Low-frequency renal sympathetic nerve activity, arterial BP, stationary "1/f noise," and the baroreflex

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Burgess, Don E., Tabitha A. Zimmerman, Marshall T. Wise, Sheng-Gang Li, David C. Randall, and David R. Brown. Low-frequency renal sympathetic nerve activity, arterial BP, stationary "1/f noise," and the baroreflex. Am. J. Physiol. 277 (Regulatory Integrative Comp. Physiol. 46): R894–R903, 1999.—The object of this study is to quantify the very low frequency (i.e., <0.1 Hz) interactions between renal sympathetic nerve activity (SNA) and arterial blood pressure (ABP). Six rats were instrumented for chronic recordings of SNA and ABP. Data were collected 24 h after surgery at 10 kHz for 2–5 h and subsequently compressed to a 1-kHz signal. The power spectra and ordinary coherence were calculated from data epochs up to 1 h in length. The very low frequency spectra for both variables were fitted to a constant times f−β. The peak magnitude squared of the coherence near 0.4 Hz was 0.82 ± 0.08, but the apparent linear coherence fell off quickly at lower frequencies so that it was close to zero for frequencies <0.1 Hz. Moreover, at these low frequencies β, as computed by a coarse grain spectral analysis, was significantly (P < 0.01) different for SNA (0.66 ± 0.12) and ABP (1.12 ± 0.14). Assuming that SNA and ABP are stationary time series, the results of our classical spectral analysis would indicate that SNA and ABP are not linearly correlated at frequencies with a period more than ~10 s. Accordingly, we tested for stationarity by computing the spectral coherence and found that SNA and ABP are not stationary "1/f noise" within the frequency range from 0.02 to 2.0 Hz. Rather the SNA exerts control over the cardiovascular system through intermittent bursts of activity. Such intermittent behavior can be modeled by nonlinear dynamics.

coherence; spectral coherence; nonlinearity; blood pressure

There is increasing recognition that the application of the tools of signal processing to biological signals can teach us a great deal about the organization and operation of biological control systems. The regulation of arterial blood pressure (ABP) is of particular interest in this regard because blood pressure is subject to a number of different physiological control mechanisms. For example, there is a great deal of evidence that neural mechanisms participate importantly in stabilizing mean ABP in the face of fairly rapid perturbations, such as postural adjustments, whereas hormonal and autoregulatory mechanisms are thought to dominate in minimizing the effects of challenges that are slower in onset and more sustained in duration.

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In this regard, we recently analyzed the relationship between renal sympathetic nerve activity (SNA) and ABP in the “frequency domain” and found that these two signals were tightly coupled in the unanesthetized rat within a narrow range centered ~0.4 Hz (2). At ~0.4 Hz, there is a spectral peak in both the ABP spectrum and the SNA spectrum. We explain this 0.4-Hz rhythm as a feedback oscillation inherent within the baroreflex using a simple mathematical model. The model predicts this oscillation on the basis of the experimentally measured time delay in the sympathetic limb of the baroreflex. The linearity of the model suggests that there is a strong linear coupling between SNA and ABP. Interestingly, the experimentally measured coupling between SNA and ABP appeared to decrease dramatically at lower frequencies. Our original study, however, was based on 9.56-min long data recordings, which did not permit us to examine this phenomenon critically at frequencies <0.1 Hz. In this paper, we will use the term “very low frequency” range to represent the frequency range f < 0.1 Hz.

Another very interesting observation within the frequency domain is that the power in cardiovascular signals appears to increase as a function of 1/fβ for very low frequencies, where β is the slope of the power spectrum curve on a log-log plot (15, 16). The origin of this “1/f noise” is not understood. In particular, the role of the autonomic nervous system, if any, in generating this scaling behavior remains unresolved. On the one hand, sinoaortic denervation (SAD) of the baroreceptors leads to an enhanced blood pressure variability (6) and to a change in the β exponent in the very low frequency range (7). However, Wagner and Persson (20) recently showed that autonomic blockade restored the shape and absolute power of the 1/f noise in the very low frequency range in the SAD animal. Gaussian fractal noise (or 1/f noise) is stationary. One property of a stationary signal is that its Fourier components have random phases (24). A coherence between phases of different frequencies can be generated by a transient fluctuation (e.g., an artifact or a physiological shift produced by transient physical activity) or by nonlinear dynamics. Intuitively, nonlinear dynamics produce phase coupling because the nonlinear interactions will mix different frequencies together. Classical spectral analysis assumes stationarity so that one can average over data segments to reduce uncertainty in spectral estimates.

