Baroreflex stabilization of the double (pressure-rate) product at 0.05 Hz in conscious rabbits

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Van Vliet, Bruce N., Francesca Belforti, and Jean-Pierre Montani. Baroreflex stabilization of the double (pressure-rate) product at 0.05 Hz in conscious rabbits. Am J Physiol Regulatory Integrative Comp Physiol 282: R1746–R1753, 2002.—The product of heart rate (HR) and systolic blood pressure (SBP), the double product (DP), is an indirect index of cardiac oxygen consumption. We used spectral analysis to test the hypothesis that baroreflex adjustments of HR stabilize the DP during spontaneous variations in SBP. SBP and HR were recorded by telemetry in five male conscious rabbits. HR and SBP power spectra each exhibited a low frequency peak at ~0.05 Hz that was associated with high (>0.5) spectral coherence and a positive phase relationship between SBP and HR (SBP leading). A prominent peak was absent in the spectra of their product, suggesting that SBP and HR interacted to reduce DP variability in this frequency region. In contrast, a prominent 0.05-Hz peak was present in the power spectrum of calculated surrogates of the DP in which reflex interactions between HR and SBP had been removed. Our results suggest that baroreflex adjustments of HR stabilize the DP during spontaneous low-frequency variations in SBP in conscious rabbits.

heart rate; systolic blood pressure

AUTONOMIC ADJUSTMENTS of heart rate (HR) are one of several effector responses of the arterial baroreflex. The physiological significance of such changes in HR has traditionally been interpreted in terms of their contribution to blood pressure (BP) regulation. However, such adjustments of HR may also have important consequences for cardiac oxygen consumption. Indeed, studies in anaesthetized open-chest animals have demonstrated that, during the pressor response to α-adrenergic agonists, baroreflex reductions in HR are capable of blunting the BP-induced increase in myocardial oxygen consumption that otherwise occurs when HR is held constant (29, 33).

We have previously suggested that the product of HR and mean or systolic blood pressure (SBP), the so-called double product or pressure-rate product, may provide a convenient framework for considering the role of baroreflex adjustments in HR in stabilizing cardiac oxygen consumption in conscious animals (30). The double product is strongly correlated with cardiac oxygen consumption (2, 15, 16, 27, 34), and it has therefore been widely used as an indirect index of cardiac metabolism (2). During an elevation of BP, baroreflex reductions in HR will tend to lessen the impact of the change in BP on the double product. The extent to which this will occur depends on the magnitude of the HR adjustment relative to the size of the initial BP disturbance. In a recent study, we showed that complete stabilization of the double product will occur when the change in HR is expressed as a per cent of the initial BP disturbance and arterial pressure and that, even though baroreflex sensitivity varies as much as 70-fold among different species, in many of the species that have been investigated the reported value of baroreflex sensitivity approximates the value calculated to provide complete stabilization of the double product (30). In addition, we also showed that, during pharmacological manipulations of BP in rabbits, baroreflex adjustments of HR were sufficient to attenuate or prevent a change in the double product (30). The results of these studies suggest that baroreflex adjustments of HR are of an appropriate magnitude to stabilize the double product in the face of experimental manipulations of BP.

The purpose of the present study was to test the hypothesis that the baroreflex control of HR contributes to the stability of the double product during spontaneous variations in SBP and HR in unrestrained conscious rabbits. This hypothesis was investigated using power spectral analysis of telemetered BP, focusing on a frequency range over which the baroreflex control of HR provided a clear and important influence on the HR and SBP power spectra. To facilitate our interpretation of the double product spectrum, we compared its spectrum with appropriately scaled spectra of HR and SBP and with that of surrogates of the double product at 0.05 Hz in conscious rabbits.
The power spectra of the double product to have features that in the double product and leading to a prominent peak in the act in a positive manner, increasing corresponding variations and SBP variations were not proportional and opposite in peak corresponding to that of HR and SBP. Conversely, if HR but opposite in direction, their variations would tend to variations in HR and SBP were proportional to each other spectral peaks in HR and SBP, if the underlying periodic peaks in HR and SBP, if the underlying periodic fl

