activity; SAD, sinoaortic baroreceptor denervated. For each variable, overall variability is expressed as variation coefficient (VC). *P < 0.01; †P < 0.001 vs. sham. Between-group comparison of mean RSNA levels was not performed, because absolute values of RSNA depend on physical factors unrelated to actual nerve traffic.

MAP and RSNA were also present in the MF band (Fig. 2). Coherence between RSNA and MAP reached a maximum (0.89 ± 0.03 at 0.42 ± 0.01 Hz). After SAD, MF spectral power was reduced by −50% for MAP and RSNA (Table 2) and residual power in the band was not organized with a clear periodicity (Fig. 2). Maximum coherence between RSNA and MAP (0.69 ± 0.06 at 0.39 ± 0.02 Hz) was significantly (P < 0.001) decreased compared with sham-operated rats in the MF band. These effects of baroreceptor denervation on Mayer waves and corresponding RSNA oscillations are illustrated in Fig. 3. Finally, SAD induced a large increase in the LF component of MAP variability, especially below 0.1 Hz, without altering the corresponding LF component of RSNA variability (Fig. 2, Table 2). In both groups of rats, coherence was usually weak in the LF band. Average coherence calculated below 0.1 Hz did not differ statistically between sham-operated (0.21 ± 0.02) and SAD (0.27 ± 0.04) rats.

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Fig. 2. Group-average power spectra of mean arterial pressure (A; MAP) and RSNA (B) computed from 1-h recordings in 10 conscious sham-operated rats (thin lines) and 10 conscious SAD rats (thick lines). In each rat, RSNA data were normalized (NU, normalized units) by the mean value calculated over the entire 1-h period. C: average coherence functions calculated between MAP and RSNA. Because peak coherence frequency slightly differed between rats, maximum values in average graphs are lower than those calculated from individual data (see RESULTS). Standard errors have been omitted for clarity. Vertical dashed lines delimit low-frequency (0.005–0.269 Hz), midfrequency (0.273–0.742 Hz), and high-frequency (0.747–5 Hz) bands.

### Table 2. Spectral powers for MAP and RSNA in conscious sham-operated and SAD rats

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<td><strong>MAP, mmHg</strong></td>
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<tr>
<td>Total power</td>
<td>4.4 ± 0.3</td>
<td>26.6 ± 3.3†</td>
</tr>
<tr>
<td>LF power</td>
<td>3.0 ± 0.3</td>
<td>25.7 ± 3.4†</td>
</tr>
<tr>
<td>MF power</td>
<td>1.13 ± 0.14</td>
<td>0.62 ± 0.06a</td>
</tr>
<tr>
<td>HF power</td>
<td>0.26 ± 0.06</td>
<td>0.32 ± 0.03</td>
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<tr>
<td><strong>RSNA, NU</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total power</td>
<td>2,164 ± 319</td>
<td>1,635 ± 262</td>
</tr>
<tr>
<td>LF power</td>
<td>215 ± 44</td>
<td>164 ± 22</td>
</tr>
<tr>
<td>MF power</td>
<td>605 ± 75</td>
<td>303 ± 39†</td>
</tr>
<tr>
<td>HF power</td>
<td>1,344 ± 209</td>
<td>1,168 ± 208</td>
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Values are means ± SE; n = 10 in each group. LF, low frequency (0.005–0.269 Hz); MF, midfrequency (0.273–0.742 Hz); HF, high frequency (0.747–5 Hz); NU, normalized units. *P < 0.01; †P < 0.001 vs. sham.

0.01 Hz) and SAD (0.046 ± 0.004 mmHg/NU at 0.39 ± 0.02 Hz) rats.

In both groups of rats, phase values were negative and tended to decline, especially starting from 0.2 Hz (Fig. 4B). Interestingly, the phase values measured at the peak coherence frequency in the MF band were similar and close to π rad (−2.82 ± 0.07 and −2.85 ± 0.06 rad in sham-operated and SAD rats, respectively), which indicates that, at this frequency, RSNA and MAP tended to vary in opposite directions.

Assuming a simple linear relation between RSNA and MAP in SAD rats and in view of the previously reported low-pass filter properties of the vasculature (18, 21, 25), we attempted to fit equations of first-order (Eq. 1) and second-order (Eq. 2) low-pass filters to experimental gain values after transformation [G = 20 log(gain), expressed in dB]

\[
G(f) = 20 \log (K) - 10 \log [1 + (ff_c)^2] \tag{1}
\]

where \(K\) is the static gain (mmHg/NU) and \(f_c\) is the corner frequency (Hz), and

\[
G(f) = 20 \log (K) - 10 \log [(1 - (ff_c)^2)^2 + 4Kf_c^2] \tag{2}
\]

where \(\lambda\) is the damping coefficient and \(f_c\) is the natural frequency (Hz).