In the present experiment we sought to quantify the interactions between SNA and ABP in the awake, undisturbed animal within the very low frequency
range. To these ends we recorded SNA and ABP in unanesthetized rats for 2–5 h while they were in their home cages. To measure the linear coupling, we computed the magnitude squared of the coherence between SNA and ABP. Second, we calculated the value of \( \beta \) for both SNA and ABP. To validate our spectral analysis, we tested for stationarity by computing the “spectral coherence” (a generalization of ordinary coherence) between the two signals (8). We found that for \( f < 0.1 \) Hz, the magnitude squared of the coherence between the two signals approached zero. Moreover, the power law exponent, \( \beta \), for the power spectrum of SNA differs from that for ABP. Assuming that ABP and SNA in the resting rat are “stationary” signals, these results would indicate that these two signals are not linearly coupled in the very low frequency range with periods >10 s. However, the spectral coherence analysis revealed significant phase coupling (\( P < 0.01 \)) between different frequencies within SNA and ABP, which indicates that the two signals are not stationary.

**METHODS**

Experiments were performed on six Sprague-Dawley rats (Harlan Industries, Indianapolis, IN) weighing between 330 and 450 g. The standards for care and use of animals of the American Physiological Society were observed at all stages of this experiment.

**Surgery**

The rats were anesthetized with pentobarbital sodium (65 mg/kg ip) in preparation for implantation of the arterial catheter and renal nerve electrodes using sterile procedures. A Teflon catheter (#90 LW, ID 0.012; Small Parts, Miami Lakes, FL) was inserted into the aorta by way of the femoral artery. A sympathetic nerve coursing over the aorta toward the kidney was identified through a flank incision. A small section of this nerve, usually from the cephalad angle formed by the renal artery and aorta, was dissected free of connective tissue and placed on fine, closely spaced (0.4–0.8 mm), bipolar gold electrodes (A-M Systems, Seattle, WA). The exposed nerve and electrode were encased in silicon gel (Wacker Chemie, Munich, Germany). The distal ends of the catheter and wires soldered to the end of the electrodes were tunneled under the skin, exited at the nape of the neck, and led through a flexible tether.

**Data Acquisition**

Data were collected 24 h after surgery in conscious Sprague-Dawley rats while they rested quietly in a cage. The arterial pressure signal from a Carus transducer attached to the femoral artery catheter was amplified and displayed by a Grass model 7 polygraph. The electrical signal from the renal sympathetic nerve was amplified (50 K) and bandpass filtered between 30 Hz and 3 kHz by a Grass P511 differential amplifier.

To obtain accurate measurements from the sympathetic nerve recordings, data were digitized at 10,000 samples/s using a Cache 486 microprocessor and Data Translation DT2821-F analog-to-digital converter. Data were collected for 2–5 h. The initial highly detailed nerve traffic signal was full wave rectified and averaged over every 10 points to produce a 1,000 sample/s signal. This process retains cumulative information from the initial 10,000 sample/s signal. The pressure signals were compressed “online” to a 1,000 sample/s signal by saving every tenth point. Because we were interested in the low-frequency range, the data were further compressed to 50 samples/s by averaging every 20 data points. Using software developed in our laboratory in Visual C++, we carefully removed artifacts from the raw time series.

**Data Analysis**

The confidence in spectral estimates can be enhanced by dividing data into multiple epochs and ensemble averaging. Although this decreases variance and increases confidence, it reduces resolution because the length of the data epoch ultimately determines the limits of the low-frequency resolution. For our classical spectral analysis, we used data segments ranging in length from 11 (32,768 points) to 87 min (262,144 points), giving a low-frequency resolution down to \( 1.9 \times 10^{-4} \) Hz.