**MATERIALS AND METHODS**

**Evaluating Baroreflex Stabilization of the Double Product by Power Spectrum Analysis**

A contribution of the baroreflex to HR and SBP spectra is often evident in terms of prominent peaks in their spectral power that are statistically linked (e.g., SBP-HR coherence values >0.5) and for which there is a positive phase relationship (i.e., SBP fluctuations precede those of HR). For such spectral peaks in HR and SBP, if the underlying periodic variations in HR and SBP were proportional to each other but opposite in direction, their variations would tend to cancel, and little or no variation in their product would be expected to occur. In such a case, the power spectrum of the double product would not be expected to exhibit a spectral peak corresponding to that of HR and SBP. Conversely, if HR and SBP variations were not proportional and opposite in direction, concurrent variations in HR and SBP would interact in a positive manner, increasing corresponding variations in the double product and leading to a prominent peak in the double product power spectrum. In practice, one may expect the power spectra of the double product to have features that are intermediate between these two extremes.

**RevHR×SBP: A Surrogate of the Double Product in Which Reflex HR and SBP Interactions Are Absent**

To evaluate where the power spectrum of the double product fits within the two extremes described above, we calculated a surrogate of the double product in which reflex interactions between HR and SBP that might stabilize the double product were prevented. This surrogate was calculated as the product of SBP and RevHR, where RevHR represents the HR signal after it has been reversed in sequence from end to end. Reversing the HR signal before calculating this surrogate of the double product disrupts the temporal coupling between variations in SBP and HR that may lead to stabilization of the double product. However, reversing the HR signal from end to end does not affect the total variance of the signal or its spectral distribution. Thus the power spectrum of the RevHR×SBP product provides a description of how the power spectrum of the double product would appear in the absence of any baroreflex adjustment of HR that might stabilize the double product. In the present study, we have determined the power spectra for the double product in conscious rabbits and compared it with that of RevHR×SBP to help evaluate the extent to which variations in HR associated with the operation of the baroreflex act to stabilize the double product.

**Contributions of HR and SBP Spectra to that of the Double Product**

In the present study, we have also calculated several additional surrogates of the double product to help clarify the contribution of variations in HR and SBP to that of the double product. The first surrogate signal, HR×MSBP, is produced by multiplying the HR signal by the corresponding mean value of the SBP signal. Because the mean value of SBP is used in place of beat-to-beat variations in SBP, variations in HR×MSBP arise solely from those of the HR signal. However, because the HR signal is multiplied by the mean SBP, HR×MSBP expresses variations in HR on the same scale as the double product (i.e., the HR×MSBP and the double product have the same mean value and units, see RESULTS). Thus the HR×MSBP spectra describes the frequency distribution of HR variability on a scale equivalent to that of the double product spectrum. The HR×MSBP spectrum can also be considered to simply represent the frequency distribution of double product variability after complete removal of any contribution of variations in SBP. Direct comparison of the HR×MSBP and double product power spectra can be used to clarify the contribution of HR variations with that of the double product.

The second signal, MHR×SBP, is a surrogate of the double product produced by multiplying the SBP signal by the mean value of the corresponding HR signal. The MHR×SBP signal presents the variability of the SBP signal on a scale of the double product signal, for which it has the same mean value and units. The MHR×SBP spectrum can be considered to represent the variability of the double product signal after complete removal of any contribution of HR. Direct comparison of the MHR×SBP and double product spectra can be used to clarify the contribution of variations of SBP to that of the double product.

The third signal is simply the sum of the HR×MSBP and MHR×SBP signals. This sum represents the variability of the double product contributed independently by the HR and SBP signals without any complex interaction (e.g., summation or cancellation) between them. Conceptually, this sum is somewhat similar to that of the RevHR×SBP signal, and the two produce similar results (see RESULTS).

**Methods**

Experiments were conducted using male lop-eared rabbits of the Belier Français strain obtained from local Swiss breeders. Rabbits were housed individually and were maintained on a 12:12-h light-dark cycle with free access to water and 180 g/day commercial rabbit chow. All procedures were conducted with the approval of the local animal care authorities and fully conform with the *Guiding Principles for Research Involving Animals and Human Beings*.

**Experimental protocol.** To permit hemodynamic recordings in conscious, unrestrained rabbits, a BP telemeter (model TA11PA-C40; Data Sciences International) was installed with its catheter positioned in the femoral artery using aseptic techniques and halothane anesthesia as previously described (1). BP data were obtained after at least 2 wk of recovery from telemeter implantation.

