Importance of Appropriate Spectral Methodology to Assess Heart Rate Variability in the Frequency Domain

To the editor:

The article "Short-term variability of blood pressure and heart rate in borderline and mildly hypertensive subjects" by Takalo and coworkers1 deserves a comment in view of some methodological oversights and statements that might engender undue confusion in this rapidly growing field of research.

In their spectral analysis of heart rate and arterial pressure variability, the authors considered three bands of interest, determined a priori and defined as low-, mid-, and high-frequency. This procedure was previously followed by authors who used the fast Fourier transform (FFT) algorithm.2 This is surprising because Takalo et al1 used an autoregressive approach that, by applying a residuals theorem,3 can instead provide automatically the number, center frequency, and associated power of oscillatory components without the need for a priori decisions. Moreover, they used a very high model order (ie, 30), which generates a noisy spectral profile similar to the one obtained with unsmoothed FFT (see middle and bottom part of the Figure). This is quite different from what is obtained when Akaike’s criterion is applied to choose an appropriate model order (ie, 11 in the case of the top part of the Figure).

This point is crucial because it has been amply demonstrated4 that in addition to a very-low-frequency or DC component below 0.03 Hz, only two rhythmic oscillations affect both heart period and arterial pressure variability, with a high degree of coherence. This is so in human subjects, conscious dogs, anesthetized cats, and unanesthetized rats.5 The center frequency of the high-frequency component corresponds to that of respiration, whereas the center frequency of the low-frequency component reflects vasomotor activity; however, the center frequency of this latter component can also vary considerably (in human subjects and conscious dogs from 0.04 to 0.13 Hz). In short, it is clear from previous studies and from the example provided in the Figure that an arbitrary cut at 0.075 Hz can only artificially subdivide into two parts the same rhythmic phenomenon.

Takalo and coworkers1 justify their methodological choice with the following statement in the “Discussion”: “Finally, our viewpoint is that components with a frequency slower than respiration should, as in Farhat et al,2 be divided into two bands, where the lower limit of the center frequency in the baroreflex rhythm, that is, 0.075 Hz, is a logical dividing line.” This a priori logic is likely to introduce a major confounding factor. Indeed, the authors could not clearly detect either the differences in day-night changes of spectral components as previously reported5 or those that exist between normotensive and hypertensive subjects.8,9 Available evidence indicates that a sound spectral methodology, by comparing the relative power of oscillations related respectively to vasomotor and respiratory activity, is providing a new tool for assessing the state of sympathovagal balance in different physiological and pathophysiological conditions, including the sympathetic overactivity of arterial hypertension.5,9

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Response

In response to the letter from A. Malliani et al regarding our study,1 we provide the following comments.

We used the autoregressive (AR) modeling method in our study because it is able to provide better frequency resolution than fast Fourier transformation. However, proper use of the method is required to obtain a high-resolution power spectrum. Crucial to the analysis is the selection of an appropriate model order. Too low a model order results in a highly smoothed spectral estimate with low resolution, and too high an order increases the resolution at the cost of introducing spurious peaks in the spectrum.2,3 Many different criteria have been introduced to guide the selection of the suitable model order, notably the Akaike Information Criteria (AIC).4 Although these criteria are found to work acceptably well in the case of a pure AR process, they have been reported to underestimate the model order in the case of non-AR or noise-corrupted processes,5,6 as is the case when analyzing blood pressure (BP) and heart rate (HR) signals. In fact, it has been observed that the AR model order chosen by AIC is usually not sufficient to resolve spectral details in noise-corrupted signals.3 Thus, when aiming at the maximization of the spectral resolution, a greater model order than that estimated with AIC should be used. Kay7 stated that as a rule of thumb in the spectral estimation, a model order between N/3 and N/2 (N being the data length) should be used for good spectral resolution and few spurious peaks. The AIC gives estimates between 6 and 22 when used with our data with N = 300. Our selection of 30 for the model order can be considered as a reasonable compromise with proper resolution; vasomotor (at around 1.0 Hz), and thermal vasomotor (at around 0.5 Hz) activities.7 There is evidence that even the renin-angiotensin system may play a significant role in short-term cardiovascular control (at around 0.4 Hz).8 So there are certainly more than two oscillations involved in BP and HR variability above 0.3 Hz.

The fact that we subdivided the oscillations between 0.02 and 0.15 Hz into two bands made it possible to detect the qualitative differences in the cardiovascular control systems between normotensive, borderline hypertensive, and mildly hypertensive subjects. In our study, there is an important message to the researchers in the field of hypertension: When BP variability is analyzed in the frequency domain, in the range 0.02 to 0.15 Hz, it is not the normalized power but the frequency content that discriminates the BP groups (in our study, the borderline hypertensive individuals had greater BP variability in the range of 0.02 to 0.075 Hz and smaller variability in the range of 0.075 to 0.15 Hz than the other groups). So far, this kind of frequency shift has been found to occur in subjects with diabetes mellitus,9,10 and it may be a common marker of dysfunction of the autonomic nervous system. Also, other researchers have divided the total spectrum into three bands.11,12 However, we agree with Malliani et al that a division of the spectrum into predetermined bands is always more or less arbitrary. Therefore, we think that future research should, among other issues, concentrate on seeking a simple and accurate way to quantify the frequency shift observed in borderline hypertensive subjects. Because of the complex nature of BP and HR fluctuations, the calculation of center frequencies and powers of the individual peaks is not a satisfactory solution, because a high-resolution power spectrum can contain several significant peaks within a particular frequency range. Our preliminary observations indicate that calculation of a median frequency, i.e., the frequency below and above which half of the power within a particular bandwidth falls, can be an accurate method for locating and measuring the frequency shift.13

The division of the subjects into three groups according to World Health Organization guidelines is of great importance. An autonomic abnormality is typically found in young subjects with borderline hypertension, but it is often difficult to show the autonomic abnormality in established hypertension.14 To our knowledge, our study is the only one in which the subjects were selected from a large population, and the subjects were followed for their BP level for 2 months before the study examination to guarantee that they really were normotensive, borderline hypertensive, or hypertensive. This is crucial before one can analyze the effect of BP level on cardiovascular regulatory phenomena.

Finally, we emphasize the importance of the calculation of physiologically relevant measures and correct interpretation of the results, as do Malik and Camm16 in their excellent editorial about the latter theme. It should be noted that the low-frequency–high-frequency ratio does not take into account the frequency shift in the range of 0.02 to 0.15 Hz, which can occur in certain groups of subjects.

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