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Spectral and symbolic analysis of heart rate data during the tilt test

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Spectral analysis of heart rate sequences is commonly used to investigate neuroauthonomic control of heart rate by means of two indexes, the low and the high frequency power. For tilt test data of normal subjects we compare the spectral indexes with new indexes defined within the framework of symbolic analysis. We define two classes of binary words of length 4: the first class is related to "acceleration" of heart rate and the second class to "stationary behavior." The new indexes measure the change in frequency of the two classes before and after the tilt. Data analysis of 13 normal subjects shows that the behavior of the new indexes is in agreement with that of spectral ones.

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I. INTRODUCTION

Head up tilt (HUT) test can be used to evaluate how the human body regulates blood pressure and heart rhythm in response to some very simple stresses. The HUT test analyzed in this paper consists of monitoring patients in two different conditions. First the patient remains in a supine position for twenty minutes; then, after the supine heart rate and blood pressure are obtained, the patient is tilted using a motorized table with a foot-board and remains in an inclined position for another twenty minutes. During this test an electrocardiogram (ECG) is performed and blood pressure is measured. The tilt is believed to produce changes in the neuroauthonomic controls consisting in an increment of the sympathetic activity and a decrease of the parasympathetic (vagal) activity. These controls can be studied by using the *RR* sequence, which is defined as the sequence of time intervals between two consecutive *R* peaks in the ECG.

In this paper we compare two methods for analyzing the neuroauthonomic control on heart rate during the HUT test: the well established method of spectral analysis and a more recent one based on symbolic analysis. Spectral analysis of the *RR* sequences has been used for providing quantitative indexes of cardiac sympathetic and vagal modulation under many circumstances including the HUT test; see Refs. [1,2] and references therein.

The symbolic method is based on the general framework of symbolic analysis of time series, which has already revealed useful in the analysis of the *RR* sequence [3–8]. This method consists in coding the data series into a symbolic series and estimating the probability distribution of words or permutations. Recently a comparison between spectral analysis and nonlinear dynamics methods, but not including symbolic ones, has been performed on the *RR* sequence [9]. We refer to this work also for some references about the controversies in the applications of spectral analysis. On the other hand, symbolic analysis has been used also for analyzing 24 hour *RR* sequences for patients with positive HUT test [7]. Note however that in this work symbolic analysis has not been used to analyze the tilt test itself.

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In this paper we study the results of a HUT test of a group of 13 healthy subjects both with spectral analysis and symbolic analysis in order to compare the results: both methods clearly detect the modification occurring in the *RR* sequences due to the tilt, suggesting that also symbolic analysis could be used as a marker of the sympathovagal activity. We summarize the two methods and give the corresponding data analysis in the next two sections; in the last section we discuss some differences between them.

II. SPECTRAL ANALYSIS

We briefly recall the basics of spectral analysis of discrete signals [10]. Every discrete signal x_t, $t=0,\ldots,N-1$ can be written as

$$x_t = \sum_{j=0}^{N-1} c(f_j) e^{2\pi i f_j t}, \tag{1}$$

where $f_j = j/N$, $j=0,\ldots,(N-1)$ and

$$c(f) = \frac{1}{N} \sum_{t=0}^{N-1} x_t e^{-2\pi i f t}. \tag{2}$$

The frequencies f_j are called *harmonic frequencies* and depend on the number N of the signal samples. The vector $c=(c(f_0),\ldots,c(f_{N-1}))$ is called *discrete Fourier transform* of x. As a consequence of orthonormality relations of complex exponentials, one has $\|x\| = N\|c\|$. In general, $c(1-f)=c(-f)$ and moreover, if x is real, $c(-f)=\overline{c(f)}$. The *raw periodogram* of a real discrete signal is the function defined, for each f in the interval $0 \leqslant f \leqslant \frac{1}{2}$, by $I(f)=N|c(f)|^2$. If x_t is the *RR* sequence, one integrates the log of the raw periodogram in the 0.04–0.15 Hz and 0.15–0.4 Hz ranges. These intervals are called low frequency (LF) and high frequency (HF) intervals and the integrals low frequency and high frequency power of the signal. Each of them can be normalized by the frequency power in the 0.4–0.5 interval to yield *normalized low frequency power* (NLFP) and *normalized high frequency power* (NHFP), respectively. It is widely assumed that NHFP reflects parasympathetic activity and NLFP reflects sympathetic activity [1,2]. If the sequence is assumed to be a stationary Gaussian process X_t, $t=0,\ldots,N-1$, it is possible to define the spectral density which characterizes the process