**Signal processing.** Each rabbit cage was outfitted with three telemetry receivers connected by a multiplexer to a calibrated pressure analog adaptor (model R11CPA; Data Sciences International). Because BP telemeters report absolute pressure (i.e., the sum of catheter and atmospheric pressures), an ambient pressure monitor (model APR-1; Data Sciences International) was also connected to the adaptor to correct for changes in atmospheric pressure. The analog pressure signal was connected to an analog-to-digital converter and was processed by a personal microcomputer using custom software to compute the diastolic, mean, and SBP, HR, and cardiac interval on a beat-to-beat basis.

To investigate the influence of the baroreflex control of HR on the double product, we first selected hemodynamic recordings in which a contribution of the baroreflex control of HR was prominent. Spectral analysis was performed on three separate 15-min segments of telemetry data in each animal. These data segments were selected from periods in which the rabbits were awake and active but otherwise undisturbed in
Table 1. Measured and calculated 15-min signals

<table>
<thead>
<tr>
<th>Variable</th>
<th>Mean</th>
<th>SD</th>
</tr>
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<tbody>
<tr>
<td>Diastolic pressure, mmHg</td>
<td>74 ± 2</td>
<td>6.5 ± 1.0</td>
</tr>
<tr>
<td>Mean pressure, mmHg</td>
<td>85 ± 2</td>
<td>6.9 ± 1.1</td>
</tr>
<tr>
<td>SBP, mmHg</td>
<td>106 ± 4</td>
<td>8.2 ± 1.2</td>
</tr>
<tr>
<td>HR, min⁻¹</td>
<td>246 ± 13</td>
<td>20.6 ± 4.0</td>
</tr>
<tr>
<td>RevHR, min⁻¹</td>
<td>246 ± 13</td>
<td>20.6 ± 4.0</td>
</tr>
<tr>
<td>Pulse interval, ms</td>
<td>248 ± 13</td>
<td>20.6 ± 3.9</td>
</tr>
<tr>
<td>HR×SBP, mmHg/min</td>
<td>26,098 ± 1,584</td>
<td>3,135 ± 756</td>
</tr>
<tr>
<td>RevHR×SBP, mmHg/min</td>
<td>26,052 ± 1,565</td>
<td>2,937 ± 355</td>
</tr>
<tr>
<td>MHR×SBP, mmHg/min</td>
<td>26,069 ± 1,567</td>
<td>2,045 ± 382</td>
</tr>
<tr>
<td>HR×MSBP, mmHg/min</td>
<td>26,069 ± 1,567</td>
<td>2,191 ± 448</td>
</tr>
<tr>
<td>MHR×SBP + HR×SBP, mmHg/min</td>
<td>52,138 ± 3,133</td>
<td>4,296 ± 727</td>
</tr>
</tbody>
</table>

Values are means ± SE for 5 rabbits. SBP, systolic blood pressure; HR, heart rate; RevHR, reverse HR; MHR, mean HR; MSBP, mean SBP.

RESULTS

Hemodynamic Values

During the day on which the hemodynamic recordings were performed, the 24-h mean values of diastolic and mean pressures and SBP were 64 ± 4, 73 ± 4, and 93 ± 5 mmHg, respectively. The corresponding 24-h mean values of HR, pulse interval, double product (HR×SBP), and the ratios of pulse interval to SBP were 212 ± 13 min⁻¹, 300 ± 21 ms, 1.98 × 10⁴ ± 1.33 × 10³ min⁻¹·mmHg, and 3.3 ± 0.3 ms/mmHg. Hemodynamic values associated with the 15-min period used to produce power spectra are listed in Table 1. The average ratio of the pulse interval to SBP during the sample period was 2.40 ± 0.15 ms/mmHg.

