Multiscale analysis of blood pressure signals

A. Marrone, A.D. Polosa, and G. Scioscia
Dipartimento di Fisica Università di Bari and Sezione INFN di Bari, Via Amendola 173, I-70126 Bari, Italy

S. Stramaglia
Istituto Elaborazione Segnali ed Immagini, Consiglio Nazionale delle Ricerche, Via Amendola 166/5, I-70126 Bari, Italy

A. Zenzola
Dipartimento di Scienze Neurologiche e Psichiatriche Università di Bari, Piazza Giulio Cesare 11, I-70100 Bari, Italy
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We describe the multiresolution wavelet analysis of blood pressure waves in vasovagal syncope-affected patients compared with those in healthy people, using Haar and Gaussian bases. A comparison between scale-dependent and scale-independent measures discriminating the two classes of subjects is made. What emerges is a sort of equivalence between these two methodological approaches, that is, both methods reach the same statistical significance of separation between the two classes. [S1063-651X(99)14205-3]

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In recent years biological time series have been considered in the more general framework of *fractal functions*. Accordingly, the analytical tools commonly used for fractal functions have been applied to study physiological time series, see, e.g., [1]. A major approach to such problems is based on the *wavelet* transform, a technique which has proved to be well suited for characterizing the scaling properties of fractal objects even in the presence of low-frequency trends [2].

In particular, the regulation of the cardiac rhythm has been recently investigated in two very interesting papers aimed at providing means of diagnosis of heart disease. The interbeat interval records for healthy and sick subjects have been studied by wavelet analysis, which can appropriately treat the nonstationarity of these signals. In Ref. [3] a scale-dependent measure, the root mean square of the wavelet coefficients $\sigma_w(s)$ at a particular scale s, has been shown to be able to sharply discriminate between healthy and sick subjects. In Ref. [4] it was observed that scale-dependent measures may reflect characteristics specific to the subject or to the choice of the wavelet basis; a scale-independent measure extracting the exponents characterizing the scaling of the partition function of wavelet coefficients was then proposed, and its performance in detecting heart disease was excellent. The scaling exponents were already studied in Ref. [3] for the second wavelet moments while in Ref. [4] they are calculated for arbitrary moments. It seems likely to us that the approaches based on scale-dependent measures and that based on scale-independent ones should be considered as qualitatively *equivalent*. Indeed some pathological conditions may alter the cardiac dynamics at a specific scale or range of scales, while the scaling behavior of the dynamics of cardiac rhythm regulation should be universal for subjects belonging to the same class. An important problem is how the choice of the wavelet basis influences the results of the analysis. Moreover, it is interesting to check whether the same kind of analysis can be used to study *other* physiological time series and pathologies.

In this work we study the temporal series of the systolic blood pressure waves' maxima in nine healthy subjects and ten subjects showing a pathology known as vasovagal syncope. We perform a wavelet analysis of these time series and consider both the scale-dependent and the scale-independent measures described above. To our knowledge this is the first time wavelets are used to study blood pressure waves' signals. We performed the analysis using two different wavelet bases, namely, the Haar basis and the third derivative of the Gaussian one (TDG). The main difference between these two bases is that the former is able to remove only zero order trends, while the latter is insensitive to higher polynomial trends. We find that the Haar basis is, with respect to the data set at hand, well suited for scale-dependent measures, i.e., measures of $\sigma_w(s)$. Indeed using these wavelets we find an evident separation among healthy and sick subjects at a particular scale $s=32$: this separation is missing when the TDG is used. On the other hand, using the TDG leads to a separation with respect to scaling exponent measures which is much less significant when the Haar basis is used. Interestingly we found that the statistical confidence of separation in the scale-dependent parameter (obtained using Haar wavelets) is very close to that obtained by the scale-independent parameter, i.e., the scaling exponent (using the TDG). Since both methods have reached the same degree of separation between the two classes, it remains to be understood whether this coincides with the intrinsic degree of separability of the data set considered here.