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[11]. This density can be estimated in two ways. The first one is a moving average of the row periodogram with respect to a window of suitable length. The second one consists in estimating the coefficients ϕ_i of an *autoregressive model of order p*, $\mathrm{AR}_{(p)}$, defined by

$$X_i = \phi_1 X_{i-1} + \cdots + \phi_p X_{i-p} + Z_i,$$

where $Z_i \sim N(0,\sigma^2)$ is an independent Gaussian sequence. The coefficients ϕ_i define a polynomial $Q(z)=1+\phi_1 z+\cdots+\phi_p z^p$. The spectral density of $\mathrm{AR}_{(p)}$ is the function

$$\frac{\sigma^2}{|Q(e^{-2\pi \mathbf{i} f})|^2}$$

defined for $f \in [0,\frac{1}{2}]$. The use of AR models for estimating the spectral density is common in medical literature [2]. We have checked that using the periodogram or AR models for estimating spectral densities makes little difference for the purposes of this paper. In Fig. 1 the *RR* sequence and the corresponding spectrum before and after the tilt are shown. The area of the spectral density above the HF interval becomes smaller after the tilt. The order of the AR models are automatically estimated by using the Akaike information criterion by the software used for analyzing the data, which is the public domain statistical package R [12]. We define the index ΔNLFP as the difference between NLFP after the tilt and NLFP before the tilt and the index ΔNHFP as the difference between NHFP after the tilt and NHFP before the tilt. The values of the spectral indexes computed in our database are reported in Table I. Both the sign tests for the positivity of ΔNLFP and for the negativity of ΔNHFP give a p-value less than 0.0003.

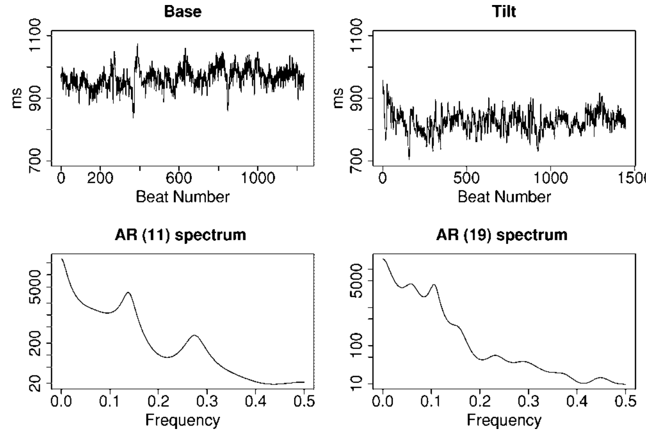

FIG. 1. The first and second panels show the *RR* sequences before and after the tilt for a typical case. The third and fourth panels show the autoregressive estimates of the corresponding spectral power densities.

III. SYMBOLIC ANALYSIS

For coding a segment of a time series into a binary word we use the following method [5]. If $\mathbb{Z}_2$ denotes the set {0,1}, the set $\mathbb{Z}_2^n$ is identified to the set of binary words of length n. We define a function $W:\mathbb{R}^{n+1}\rightarrow\mathbb{Z}_2^n$ in the following way: $W(x_1,\ldots,x_{n+1})=(w(1),\ldots,w(n))$, where

$$w(i)=\begin{cases}0, & \text{if } x_i \geqslant x_{i+1},\\ 1, & \text{if } x_i < x_{i+1}.\end{cases} \quad (3)$$

For example, $W(181,32,42,115,130)=(0,1,1,1)$. For a given time series we code each segment of consecutive n

TABLE I. In this table we report spectral indexes computed with log-raw periodogram. All values are rounded. Rows refer to patients. Column NLFPb contains the normalized low frequency power index before the tilt. Column NLFPt contains the same after the tilt. Column ΔNLFP contains the difference between the first two. Column Δnlfp contains the relative difference, i.e., the ratio of the third column to one-half of the sum of the first two. The remaining four columns are built in the same way by using the normalized high frequency power index.

Spectral indexes							
Low frequency				High frequency			
NLFPb	NLFPt	ΔNLFP	Δnlfp	NLHPb	NLHPt	ΔNHFP	Δnhfp
0.29	0.36	0.08	0.23	0.55	0.50	−0.05	−0.10
0.38	0.47	0.09	0.21	0.51	0.43	−0.08	−0.16
0.27	0.32	0.04	0.14	0.54	0.52	−0.02	−0.03
0.31	0.44	0.12	0.32	0.52	0.48	−0.04	−0.07
0.25	0.28	0.02	0.09	0.57	0.54	−0.03	−0.06
0.36	0.43	0.07	0.18	0.53	0.43	−0.09	−0.20
0.28	0.33	0.05	0.16	0.53	0.50	−0.03	−0.05
0.29	0.35	0.05	0.17	0.55	0.50	−0.04	−0.08
0.30	0.35	0.06	0.17	0.55	0.49	−0.06	−0.11
0.28	0.31	0.04	0.12	0.56	0.51	−0.05	−0.09
0.29	0.32	0.03	0.10	0.54	0.50	−0.04	−0.08
0.29	0.39	0.10	0.28	0.54	0.48	−0.06	−0.12
0.27	0.32	0.05	0.16	0.57	0.53	−0.04	−0.08