Auto- and cross-spectral estimates were computed using Welch’s method (21). For each variable, a discrete Fourier transform was computed using the fast Fourier algorithm. Before computing the discrete Fourier transform, linear trends were removed from the data, and data were tapered using the Welch window. Squared magnitudes and the products of the computed discrete Fourier transforms were averaged to obtain spectral estimates. Estimates for the magnitude squared of the coherence function between ABP and SNA were computed as the ratio of the magnitude squared of the cross-spectra divided by the product of the autospectra (13) (refer to equation 1). The normalized random error in the magnitude squared of the coherence \( \left| C \right|^2 \) (1) depends on both the number of data segments \( K \) and the magnitude of the coherence according to

\[
\frac{\Delta C^2}{|C|^2} = \sqrt{2} \left( 1 - \frac{|C|^2}{|C|/K} \right)
\]

The low-frequency portion of each spectrum was modeled as a power law, namely

\[
P \sim 1/f^\beta
\]

where \( P \) is the power spectral density, and \( f \) is the frequency. To aid in characterizing this “fractal” or spectrally self-similar region, we used Yamamoto’s coarse-graining technique (5, 23) to minimize the harmonic peaks in the spectrum. The \( \beta \) exponent was then determined from the slope of the least-squares fit to the log-log plot of the coarse-grained power spectrum. The uncertainty in the fitted parameter \( \beta \) is given by the square root of the corresponding diagonal entry in the covariance matrix for the least squares fit. The fit covered frequencies ranging from 0.001 to 0.5 Hz.

To determine if SNA and ABP are stationary, we calculated the spectral coherence, which is a generalization of the ordinary coherence (8). The coherence \( C_{xy} \) between two time series \( x(t) \) and \( y(t) \) is defined as

\[
C_{xy}(f) = \frac{\langle X^*(f) Y(f) \rangle}{\left[ \langle X^*(f) X(f) \rangle \langle Y^*(f) Y(f) \rangle \right]^{1/2}}
\]

where \( X(f) \) and \( Y(f) \) are the Fourier transforms of \( x(t) \) and \( y(t) \), respectively. The symbol \( X^* \) represents the complex conjugate, and the angular brackets \( \langle \rangle \) denote the expected value of \( X \). This definition of coherence can be generalized to

\[
C_{Xx}(f, g) = \frac{\langle X^*(f) X(g) \rangle}{\left[ \langle X^*(f) X(f) \rangle \langle X^*(g) X(g) \rangle \right]^{1/2}}
\]
for the spectral coherence within a single time series. \( C_{xy}(f, g) \) measures the correlation coefficient between two different frequencies \( f \) and \( g \). The numerator \( \langle X^*(f) Y(g) \rangle \) is the generalized spectrum of \( x(t) \) (24). Note that \( C_{xy}(f, g)^2 = 1 \) and that the diagonal is always 1. So, information is only contained in the off-diagonal terms. The concept of coherence can also be generalized to

\[
C_{xy}(f, g) = \frac{\langle X^*(f) Y(g) \rangle}{\left| \langle X^*(f) X(f) \rangle \langle Y^*(g) Y(g) \rangle \right|^{1/2}}
\]

for the spectral coherence between two different time series. Here the numerator is the generalized cross-spectrum. The diagonal term is simply the ordinary coherence defined in equation 1 above.

To compute the spectral coherence, we filtered the compressed time series with an eighth-order Butterworth low-pass filter (cutoff frequency was set equal to 2.0 Hz). We further compressed the two time series to obtain a 5-Hz sampling rate. Each time series was then divided into ~700 segments containing 256 points (or a period of 51.2 s). For each data segment, the Fourier transform was computed as in the classical spectral analysis above. To obtain estimates of the expected values in equation 2 and in equation 3, we formed a matrix by taking the outer product of the appropriate Fourier transform pairs and averaging this matrix over the 700 data segments.

When \( x(t) \) is a stationary zero mean, Gaussian noise time series, Goodman (9) gave the probability distribution of equation 2 as

\[
P[C_{xy}(f, g; K)^2 > c_0] = (1 - c_0)^{K-1}
\]

where \( c_0 \in [0, 1] \), and \( K \) is the number of segments averaged over. In other words, if \( x(t) \) is Gaussian noise, then random fluctuations will lead to estimates that exceed \( c_0 \) in \( (1 - c_0)^{K-1} \times 100\% \) of the computational values (elements of the matrix). [Note: in our data, the data segments were not statistically independent because we used overlapping segments. So, we adjusted the number of segments according to Welch's correction factor, namely: \( K \rightarrow 9K/11 \) (21).]