Vasovagal syncope is a sudden, rapid, and reversible loss of consciousness, due to a reduction of cerebral blood flow [5] attributable to a dysfunction of the cardiovascular control, induced by that part of the autonomic nervous system (ANS) that regulates the arterial pressure [5,6]. In normal conditions the arterial pressure is maintained at a constant level by the existence of a negative feedback mechanism localized in some nervous centers of the brainstem. As a consequence of a blood pressure variation, the ANS is able to restore the haemodynamic situation acting on heart and vases, by means of two efferent pathways, the vasovagal and

sympathetic one, the former acting in the sense of a reduction of the arterial pressure, the latter in the opposite sense [7]. Vasovagal syncope consists of an abrupt fall of blood pressure corresponding to an acute haemodynamic reaction produced by a sudden change in the activity of the ANS (an excessive enhancement of vasovagal outflow or a sudden decrease of sympathetic activity) [5].

Vasovagal syncope is a quite common clinical problem and in 50% of patients it is undiagnosed, being labeled as syncope of unknown origin, i.e., not necessarily connected to a dysfunction of the ANS action [6,8,9]. Anyway, a rough diagnosis of vasovagal syncope is practicable [8,10] with the help of the head-up tilt test (HUT) [11]. During this test the patient, positioned on a self-moving table, after an initial rest period in horizontal position, is suddenly brought into a vertical position. In such a way the ANS registers a sudden stimulus of reduction of arterial pressure due to the shift of blood volume to inferior limbs. A badly regulated response to this stimulus can induce syncope behavior.

According to some authors, a positive finding on the HUT means an individual predisposition toward vasovagal syncope [12]. This statement does not find general agreement because of the low reproducibility of the test [13] in the same patient and the extreme variability of the sensitivity in most of the clinical studies [10]. For this reason a long and careful clinical observation period is needed to establish with a certain reliability whether the patient is affected by this syndrome. What we want to stress here is that, from a clinical standpoint, there is *not* a neat way of discriminating between healthy and syncope-affected subjects, while, in the case of heart disease, studied in [3,4], there is always a very clear clinical picture. For this reason in recent years a great deal of work has been devoted to the investigation of signal patterns that could characterize syncope-affected patients. This has been done especially by means of Fourier analyses of arterial pressure and heart rate which have not proven to be successful for this purpose [14].

The temporal behavior of blood pressure is the most clinically relevant aspect to study vasovagal syncope since it is the result of the combined activity of ANS on heart and vases. Therefore we extract blood pressure wave maxima from a 20 minutes long recording period (which is the best we can do for technical reasons). During this time the following biological signals of the subject are recorded: electrocardiogram, electroencephalogram, the thoracic breath, the arterial blood pressure (by means of a finapres Ohmeda 2300 system from Eglewood Co., measuring from the second finger of the left hand).

We denote by $\{P_i\}$ the time series of systolic pressure maxima. The coefficients of the discrete wavelet transform at scale s are given by

$$W_s(n)=s^{-1}\sum_{i=1}^{M} P_i\psi((i-n)/s), \tag{1}$$

where ψ is the generating wavelet, M is the number of points in the time series (we have $M=2^{10}$), and n is the point for which the coefficient is calculated. The scale-dependent measure proposed in [3] corresponds to evaluating the root mean square of wavelet coefficients at fixed scales. The scale-independent measure deals with the sums of the moments of the wavelet coefficients

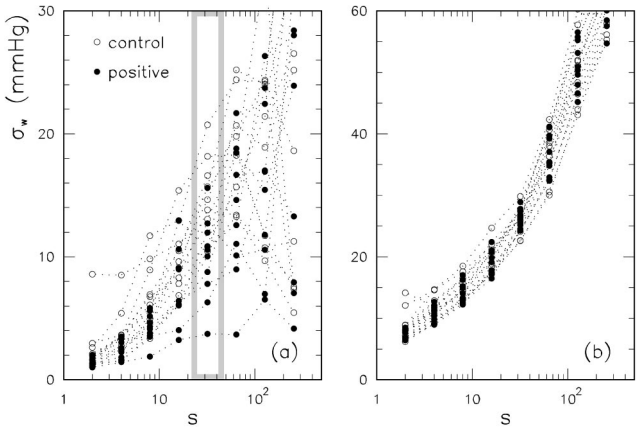

FIG. 1. Standard deviations of the wavelet coefficients of the systolic pressure in syncope-affected patients (positives) and healthy people (controls) drawn both in Haar basis (a) and Gaussian basis (b). Note the evident separation among positives and controls at $s=32$ in (a). This separation is completely lost in (b). We believe that the discrimination pattern is not as sharply evident as in Ref. [3] due to the restricted temporal extension of our data set. We use different σ_w ranges in (a) and (b) only in order to have the best visual impact.