+1 values into a length n binary word as above. This allows one to consider, for each n, the histogram of length n binary words. This histogram is computed in the following way. Given a data series $x_1, \ldots, x_N$ we compute, for each binary word ω, the number of matchings of the word in the data series, i.e., the number of segments $s_i=(x_i, x_{i+1}, \ldots, x_{i+n})$ extracted from the data series such that $W(s_i)=\omega$. Note that in this work the segments s_i's are not disjoint. For example, the binary words of length 4 extracted from the series {181,32,42,115,130,100,87,123,91,121,123,124,132} are {(0,1,1,1), (1,1,1,0), (1,1,0,0,), (1,0,0,1), (0,0,1,0), (0,1,0,1), (1,0,1,1), (0,1,1,1), (1,1,1,1)}. The histogram gives, for each word, its relative frequency in the data series, i.e., the number of occurrences divided by the total number of extracted words. The model we adopt in order to describe our data is that the observed sequence $x_1, \ldots, x_N$ is considered to be a realization of the sequence of random variables $X_1, \ldots, X_N$. The dependence among the variables is given by the joint distribution of the $k+1$ dimensional vectors $(X_i, \ldots, X_{i+k})$ which does depend on i if we assume that the sequence is stationary. The observed data are not sufficient to estimate the joint distribution even for small values of k; the histogram of binary words captures however some relevant features of the dependence among the variables. Simple but important operations can be defined for words. The *shift* of the word $(a_1, \ldots, a_{n-1}, a_n)$ is the word $(a_n, \ldots, a_1, a_{n-1})$. The *flip* of a word ω is obtained by changing 0 to 1 and 1 to 0 in ω. The *time reversal* of the word $(a_1, \ldots, a_n)$ is the flip of the word $(a_n, \ldots, a_1)$. These operations can be used for analyzing nontrivial properties of data series, like time reversibility [8]. One striking feature of binary words is that if these words are extracted from a sequence X_i of independent random variables with the same distribution, then the binary words distribution does not depend on the distribution of the X_i's [5]. We refer to this property as "i.i.d.-universality" of the distribution of binary words. The consequences are relevant also for data analysis, as is shown in Ref. [6] where atrial fibrillation has been investigated. The histograms of binary words for atrial fibrillation are extremely close to the i.i.d.-universal distribution. For normal subjects the histograms are very different [5]. At the moment there exists no theoretical model for explaining the main features of the histogram of binary words of normal subjects. The present paper addresses the specific question of analyzing the modifications of this histogram under the basic stress induced by the tilt test. In Fig. 2 we show the histogram of length 4 binary words before and after the tilt for a typical case. By inspecting these diagrams for all our patients, we have found out that the frequency of occurrence of the length 4 binary words

$$W_A = \{(0,0,0,0),(1,1,1,1)\} \quad (4)$$

increases from base to tilt, while the frequency of occurrence of the binary words

$$W_S = \{(0,0,1,1),(0,1,1,0),(1,1,0,0),(1,0,0,1)\} \quad (5)$$

decreases. The words W_A have already been proved to be useful for analyzing different pathological situations, see for example, Ref. [3]. We call the words (4), A-words (A stands for *acceleration*) and the words (5), S-words (S stands for *stationary*). Note that both W_S and W_A are closed under the operations of shift and time reversal. One heuristic motivation for our choice of these two classes of words is that in rest conditions S-words describe the most common pattern in the RR sequence while A-words are the most sensitive to sudden changes. This suggests the introduction of two indexes. The index ΔA is defined in the following way: let A_b be the sum of the relative frequencies of occurrence of the words in W_A before the tilt and let A_t be the sum of the relative frequencies of occurrence of the same words after the tilt. Define $\Delta A = A_t - A_b$. The index ΔS is defined analogously: S_b is the sum of the relative frequencies of occurrence of the words in W_S before the tilt and S_t is the sum of the relative frequencies of occurrence of the same words after the tilt. Define $\Delta S = S_t - S_b$.