The fitting of equations used an iterative least-squares procedure (SYSTAT 8.0, SPSS, Chicago, IL). Only gain values associated with a significant coherence were used (n = 130 ± 11 in the 0.005- to 1-Hz frequency band).

Both models provided satisfactory fittings of the experimental data. However, the regression coefficients \(r^2\), observed vs. predicted values were always higher in the case of a second-order, low-pass filter (0.931 ± 0.013 and 0.912 ± 0.014 for Eqs. 2 and 1, respectively). An individual example is shown in Fig. 5A. The estimated parameters obtained from the 10 SAD rats were 0.439 ± 0.086 mmHg/NU, 0.186 ± 0.023 Hz, and 2.25 ± 0.26 for \(K\), \(f_c\), and \(\lambda\), respectively.

Theoretically, in a system including a low-pass filter with a fixed time delay, the linear portion of the phase function mainly reflects the influence of the time delay. Therefore, to estimate the time delay between RSNA
and MAP fluctuations, individual linear fittings of phase functions were performed in the group of SAD rats. Because at low frequencies the influence of the time delay is weak, phase values below 0.2 Hz were excluded. Linear regression analysis (SYSTAT 8.0) was thus performed between 0.2 and 1 Hz, with consideration of only phase values associated with a significant coherence ($r^2 = 0.809 \pm 0.038, n = 107 \pm 8$).

An individual example is presented in Fig. 5B. The time delay ($\tau$, s) was calculated from the slope (rad/Hz) of the linear regression: $\tau = \text{slope}/2\pi$. The time delay estimated in the group of SAD rats was $0.46 \pm 0.03$ s.

![Fig. 4. Group-average transfer gain (A) and phase (B) functions from RSNA to MAP computed from 1-h recordings in 10 conscious sham-operated rats (thin lines) and 10 conscious SAD rats (thick lines). Standard errors have been omitted for clarity. NU, normalized unit.](image)

![Fig. 5. Linear modeling of the experimental transfer function from RSNA to MAP in 1 conscious SAD rat. A: gain function of a second-order low-pass filter that was fitted to experimental gain values associated with a significant ($P < 0.01$) coherence. $K$, static gain; $f_n$, natural frequency; $\lambda$, damping coefficient. B: regression line fitted to experimental phase values (0.2–1 Hz) associated with a significant coherence. Fixed time delay ($\tau$) between RSNA and MAP fluctuations was calculated using the slope of the line.](image)
DISCUSSION

In the baroreceptor-intact rat, AP is altered by SNA, mainly through its direct influence on the resistance vasculature, and SNA is altered by BP, mainly through the operation of the arterial baroreceptor reflex. This closed-loop situation makes it difficult, if not impossible, to disentangle the feedforward and feedback effects when spontaneous AP and SNA variabilities are considered. The SAD rat provides the unique condition under which the main feedback control loop has been opened. On the one hand, feedforward effects that are unopposed by the baroreceptor reflex become apparent. On the other hand, elimination of feedback effects allows inference of the reflex origin of some SNA rhythms.

SAD rats exhibited HF respiratory-related fluctuations of MAP and RSNA that did not differ in amplitude from those measured in sham-operated rats. This observation was not unexpected with respect to HF oscillations of MAP, which are essentially of mechanical origin in the rat (17). Regarding HF oscillations of RSNA, the results of the present study suggest that the baroreceptor reflex contributes little to their genesis and/or modulation. It has been shown in the anesthetized, vagotomized rat that the respiratory-related oscillations of RSNA have a mixed central and baroreflex origin (14). In the conscious SAD rat, it has been reported that HF oscillations of RSNA are absent most of the time but can appear sporadically (23). Inasmuch as we did not examine the stability over time of the HF RSNA fluctuations, we cannot exclude that, in some animals, this component was not always present and that sporadic large-amplitude fluctuations produced spectral power in the HF band.

In sham-operated rats, 0.4-Hz oscillations of AP (the so-called Mayer waves) were associated with large, coherent oscillations of RSNA, which confirms previous observations (4, 7). These oscillations were strongly attenuated in SAD rats, which is consistent with a recent report (23). The latter observation further supports the hypothesis that Mayer waves and accompanying RSNA oscillations are resonant oscillations within the baroreceptor reflex loop (2, 5). There was significant residual power in the MF band for MAP and RSNA in SAD rats, although no clear peaks could be discerned. This finding is in keeping with the previous observation that acute ganglionic blockade abolishes MF power of MAP in conscious SAD rats (10). The origin of this residual sympathetic rhythmicity is unclear. One possibility is that the surgical procedure used to produce SAD spared some baroreceptor fibers, which is indeed suggested by the persistence of reflex HR and RSNA responses to drug-induced changes in AP (31). Another possibility is that, in the MF band, endogenous RSNA rhythms of small amplitude and seemingly random frequency are generated by central nervous structures. Whatever the mechanism of their production may be, calculation of the coherence function indicated that these RSNA and MAP rhythms were linearly correlated in SAD rats. This finding is consistent with the proposal that MF fluctuations of AP are mainly, if not solely, mediated by the sympathetic nervous system (18, 25), with a possible modulation by the cyclic release of nitric oxide (28). Other factors known to alter AP, such as myogenic reactivity of resistance vessels or humoral systems activation, act with rather slow time constants and, thus, induce AP fluctuations at frequencies below the MF band (6, 11, 24).