To determine whether a time series is stationary, we made a contour plot of the magnitude squared of the spectral coherence. To calculate the statistical significance of an off-diagonal contour in a plot, we multiplied the probability \( P \) of an exceedance by the number of independent values based on symmetry. For the spectral coherence between two different signals, the number of independent values is \( 1/2 \ N^2 \), whereas for the spectral coherence within a time series, the number of independent values is \( 3/8 \ N^2 \).

Simulations

To test the efficacy of spectral coherence contour plots to detect nonstationarity, we ran two simulations.

Narrow-band noise. This was a linear model driven by two independent stationary random sources, namely

\[
x_1(t) = -x_1(t) + 2\pi x_2(t) + z_1(t),
\]

\[
x_2(t) = -2\pi x_2(t) - x_1(t) + z_2(t)
\]

where \( z_1(t) \) and \( z_2(t) \) are two independent random Gaussian time series with zero mean and unit variance. The linear coupling between \( x_1 \) and \( x_2 \) leads to a resonance oscillation at 1.0 Hz. This model was integrated using a fourth-order Runge-Kutta method with a time step of 0.001 s. After discarding the first 1,000 time steps to get rid of initial transients, a file was made of 1,048,576 points spaced at a sampling rate of 10 Hz.

Strange attractor. This model was the Rossler attractor (19) and has both linear and nonlinear coupling between variables. The system is defined by

\[
x = -z - y,
\]

\[
y = x + ay,
\]

\[
z = b + z(x - c)
\]

The linear coupling between \( x \) and \( y \) produces an oscillation at \( 2\pi Hz \), whereas \( z \) acts as a variable damping term to the \( x \) - \( y \) system. The parameter \( a \) gives rise to positive damping, which puts energy into the \( x \) - \( y \) system. As a result of the nonlinear interactions, the \( z \) variable exhibits intermittent, positive amplitude bursts.

We used parameter values \( a = 0.15, b = 0.20, \) and \( c = 10.0 \). The trajectory was integrated using a fourth-order Runge-Kutta method with a fixed time step of \( \pi/100 \). After discarding the first 1,000 time steps to allow the trajectory to fall onto the attractor, a file was made of 1,048,576 points spaced at a sampling rate of \( \pi/10 \). For both simulations, the data file was divided into 8,191 overlapping segments of 256 points each. Then estimates were computed for the spectral coherences as described above.

RESULTS

Filtered time series for SNA and for ABP from rat sds are shown in Fig. 1. These data were passed through an eighth-order Butterworth low-pass filter with a cutoff frequency of 0.2 Hz and compressed to a sampling rate of 0.5 Hz. Both time series display large amplitude, intermittent fluctuations separated by quiet periods consisting of smaller fluctuations. In particular, notice the three prominent bursts in SNA and the corresponding fluctuations in ABP at roughly \( t = 8,500, 9,000, \) and \( 9,500 \) s. The duration of each of these bursts is close to 1 min.

Spectral Analysis

Log-log plots of typical power spectra for SNA and ABP are shown in Fig. 2. A and B, respectively, for rat sdm. For this analysis, we divided the original data set into 54 segments, each 11 min long, with 50% overlap. The peaks in both spectra at 7.0 Hz and higher are associated with pulse pressure. The spectral peak near 2.0 Hz is related to the respiratory rate. We (3) and others (11, 12) have shown that the prominent peak in both the SNA and the ABP spectra at \( -0.4 \) Hz is mediated by the sympathetic limb of the baroreflex. Notice that, as mentioned in the introduction, spectral power increases with decreasing frequency for both SNA and ABP.

The magnitude squared of the coherence between SNA and ABP corresponding to the power spectra from Fig. 2, A and B, is shown in Fig. 2C. The confidence interval around a computed coherence value depends on the coherence value. For example, the 95% confidence interval for a squared coherence value of 0.8 is 0.74–0.86, whereas the 95% confidence interval for a squared coherence value of 0.2 is 0.06–0.34. For each of the three peaks in spectral power associated with pulse
pressure (~8 Hz), respiration (~2 Hz), and the baroreflex (~0.4 Hz), there is a corresponding peak in the coherence. Notice the apparent lack of coherence at very low frequencies <0.1 Hz, where the majority of spectral power within SNA and ABP exists.