$$Z_q(s)=\sum_n |W_s(n)|^q, \tag{2}$$

where the sum is only over the maxima of $|W_s|$. One can show that Z_q scales as

$$Z_q(s)\sim s^{\tau(q)}. \tag{3}$$

The exponents $\tau(q)$, especially for $q=2$ and $q=5$, were found to provide a robust degree of separation in the case of heart disease diagnosis [4].

First we discuss the results we obtained on the data set considered here by evaluation of the rms of wavelet coefficients. In Fig. 1(a) the rms of the Haar wavelet coefficients are plotted versus the scale, for both sick and healthy subjects, while in Fig. 1(b) the same quantities are plotted in the case of the TDG basis. One can see that in the Haar case an evident separation between healthy and sick subjects holds at the scale $s=32$: healthy subjects have greater fluctuations in the wavelet coefficients. We performed the Wilcoxon-Mann-Whitney (WMW) test to check the hypothesis that the two kinds of samples, positive and control subjects, have been drawn from the same continuous distribution function. The WMW test gives a 3.5×10^{-3} probability to the above cited hypothesis, i.e., the statistical hypothesis is rejectable at the level of significance of 1%. On the other hand, using the TDG as the wavelet basis does not lead to separation at any scale. Therefore a scale-dependent measure can highlight an evident separation at a particular scale but the result depends on the wavelet basis one uses.

Let us now turn to consider scaling exponent measures. We have calculated the partition functions $Z_q(s)$ using both Haar wavelets and the TDG basis. A measure of the expo-

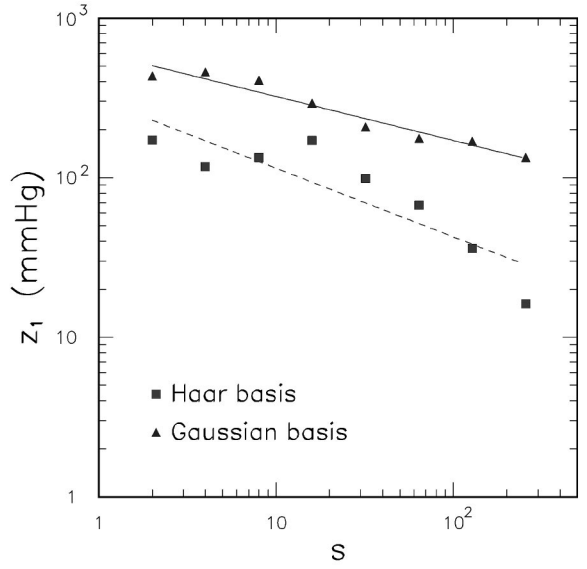

FIG. 2. Log-log plots of $Z_1(s)$ vs s drawn in the Haar basis and in the Gaussian basis for a subject. Analogous plots have been obtained for the other subjects we have examined. The scaling behavior is evident only in the Gaussian basis, while the points from the Haar basis are not as well linearly fitted.