Power Spectra of SBP and HR

Figure 1 shows an example of a 15-min period of data, the associated HR, SBP, double product power spectra, and the HR-SBP coherence spectra. The mean HR and SBP spectra for five rabbits is shown in Fig. 2. Power spectra of SBP and HR exhibited an approximate "1/f" distribution of spectral power, that is, the shape of the spectra was approximately linear when graphed using logarithmic axes (31 and see Fig. 2, insets). HR and SBP spectra contained a peak at ~0.05 Hz that corresponded to a peak in the SBP-HR coherence spectra (Figs. 1 and 3) and a positive phase in the SBP-HR transfer function (Fig. 3). These characteristics suggest that the baroreflex represents a dominant influence on HR and SBP spectra in the vicinity of 0.05 Hz. At 0.05 Hz, the mean SBP-HR transfer function gain amounted to 2.1 ± 0.4 min⁻¹/mmHg. The corresponding gain value for the transfer function between SBP and pulse interval amounted to 2.0 ± 0.6 ms/mmHg (transfer function not shown).

A prominent high-frequency peak was not regularly observed in the SBP-HR coherence spectra (Fig. 3) or in
the SBP or HR power spectra when plotted on linear axes. However, evidence of a small high-frequency peak could be discerned at $\sim1$ Hz in terms of a small departure from the expected $1/f$ distribution of power when HR and SBP spectra were plotted on log-log axes (see Fig. 2, insets).

**RevHR Spectra**

As shown in Fig. 2, the RevHR spectrum was virtually identical to that for the original HR signal. The RevHR signal was also similar to the HR signal in terms of its mean value (246 ± 13 vs. 246 ± 13 min$^{-1}$) and standard deviation (20.6 ± 4.0 vs. 20.6 ± 4.0 min$^{-1}$; Table 1).

**Power Spectra of the Double Product and Its Surrogate Signals**

The power spectrum of the double product is shown for an individual rabbit in Fig. 1. The mean spectrum for five rabbits is shown in Fig. 4. As in the case of the SBP and HR spectra, the double product spectra had an approximate $1/f$ distribution of spectral power. However, in contrast to the SBP and HR power spectra which exhibited a prominent peak at $\sim0.05$ Hz (Fig. 2), a corresponding peak in the power spectrum of the double product was absent (Fig. 4).

**Comparison of the Double Product Spectra with that of RevHR×SBP**

The power spectrum of the RevHR×SBP signal represents how the double product spectra would appear in the absence of nonrandom (e.g., baroreflex) interactions between HR and SBP, which might stabilize the double product. Thus comparison of this spectra with that of the double product can be used to reveal regions of the power spectrum in which interactions between HR and SBP increase or decrease the variability of the double product.
In Fig. 4, the power spectrum of the double product is compared with that of the RevHR×SBP signal. Similar to the HR and SBP spectra, but in contrast to the double product spectrum, the RevHR×SBP power spectrum exhibited a prominent peak at ~0.05 Hz (Fig. 4). The difference between the RevHR×SBP and double product spectra was greatest at 0.05 ± 0.004 Hz, at which the spectral power of the HR×SBP signal fell to 31 ± 5% of that of the RevHR×SBP signal (normalized spectra). The maximum difference between the nonnormalized spectra amounted to 0.051 ± 0.004 Hz when the double product spectral power fell to 32 ± 6% of that of the RevHR×SBP spectrum. The peak in the RevHR×SBP spectrum represents the variability that would have been expected to be evident in the HR×SBP spectrum in the absence of any interaction between SBP and HR to stabilize the double product. The absence of this peak in the double product spectrum suggests that SBP and HR normally interact in a manner to attenuate variations in the double product.

Comparison of the Double Product Spectra with that of HR×MSBP, MHR×SBP, and Their Sum

The MHR×SBP and HR×MSBP signals represent the respective contributions of SBP and HR variability to that of the double product. Their sum represents the combined contributions of HR and SBP to the variability of the double product, excluding nonrandom interactions between HR and SBP such as those imposed by the baroreflex. In Fig. 5, the power spectrum of MHR×SBP, HR×MSBP, and their sum are compared with that of the double product.