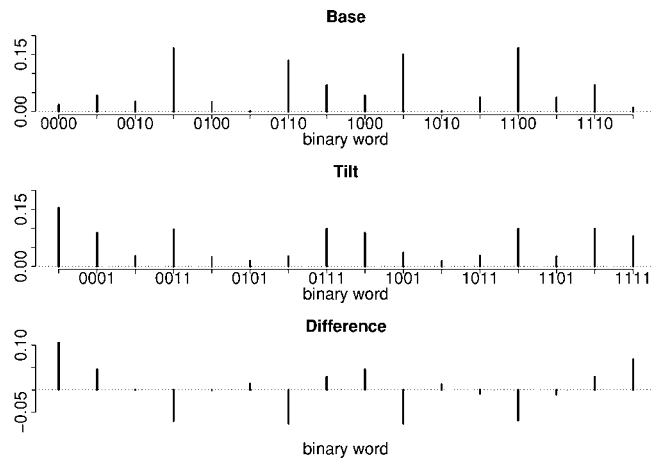

FIG. 2. The histograms of length 4 binary words for a typical case: before the tilt (first row) and after the tilt (second row). We have labeled half of the words in the x axis of the first picture and the other half in the x axis of the second picture. In the y axis of both pictures we put the relative frequency of occurrence of each word. In the third row we plot, for each word, the difference of the frequency after the tilt minus that before.

The values of the symbolic indexes computed in our database are reported in Table II. Both the sign tests for the positivity of ΔA and for the negativity of ΔS give a p value less than 0.0003.

IV. CONCLUSIONS

According to the results of the data analysis presented here, which should be further validated in larger data sets, both spectral analysis and symbolic analysis clearly detect the modification occurring in the RR sequences due to the tilt. An increment of sympathetic activity is measured by positivity of ΔNLFP in spectral analysis and by positivity of ΔA in symbolic analysis. A decrement of parasympathetic activity is measured by negativity of ΔNHFP in spectral analysis and by negativity of ΔS in symbolic analysis. There are however some differences in the two methods that we elucidate here.

First, spectral analysis is mathematically more sophisticated than symbolic analysis. For this reason we believe that

TABLE II. In this table we report symbolic indexes computed with length 4 binary words. All values are rounded. Rows refer to patients. Column A_b contains the frequencies of the "acceleration" words before the tilt. Column A_t contains the same after the tilt. Column ΔA contains the difference between the first two. Column Δa contains the relative difference, i.e., the ratio of the third column to one-half of the sum of the first two. The remaining four columns are built in the same way by using the frequencies of the "stationary" words.

Symbolic indexes							
A-words				*S*-words			
A_b	A_t	ΔA	Δa	S_b	S_t	ΔS	Δs
0.03	0.23	0.20	1.56	0.62	0.27	−0.36	−0.92
0.18	0.31	0.12	0.50	0.30	0.22	−0.08	−0.28
0.00	0.07	0.06	1.72	0.60	0.35	−0.25	−0.53
0.10	0.33	0.23	1.06	0.42	0.23	−0.19	−0.58
0.00	0.02	0.02	1.19	0.65	0.51	−0.15	−0.27
0.05	0.24	0.19	1.34	0.50	0.18	−0.32	−0.94
0.22	0.31	0.10	0.38	0.31	0.22	−0.09	−0.33
0.03	0.17	0.13	1.32	0.61	0.28	−0.33	−0.72
0.03	0.23	0.21	1.60	0.42	0.28	−0.14	−0.39
0.02	0.06	0.04	1.08	0.61	0.39	−0.23	−0.46
0.09	0.23	0.15	0.93	0.45	0.26	−0.18	−0.51
0.04	0.32	0.28	1.55	0.47	0.22	−0.25	−0.70
0.00	0.07	0.06	1.63	0.61	0.43	−0.17	−0.34

the last one can be used and understood more easily. This is important for avoiding wrong uses of mathematical models. For example, in the medical literature linear autoregressive models are often used to estimate spectral densities. However, it is widely believed that linear models are not always adequate for describing *RR* sequences.

Second, data series, for example, long *RR* series, may contain many missing values. Methods based on the distribution of short words can easily cope with this problem by simply avoiding strings containing missing values. Spectral analysis needs to interpolate missing values according to more or less arbitrary criteria.

Third, data series are often nonstationary, for example, the *RR* sequence soon after the tilt. A method widely used in time series analysis for reducing nonstationary behaviors is to differentiate the series. Symbolic analysis, which is based on coding differences, directly embeds this method.

Finally, note that the values of the relative indexes for symbolic analysis, in columns 4 and 8 of Table II, are greater than the corresponding ones for spectral analysis, in columns 4 and 8 of Table I. This seems to suggest that the former method is more sensitive than the latter.

The application of symbolic methods in the analysis of *RR* sequences has a lot of flexibility and can be improved in several directions: one can consider longer binary words, define ternary words by using a threshold coding, introduce different grouping of words, or consider permutation instead of words. At this stage of the research it is not possible to state *a priori* which is the best method. On the base of our previous work our opinion is that this must be settled case by case depending on the nature of the data to be analyzed.

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