The least-squares fit to the coarse-grained power spectrum of SNA from rat sdm is shown in Fig. 3A. Recall that the coarse-graining algorithm minimizes the spectral power attributable to periodic sources, such as the 0.4-Hz rhythm, so that the 0.4-Hz rhythm seen in Fig. 2A is virtually gone. The surviving power is now readily characterized by a power law exponent. However, coarse-graining did not eliminate the shelf in the spectrum beginning at ~0.1 Hz. To obtain an objective estimate for $\beta$, we performed a nonlinear least squares fit to a combination of two line segments with two different slopes. The fit covered frequencies ranging from 0.001 to ~0.5 Hz and computed the location of the point of intersection so that we did not have to guess where the 1/f trend ended. The slope of the first line segment (over the very low frequency range) yielded $\beta = 0.69 \pm 0.03$. For even lower frequencies, we expect there to be different slopes for different frequency ranges, but we did not try to fit to frequencies <0.001 Hz because these frequencies were influenced by detrending.

Similarly, the least squares fit to the coarse grained power spectrum of ABP from rat sdm is shown in Fig. 3B. Again, although coarse graining reduced the harmonic components in the spectrum, it did not remove the "shelf" in the spectrum at ~0.1 Hz. So, we again performed a nonlinear least squares fit to a combination of two line segments with two different slopes. The slope of the first line segment (over the very low frequency range) yielded $\beta = 1.15 \pm 0.06$. For this coarse-grained analysis, we divided the data set into 10 overlapping segments each of width 44 min.

We performed a similar analysis to determine the set of $\beta$s for each remaining rat. As summarized in Table 1, we find that the $\beta$ exponents for the two variables are significantly different. The (mean ± SD) $\beta$ exponent for SNA is 0.66 ± 0.12, whereas the $\beta$ exponent for ABP is 1.12 ± 0.14 ($P < 0.01$, Student’s $t$-test for paired samples).

To summarize our classical spectral analysis, in Fig. 4 we show an ensemble average of the coherence curves between SNA and ABP for all six rats. In agreement with earlier work by Brown et al. (2), we find a robust coherence peak between 0.1 and 1.0 Hz, but an apparent lack of coherence <0.1 Hz down to ~0.001 Hz. Near 0.4 Hz the peak coherence was 0.82 ± 0.08, whereas <0.1 Hz the average coherence from all six animals was <0.2.

Modeling

Before proceeding to the generalized spectral analysis of these same data sets, we first consider two simulations. The power spectrum for variable $x_1$ in the narrow-band noise simulation is shown in Fig. 5A. The spectrum for $x_2$ is identical. The peak in the power spectrum at 1.0 Hz corresponds to the resonance oscilla-
tion generated by the linear coupling. Figure 5B shows the magnitude squared of the resulting coherence. In the frequency range where the resonance oscillation dominates the background noise, there is a corresponding coherence peak. The 0.1-Hz rhythm in humans (which corresponds to the 0.4-Hz rhythm in rats) can be described as narrow-band noise (22). A contour plot of the spectral coherence between $x_1$ and $x_2$ is shown in Fig. 5C. The diagonal of this contour plot corresponds to the ordinary (i.e., linear) coherence displayed in Fig. 5B. Because there are no nonlinear interactions in this model, any off-diagonal structure would be due to random statistical variations. For a threshold of $c_0 = 0.002$, $P < 0.01$ that the spectral coherence at any computational node would exceed this value by chance. As expected, there are no off-diagonal contours in this plot of a stationary time series.

Next we consider the strange attractor simulation, which involves both linear and nonlinear interactions. Contour plots of the spectral coherences for the $y(t)$ and $z(t)$ coordinates of the Rossler attractor are shown in Fig. 6. Notice that each contour plot is unique and complementary to the other two plots. The Rossler attractor does have nonlinear interactions. These nonlinear dynamics produce phase coupling between different frequencies, which results in a nonstationary signal. So, we expect to see off-diagonal structure produced by this nonlinear coupling. In Fig. 6, the dramatic pattern in the off-diagonal contours confirms that this analysis is sensitive to the presence of nonlinear dynamics.