HR×MSBP and MHR×SBP each exhibited a peak in the low-frequency range of the spectrum at ~0.05 Hz. At low frequencies below 0.2 Hz, MHR×SBP and HR×MSBP were similar in value, suggesting that HR and SBP signals contribute equally to the variability of the double product at very low frequencies. At high frequencies >0.2 Hz, HR×MSBP increased and MHR×SBP decreased with frequency, suggesting that the HR signal provided a progressively increasing contribution to the variability of the double product at high frequencies. The spectrum of the sum of HR×MSBP and MHR×SBP peaked at 0.054 ± 0.008

In Fig. 4, the power spectrum of the double product is compared with that of the RevHR×SBP signal. Similar to the HR and SBP spectra, but in contrast to the double product spectrum, the RevHR×SBP power spectrum exhibited a prominent peak at ~0.05 Hz (Fig. 4). The difference between the RevHR×SBP and double product spectra was greatest at 0.053 ± 0.004 Hz, at which the spectral power of the HR×SBP signal fell to 31 ± 5% of that of the RevHR×SBP signal (normalized spectra). The maximum difference between the nonnormalized spectra amounted to 0.051 ± 0.004 Hz when the double product spectral power fell to 32 ± 6% of that of the RevHR×SBP spectrum. The peak in the RevHR×SBP spectrum represents the variability that would have been expected to be evident in the HR×SBP spectrum in the absence of any interaction between SBP and HR to stabilize the double product. The absence of this peak in the double product spectrum suggests that SBP and HR normally interact in a manner to attenuate variations in the double product.

Fig. 4. Power spectra of the DP (●) and RevHR×SBP signal (○). Each point represents the mean ± SE of 5 rabbits. Data are presented in normalized units in A and in original units in B. *Points at which the DP and RevHR×SBP signals are significantly different. Log-log plots of the DP and RevHR×SBP spectra are shown in inset in B. AU, arbitrary units.

Fig. 5. Contribution of HR and SBP to the variability of the DP. A: power spectra of the DP, HR×MSBP, MHR×SBP, and the sum of HR×MSBP and MHR×SBP. B: replotting of the spectra in A with spectral power expressed as a fraction of that of the DP. The line at y = 1 highlights the position at which the spectral power is at the level of that of the DP. Each point represents the mean of 5 rabbits. Error bars are omitted for clarity. *Significant difference between the DP and the sum of the HR×MSBP and MHR×SBP spectra.
Hz, reaching a level of spectral power 3.16 ± 0.59 times that of the double product (i.e., spectral power of the double product was only 32% of that of the sum of HR×MSBP + MHR×SBP). At very low frequencies (<0.02 Hz), the power spectrum of the sum fell slightly below that of the double product, suggesting that positive interactions between HR and SBP may contribute to the variance of the double product in this frequency region. At high frequencies, the spectrum of the sum of HR×MSBP and MHR×SBP signals approached that of the double product, suggesting that the double product was relatively unaffected by interactions of HR and SBP at high frequencies (>0.2 Hz).

Mean values of spectral powers for the sum of MHR×SBP and HR×MSBP were highly correlated with those of RevHR×SBP [log(Power_RevHR/MSBP + HR×MSBP) = 1.005 Power_RevHR×SBP − 0.041, adjusted R² = 0.986, n = 256, P < 0.001].

**DISCUSSION**

In the present study, we used spectral analysis of BP and HR to test the hypothesis that baroreflex adjustments of HR stabilize the double product in conscious, unrestrained rabbits. We focused our analysis on a low-frequency band of the power spectrum for which the influence of the baroreflex was evident in terms of prominent peaks in the HR and SBP spectra, a high coherence between HR and SBP, and an appropriate phase between HR and SBP (HR after SBP). Our results showed that, despite the observation of a prominent low-frequency (0.05 Hz) peak in SBP and HR spectra (Figs. 1 and 2), a corresponding peak was absent in the power spectrum of their product (Figs. 1 and 4), suggesting that the variability of the double product in this low-frequency region is attenuated by interactions between the HR and SBP signals. This conclusion is consistent with the presence of prominent low-frequency peaks in the power spectra obtained for calculated surrogates of the double product signal in which normal interactions between HR and SBP were absent (discussed below). Thus our data suggest that, in conscious rabbits, spontaneous fluctuations in HR and SBP interact in a manner that tends to stabilize their product.