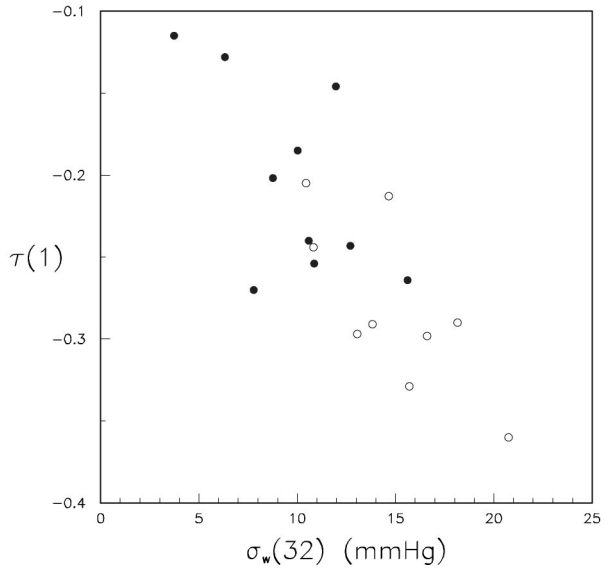

FIG. 3. $\sigma_w(32)$-$\tau(1)$ plot, i.e., the Haar wavelet coefficient fluctuation at the scale $s=32$ vs the scaling exponent of Eq. (3) in the Gaussian basis. ● refers to syncope-affected patients, ○ refers to healthy subjects. Projecting the points lying in the σ-τ plane on σ and τ axes we obtain two separation patterns between positives and controls which are quite similar from a statistical point of view (see the WMW analysis in the text).

nents $\tau(q)$ can then be obtained through log-log plots of Z_q versus s. In the case of the TDG, the log-log plots of Z_q versus s showed a neat scaling behavior: in Fig. 2 the $q=1$ case, the most significant with our data, is shown. In the case of Haar wavelets, the log-log plots show some curvature (see Fig. 2), but calculating linear correlation coefficients we discover that it still makes sense to evaluate $\tau(q=1)$ exponents. For the moment let us refer to the TDG case. We found that the exponent $\tau(q=1)$ acts as a discriminating parameter between healthy and sick subjects, while exponents for the other values of q did not succeed in obtaining equally convincing results. Healthy subjects have lower $\tau(q=1)$ values than do syncope-affected ones (see Fig. 3). By the WMW test, the probability that the values of the exponents found for the two classes of subjects, healthy and sick, were sampled from the same continuous distribution was estimated to be 4.5×10^{-3}, a level of significance very close to the one found in the case of the scale-dependent measure. On the other hand, considering the $\tau(q=1)$ as computed in the Haar basis, we find that the latter probability value grows by about one order of magnitude, reaching a value of 2.1×10^{-2}.

In Fig. 3 we have shown the points corresponding to the 19 subjects under consideration in the σ_w-τ plane, where the coordinates correspond to the measured quantities $\sigma_w(32)$ (by Haar wavelets) and $\tau(q=1)$ (by the TDG basis). It is evident that the two measures separate, *at the same degree*, the two classes.

We observe that it is reasonable that the Gaussian basis is more effective in detecting the scaling behavior of these time series with respect to the Haar basis. On the other hand, the same degree of separation is obtained by Haar wavelets at a given scale, while the TDG seems insensitive to the single scale features. It follows that these two kinds of measures are going in the same direction rather than excluding each other. A very careful analysis in Ref. [15] shows that in the case of diverse heart pathologies, scale-dependent measures, namely, measures of $\sigma_w(s)$ at a particular scale s, outperform measures of scaling exponents. Due to the size of our data set, we may encounter problems in reproducing the kind of analysis performed in Ref. [15], but we look forward to investigating this aspect. In Ref. [15] it is also stressed that baroflex modulations of sympathetic and parasympathetic tone lie in a frequency range which corresponds to the scale $s=32$ which is also, for us, the best discrimination between controls and positives.

We are, at the moment, not able to provide the physiological explanation of the phenomena described here. However, these results might be useful to get a better understanding of the very complicated vasovagal syncope pathology.

Some conclusions are in order. We analyzed signals from healthy subjects and subjects positive to vasovagal syncope pathology by wavelet blood pressure. We evaluated two quantities, one depending on a fixed scale and a scaling exponent, which have been recently proposed as diagnostic tools for heart disease. We have shown that both the measures succeed in separating the two classes within the same degree of significance. We are working to have longer records and an enlarged number of positives and controls so as to refine our analysis. At the moment we are aware of being far from being able to propose an alternative diagnostic tool. This would be very useful because of the particular difficulty that the clinical diagnosis of vasovagal syncope still presents.

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