Generalized Spectral Analysis

Contour plots for the spectral coherences of rat sdm are displayed in Fig. 7. Figure 7A represents the spectral coherence between SNA and ABP (equation 3), Fig. 7B represents the spectral coherence within SNA (equation 2), and Fig. 7C represents the spectral coherence within ABP (equation 2). The contour levels are

![Fig. 2. Power spectra for SNA (A), ABP (B), and squared coherence (C) for rat sdm. Prominent peak in both SNA and ABP spectra at ~0.4 Hz is mediated by sympathetic limb of baroreflex (3). Notice that coherence between SNA and ABP drops to low values for frequencies <0.1 Hz.](image-url)
color coded, with light blue contours representing the highest coherence (i.e., coherence $\geq 0.8$). In Fig. 7A, the light blue contour near 0.5 Hz on the diagonal represents the “0.4 Hz” coherence peak for this rat seen in Fig. 2B. Notice that the diagonal structure ends below 0.1 Hz in agreement with our ordinary coherence analysis. The small red diagonal contours near the origin represent a small, but statistically significant ($P < 0.05$) linear coherence between SNA and ABP in Fig. 3. Coarse-grained power spectra for SNA (A) and for ABP (B) from rat sdm. Least squares fit to low frequencies is shown as a solid line in each plot. Coarse-graining removed 0.4-Hz rhythm, but not “bend” in each power spectrum near 0.1 Hz. Because of “bend” in both spectra $\sim 0.1$ Hz, we performed a nonlinear least squares fit to a “knee” function consisting of 2 line segments with 2 different slopes. We obtained parameter $\beta$ from slope of first line segment. For SNA spectrum, $\beta = 0.69 \pm 0.03$. For ABP spectrum, $\beta = 1.14 \pm 0.06$. Although coarse graining reduced harmonic power at pulse pressure, it by no means eliminated this strong harmonic component in blood pressure.

Table 1. $\beta$ exponents for SNA and ABP

<table>
<thead>
<tr>
<th>Rat</th>
<th>$\beta$ SNA</th>
<th>$\beta$ ABP</th>
</tr>
</thead>
<tbody>
<tr>
<td>sdd</td>
<td>0.58 ± 0.02</td>
<td>1.10 ± 0.02</td>
</tr>
<tr>
<td>sdk</td>
<td>0.70 ± 0.03</td>
<td>0.96 ± 0.02</td>
</tr>
<tr>
<td>sdl</td>
<td>0.55 ± 0.01</td>
<td>1.21 ± 0.03</td>
</tr>
<tr>
<td>sdm</td>
<td>0.69 ± 0.02</td>
<td>1.15 ± 0.06</td>
</tr>
<tr>
<td>sds</td>
<td>0.58 ± 0.04</td>
<td>1.34 ± 0.05</td>
</tr>
<tr>
<td>sdt</td>
<td>0.88 ± 0.03</td>
<td>0.97 ± 0.06</td>
</tr>
</tbody>
</table>

Values are means ± SD. SNA, sympathetic nerve activity; ABP, arterial blood pressure.
the very low frequency range. The green off-diagonal contours represent coherences between very low frequencies in SNA and frequencies \( \sim 1.0 \) Hz in ABP, with a statistical significance of \( P < 0.01 \). In Fig. 7B, the most significant off-diagonal contours (in light blue) are confined to the low frequencies within SNA. Notice how the pattern of off-diagonal contours in Fig. 7C complements the pattern of off-diagonal contours in Fig. 7B.

A summary of our findings for nonlinear phase coupling is shown in Table 2. In three of six rats, the contour plots showed significant (\( P < 0.05 \)) off-diagonal contours reflecting nonlinear phase coupling of different frequencies in ABP and SNA as well as within ABP and within SNA. Of the three remaining rats, one (rat sdk) displayed a well-defined pattern of nonlinear phase coupling within ABP and another (rat sdt) displayed a well-defined pattern within SNA. In only one (rat sdd) did we fail to detect the presence of nonlinear dynamics. The detection of nonlinear dynamics within ABP is consistent with the finding of nonlinear interactions within heart rate fluctuations reported by Ivanov et al. (10).