The RSNA of SAD rats clearly exhibited slow fluctuations, such that LF power contributed ~10% of the total power. Such slow changes in RSNA can be evoked as part of the response to environmental stressors (29) or can accompany the performance of natural behaviors (27). The intriguing finding of the present study is that LF power of RSNA did not significantly differ in sham-operated and SAD rats. This can be taken to indicate that, in the conscious baroreceptor-intact rat, baroreflex-induced changes in RSNA contribute little to its slow variability. Alternatively, it is possible that RSNA fluctuations evoked by the central command would be attenuated by the baroreceptor reflex in such a way that it would then compensate for the increase in RSNA variability directly caused by the reflex. An exaggeration of vasoconstrictor responses to acute environmental stress has indeed been demonstrated in the conscious SAD rat (34). Finally, it is possible thatafferent renal nerves contributed to slow RSNA variability, which could not be evaluated in the present study because the renal nerve was not cut distal from the electrode.

Despite the unchanged LF power of RSNA in SAD rats, there was an eightfold increase in the LF power of MAP, which indicates that sympathetic influences were not responsible for the major part of the increased AP variability after baroreceptor denervation. Accordingly, rank correlation analysis has revealed that MAP and RSNA are positively correlated for only 25% of the time in conscious chronically SAD rats (1), whereas linear regression analysis did not disclose any consistent relation between the two signals in this model (15). In the present study, although coherence values were usually low in the LF band, they did reach significance in some instances. Therefore, using transfer gain values that were associated with a significant coherence, we attempted to characterize in SAD rats the feedforward effects of RSNA on MAP by means of linear modeling analysis. In all cases, the equation of a second-order low-pass filter could be satisfactorily fitted to experimental gain values. Model parameters were in good agreement with those obtained for the transfer function relating stimulation of the lumbar sympathetic chain and hindlimb vascular conductance in the urethane-anesthetized rat (4). In addition, with the use of the linear portion of the phase function, it was possible to reliably estimate a fixed time delay between RSNA and MAP changes. The 0.46-s value we report here is close to that reported previously in the rat with use of time- (29) or frequency-domain (4) methods. Therefore, despite a relatively weak coupling in the LF range, the modeling analysis was robust.
enough to extract linear causality between RSNA and MAP after baroreceptor denervation. However, ~70% of the variance of MAP below 0.15 Hz could not be explained by the variance of RSNA. This indicates that internal noise sources (hemodynamic perturbations) unrelated to the sympathetic nervous system powerfully affect AP in this frequency range. We and others have provided evidence that transient changes in stroke volume, autoregulatory responses of regional circulations, and active muscular vasodilations are important contributors to these slow hemodynamic perturbations (20, 24, 35).

Linear systems analysis predicts that the input-output relations (i.e., the transfer function) between two signals in a control loop would be identical in the open- and closed-loop configurations, provided there are no independent noise sources affecting either signal (21). This theoretical assumption was verified in the MF band, where the gain functions were almost indistinguishable in sham-operated and SAD rats. As discussed above, this can be interpreted as sympathetic influences being predominant in this frequency range. Additionally, this indicates that vascular responsiveness to sympathetic stimulation is essentially unaltered in the SAD rat. On the contrary, the gain functions clearly differed at frequencies below 0.15 Hz, which can be explained by the strong interference of noise sources unrelated to RSNA in this frequency range. In the SAD rat, any slow hemodynamic perturbation increases MAP power and the gain of the RSNA-MAP transfer function in the LF band. This is because the transfer gain at a given frequency is proportional to the square root of the ratio of MAP to RSNA powers, i.e., the ratio of the amplitude of MAP to RSNA fluctuations. In the baroreceptor-intact rat, the same hemodynamic perturbation induces an opposite change in RSNA through the baroreflex transfer function, which increases RSNA power. The RSNA variation then attenuates the impact of the hemodynamic perturbation on MAP power. Both effects result in a lowered transfer gain.

Perspectives

Although the feedforward influence of SNA on AP cannot be neglected, it explains only a small portion of slow AP variability after baroreceptor denervation in the conscious rat. The baroreceptor reflex limits AP variability in the LF range without increasing the SNA variability, which suggests that the reflex generates SNA fluctuations in response to AP perturbations but also limits the amplitude of SNA changes originating from the central command. We speculate that, in baroreceptor-intact rats, the weak coherence observed between SNA and AP in the LF range results from the continuous mixing of these two types of events.

REFERENCES