The conclusions of our study rely on calculated surrogates of the double product signal. In the case of RevHR×SBP, reversal of the HR signal from end to end before calculating its product with SBP was performed to disrupt the temporal coupling of the HR and SBP signals, thereby preventing complex (nonrandom, temporally coupled) interactions between them that would otherwise alter the variability of the double product. The nonrandom interactions we intended to remove were reflex adjustments of HR occurring during baroreflex activation. Though temporally coupled interactions between HR and SBP arising from any other source would also be eliminated, the SBP-HR phase relationship (SBP leading HR at 0.05 Hz; Fig. 3) suggests that the dominant behavior of HR and SBP in the vicinity of the low-frequency peaks is consistent with the operation of a baroreflex. The presence of a prominent peak in the RevHR×SBP spectrum but not that of the double product at 0.05 Hz suggests that reflex interactions between HR and SBP attenuate the variability of the double product in this low-frequency band. On average, the interaction between HR and SBP reduced the spectral power of the double product to ~32% of RevHR×SBP, that is, 32% of the level that would otherwise be predicted to occur if such SBP-HR interactions were absent. Conversely, the tendency for the double product to have greater spectral power than RevHR×SBP at frequencies <0.02 Hz suggests that positive, nonrandom interactions between HR and SBP may lead to increased variation of the double product in the very low frequency region. This tendency did not reach statistical significance, although it might have if a larger group of animals was studied. In any case, the zero phase and low coherence of the HR-SBP transfer function in this very low frequency region suggests that the tendency of HR and SBP interactions to increase the variability of the double product was the result of covariation in HR and SBP, presumably in association with episodes of excitement or arousal of the animals.

In the case of MHR×SBP and HR×MSBP, these calculated signals are surrogates of the double product in which the contribution of variations in either HR or SBP was eliminated by substituting the mean value of HR or SBP in place of the HR or SBP signal. Thus the MHR×SBP scales the variations in SBP to that of the double product and does not include any contributions of variability from the HR signal. Similarly, HR×MSBP scales the contribution of HR variations to that of the double product without a contribution of variability from the SBP signal. Using these surrogates, we found (Fig. 5) that, in the low-frequency region of ~0.05 Hz, each of the HR and SBP signals alone (i.e., HR×MSBP and MHR×SBP) provided as much if not more power than that of the double product. Furthermore, the sum of the spectral power contributed independently by SBP and HR (i.e., HR×MSBP + MHR×SBP) exceeded that of the double product by up to 3.2-fold, suggesting that the nonrandom interactions between HR and SBP had attenuated the variability of the double product by 69%. The sum of the HR×MSBP and MHR×SBP signals represents the contributions of variability of the individual HR (represented by HR×MSBP) and SBP (represented by MHR×SBP) signals and does not include the temporally coupled interactions between them such as may be produced by the baroreflex. Thus the sum of HR×MSBP and MHR×SBP is analogous to RevHR×SBP, and the two produce highly similar values and spectral results.

The physiological significance of our results lies in our understanding that HR and SBP are both important determinants of cardiac metabolism and that the product of HR and SBP is highly correlated with cardiac oxygen consumption (2, 15,16, 27, 34). By stabilizing the HR×SBP product, the interaction of HR and SBP will also tend to stabilize cardiac oxygen consumption. Thus the baroreflex may help isolate the heart...
from the metabolic impact of sudden hemodynamic disturbances not only by attenuating perturbations of BP but also by stabilizing the double product in the face of the BP perturbations that do occur. Such a mechanism may be of particular importance during sudden changes in SBP, since baroreflex adjustments of HR occur within the time scale of a few beats, whereas the metabolic autoregulation of coronary blood flow, the main mechanism by which the heart adjusts oxygen delivery in the face of changing oxygen demand, requires ~10 s to adjust to a change in hemodynamic load (3, 20). Aside from baroreflex adjustments of HR, we are not aware of another mechanism that would help to maintain the balance between myocardial oxygen supply and demand on such a rapid time scale.

Because the baroreflex is well known to impose an inverse relationship between HR and SBP during perturbations in BP, it is self evident that such a relationship will tend to attenuate variations in the product of HR and SBP. However, the extent to which such variations will be reduced depends on the size of the reflex adjustment of HR for a given change in SBP. In a previous study (30), we showed that ideal (complete) stabilization of the double product by the baroreflex will occur when the value of baroreflex sensitivity (in ms/mmHg) is equal to the ratio of pulse interval and arterial pressure. In the present study, the transfer function gain between the pulse interval and SBP, where their coherence was maximum (0.05 Hz), amounted to 2.0 ± 0.6 ms/mmHg, which is relatively close to the ratio of pulse interval and SBP during the sample period (2.4 ± 0.15 ms/mmHg). The fact that these values were similar, but not identical, is consistent with our finding that stabilization of the double product was observed to occur but was not complete (i.e., at 0.05 Hz, spectral power of the double product amounted to ~32% of that of surrogates of the double product in which the temporal coupling of HR and SBP interactions was prevented).