DISCUSSION

The action of the arterial baroreflex naturally implies a very high (linear) coherence between SNA and ABP. This must be true, of course, because increases in blood pressure reflexly decrease SNA when this reflex is functioning within its normal closed loop. Although changes in parasympathetic activity might be expected to confound this relationship, this limb of the nervous system is apparently modestly involved in cardiac regulation in the Sprague-Dawley rat (18). We have, in fact, demonstrated that the natural periodicity in both SNA and ABP centered \( \sim 0.4 \) Hz can be explained in this animal by using a simple linear mathematical model involving only the sympathetic limb of the baroreflex (3). Therefore, the present findings of a very high coherence between SNA and ABP centered \( \sim 0.4 \) Hz dramatically affirm this fundamental physiological principle.

Classical spectral analysis can be misleading, however, when the time series being analyzed is nonstationary. The 0.4-Hz rhythm is relatively stationary, and the ordinary coherence correctly identifies the linear coupling between SNA and ABP mediated by the baroreflex. However, the coupling between SNA and ABP < 0.1 Hz is obscured in the classical spectral analysis by the intermittent nature of the time series for both variables. Visual inspection of the raw data shows that SNA comes in intermittent bursts (Fig. 1; see also Ref. 2). During many of these bursts there is a corresponding fluctuation in ABP. Because the bursts in SNA are intermittent, they are present in some data segments, but are absent in many others; as a result, the direct coupling between SNA and ABP is washed out by averaging. Such intermittent behavior can be produced by simple nonlinear dynamics.

Our finding that SNA and ABP are not stationary implies that their time series cannot be characterized by the \( \beta \) exponents of their corresponding power spectra. That is, at the start of the very low frequency range, SNA and ABP cannot legitimately be modeled as fractal Gaussian noise.

Limitations

Our generalized spectral analysis of the phase coupling between frequencies covered the frequency range.
range from 2.0 to 0.02 Hz. So, we can only say that SNA and ABP are nonstationary within this frequency range. Perhaps at frequencies < 0.02 Hz, the time series are stationary noise. In addition, it must be noted that our measurement of SNA is actually renal SNA. It is possible that SNA to other vascular beds (e.g., skin and muscle) contribute to very low frequency ABP fluctuations that are uncorrelated with renal SNA.

Perspectives

Taking into account the nonstationarity of SNA and ABP helped us understand the results of our classical spectral analysis. That is, the direct coupling between SNA and ABP at frequencies < 0.1 Hz is hidden by the intermittent nature of the time series. Perhaps the nonstationarity of ABP can provide insight into the results of SAD experiments. It is well known that SAD of baroreceptors leads to an enhanced blood pressure variability and to a change in the β exponent at very low frequencies (6, 7). Recent experiments by Just et al. (14) show that the increased blood pressure variability is generated by the central nervous system and can be eliminated through ganglionic blockade. However, Wagner and Persson (20) showed that autonomic blockade restored the shape and absolute power of the 1/f noise in the very low frequency range. They concluded that this lower frequency 1/f noise does not appear to be directly modulated by the baroreceptor feedback loop. Seemingly, we have a paradox: the central nervous system can influence very low frequency fluctuations in ABP, but does not seem to directly mediate these fluctuations in the intact, resting animal. We would argue that the shape of the power spectrum does not necessarily characterize ABP fluctuations because the phases of the Fourier modes are not random in an intact animal. Accordingly, denervation followed by ganglionic blockade could affect the nature of ABP.
fluctuations without changing the shape of the ABP power spectrum.

The underlying dynamics of the baroreflex and sympathetic nervous system are imprinted on SNA and ABP regardless of the coupling (linear and/or nonlinear) that exists between them. Specifically, the intermittent nature of SNA reflects some sort of underlying nonlinear dynamics that produces the observed phase coupling between different frequencies within SNA. Such intermittent behavior occurs in simple nonlinear models. Notice the qualitative similarity between Fig. 6 for the Rossler attractor and Fig. 7 for rat sdm. The \( z \) variable is analogous to SNA, whereas the \( y \) variable is analogous to ABP. Both the \( z \) variable and SNA occur in “bursts.” In the Rossler attractor, the \( z \) variable exerts nonlinear control over the \( x - y \) system through energy dissipation. The \( y \) variable is a controlled variable in the sense that it fluctuates within a limited range. Just as in the Rossler attractor, the sympathetic nervous system exerts control over the cardiovascular system through concentrated bursts of activity, which result in energy dissipation in the arterioles.

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