We have based our present conclusions on the low-frequency band in the vicinity of 0.05 Hz because this was the only segment of power spectra in which periodic fluctuations of SBP occurred and in which a dominant influence of the baroreflex on the behavior of SBP and HR was evident in terms of a high HR-SBP coherence and appropriate HR-SBP phase relationship (Fig. 3). Baroreceptor denervation led to the loss of the 0.05-Hz peak in HR and SBP (data not shown), thereby precluding an analysis of the contributions of variations in HR and SBP to that of the double product in denervated animals. In our previous study (30), we demonstrated that the baroreflex acts to stabilize the double product during pharmacological manipulation of BP in conscious rabbits. Because the BP perturbations in that study clearly included frequencies below the 0.05-Hz range, we presume that the baroreflex is capable of stabilizing the double product at frequencies outside the vicinity of 0.05 Hz that we focused on in the present study. However, the application of power spectra and transfer functions to investigate the reflex stabilization of the double product requires a periodic SBP input to the baroreflex, which was only present in the ~0.05-Hz region in the present study. We speculate that baroreflex stabilization of the double product may also be evident within other frequency bands of the double product power spectrum under other experimental conditions in which periodic fluctuations of SBP sufficient to activate the baroreflex at those frequencies were present.

In addition to a high-frequency BP rhythm occurring at the ventilatory frequency (>0.75 Hz), a 0.3-Hz rhythm in BP and has also been recognized in New Zealand White rabbits (14, 18). In the present study, a prominent peak in the SBP and HR spectra occurred at a considerably lower frequency of 0.05 Hz. This 0.05-Hz rhythm may correspond with a distinct ~0.03-Hz rhythm that was previously described for HR in rabbits (6). In addition, a prominent low-frequency rhythm in BP and HR also appears evident in the 0.05- to 0.1-Hz range of spectra published by Malpas et al. (Figs. 2 and 4 of Ref. 19). The description of multiple low-frequency rhythms in rabbits is reminiscent of the situation in other species. An ~0.4-Hz BP rhythm has been widely recognized in rats (4, 5, 7–9, 11, 12, 25, 28) and mice (13), but slower (0.05- to 0.1-Hz) rhythms have also been described in rats (4, 5, 7–9, 24, 25, 28). In dogs, low-frequency peaks have been described in BP spectra at ~0.1 (10, 22, 26) and ~0.05 (10, 17, 21, 23, 32) Hz. Based on these findings in other species, we would suggest that the 0.05-Hz rhythm observed in rabbits in the present study should be considered distinct from the previously recognized 0.3-Hz rhythm. The main features of the 0.05-Hz rhythm that we have observed so far are that it involves both SBP and HR, with high coherence between the two at this frequency, and that the 0.05-Hz rhythm is absent after sinoaortic denervation (data not shown). However, the mechanisms underlying the 0.05-Hz rhythm, and the factors that favor the appearance of the 0.05-Hz vs. the 0.3-Hz rhythm in rabbits, remain to be determined.

Perspectives

Arterial BP is an important determinant of cardiac oxygen consumption. It is well established that the baroreflex acts to attenuate BP perturbations, and, in this way, it may also attenuate the impact of such perturbations on cardiac metabolism. Recently, we have suggested that, because the product of HR and BP is a correlate and indirect index of cardiac oxygen consumption, baroreflex adjustments of HR that stabilize the product of HR and BP may help isolate cardiac metabolism from the BP disturbances that do manage to occur. We have previously demonstrated that baroreflex sensitivity is of an appropriate magnitude to stabilize the product of HR and BP in a variety of species and that baroreflex adjustments of HR do tend to attenuate or prevent changes in the product of HR and BP when BP is pharmacologically manipulated in rabbits. Using a spectral analysis approach, our present results confirm this for spontaneous fluctua-
tions in BP in freely behaving, conscious rabbits. These results suggest that baroreflex adjustments of HR may help attenuate fluctuations in cardiac metabolism during spontaneous hemodynamic disturbances in conscious animals.

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REFERENCES


