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Empirical Mode Decomposition to Assess Baroreflex Gain from Spontaneous Variability during Exercise in Humans

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Abstract—**Estimation of the baroreflex gain has become an important tool in clinical practice in order to assess cardiac autonomic system control. Spectral analysis and sequence analysis techniques based on the spontaneous variability of systolic arterial pressure and heart period have been proposed to evaluate the baroreflex gain. These analyses can be significantly altered by the presence of nonstationarities. Recently, the empirical mode decomposition (EMD), a signal processing technique particularly suitable for nonstationary series, has been proposed as a new tool for data analysis. The aim of this study is to propose EMD-based approaches to the evaluation of the baroreflex gain to account for the possible presence of nonstationarities of systolic arterial pressure and heart period series.**

I. Introduction

THE observation that oscillations in the heart period (RR interval) and the systolic arterial pressure (SAP) are correlated around 0.1 Hz and at the frequency of respiration has prompted many researchers to focus on the interrelationship between these two signals.

Usually, to study this phenomenon, an experimental protocol capable of evoking an autonomic response (i.e., the head-up tilt test), is applied to patients in standardized conditions [1], and the magnitude of the heart rate variability (HRV) changes is assessed and compared with values derived from a healthy population. Among the possible autonomic tests that can be utilized to evoke a cardiovascular response, physical exercise is a good candidate as it can evoke an important cardiovascular response especially when protocols using incremental loads over treadmill [2] or cycloergometer [3] are applied.

Several techniques have been proposed to evaluate the baroreflex gain based on the spontaneous variability of SAP and RR intervals [4]. Among them, the baroreflex sequence analysis is based on the detection of sequences of SAP and RR values characterized by the simultaneous increase or decrease of both variables [5], while the spectral method relies on the calculation of the power spectrum of RR interval and SAP variability series [6].

One important limitation of both these methods is that results can be significantly distorted by nonstationarities characterizing the RR and SAP series. Indeed, using the spectral method the presence of nonstationarities might produce shifts of the central frequency of the rhythms outside the inferior and superior limits defining the frequency bands, while using the baroreflex sequence analysis, nonstationaries might reduce the number of baroreflex sequences and the resulting correlation between RR and SAP samples.

Recently, the empirical mode decomposition (EMD), a signal processing technique particularly suitable for nonstationary series, has been proposed as a new tool for data analysis. This technique performs a time adaptive decomposition of a complex signal into elementary components [7]. The RR time series can be decomposed into oscillatory modes from which the corresponding powers can be calculated.

The aim of this study is to propose two EMD-based approaches for the evaluation of the baroreflex gain capable to deal with nonstationarities characterizing RR and SAP variabilities during a mild supine progressive bicycle exercise protocol. The EMD-based approaches were compared with standard baroreflex gain estimate methods.

II. Methods

A. Experimental Protocol

A progressive exercise effort able to evoke a-priori well known modifications on the autonomic nervous system response was utilized to test the performances of the developed methods in assessing changes of the baroreflex gain in 13 healthy volunteers. More specifically after a 10-min period which is necessary for stabilization, 10-min of control recording at rest was obtained with the subject in recumbent position. Subsequently every subject performed a three-step, progressive, supine, electronically braked, bicycle exercise on the horizontal bicycle. The incremental work test consisted of three exercise stages of 4-min each at 10% (Exe1), 20% (Exe2), and 30% (Exe3) of the nominal individual maximum effort ($V_{O2,max}$). The electrocardiogram (ECG), the arterial pressure signal (via a pletysmographic

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non-invasive device: Finapress, Ohmeda, Englewood, USA) and the respiratory signal obtained with a piezoelectric transducer (Marazza, Monza, Italy) were recorded and sampled at 300 Hz in thirteen normal subjects.

B. Signal Analysis

From the ECG, the heart period was measured. The QRS detection was performed by means of a threshold-derivative algorithm. After fixing the R peak with minimum jitters by means of parabolic interpolation, the temporal distance between two consecutive R peaks (RR interval) was measured. From the arterial pressure signal, the i-th systolic arterial peak was searched inside the i-th RR interval, thus obtaining the beat-to beat-series of the SAP values. The RR interval was expressed in ms and the SAP series in mmHg.

B.1. Spectral Analysis

Variability series of approximately 300 beats were analyzed by means of autoregressive (AR) spectral methods with software developed in-house. The Levinson–Durbin recursion was used to identify the coefficients of the AR model [8] and the order was chosen (between 4 and 12) accordingly to the Akaike figure of merit. The AR spectral decomposition procedure was applied to calculate the power of the oscillations embedded in the series [9]. The rhythms were classified [10] as very low frequency (VLF, <0.04 Hz), low-frequency (LF, ranging from 0.04 to 0.14 Hz) and high frequency (HF, ±0.03 Hz around the respiratory frequency detected on the respiratory signal) oscillations. The power indexes were expressed in absolute units (LF_{RR}, HF_{RR}, LF_{SAP} and HF_{SAP}).

B.2. Empirical Mode Decomposition Analysis

The EMD is able to empirically identify and extract all the oscillatory modes present in a signal at different length scales. Each extracted mode, named intrinsic mode function (IMF), is characterized by the following properties: it is symmetric with respect to zero, has a unique local frequency, and different IMFs do not share the same frequency at the same time [7].

The decomposition of a series *X* is trained by an iterative procedure in six steps:

1) Identification of all the extrema (maxima and minima) of the series *X*.

2) Generation of the upper and lower envelope of *X* via cubic spline interpolation among all the maxima and minima of *X*, respectively.

3) Point by point averaging of the two envelopes to compute the local mean series *m*.

4) Subtraction of the local mean series *m* from the data to obtain an IMF candidate $h=X-m$.

5) Check the properties of *h*:

- if *h* doesn't satisfy the previously defined properties necessary to be an IMF, replace *X* with *h* and repeat the procedure from step 1.
- if *h* has the above mentioned properties to be an IMF, evaluate the residual $r= X-h$.

6) Repetition of the procedure on the residual signal from step 1 to step 5.

The process ends when the range of the residual *r* satisfies a predefined stopping criterion (i.e., *r* is below a predetermined level, or has a monotonic trend [7]). At the end, a collection of *n* components h_i (i=1,..,n) and a residual *r* are obtained. The original series *X* can be exactly reconstructed as a linear combination by:

$$X = \sum_{i=1}^{n} h_i + r \qquad (1)$$

Each IMF has a well defined Hilbert transform from which the instantaneous frequencies can be calculated [7].

In order to extract parameters that could be comparable to the spectral indexes, we considered: the mode with the characteristic frequency (defined as the median value of the instantaneous frequency obtained by means of the Hilbert spectrum [11]) closest to 0.1 Hz (LF1); the first mode with characteristic frequency lower than LF1 (LF2) if it belongs to the LF band as defined for spectral analysis; and the modes with characteristic frequencies greater than LF1 (HF1, HF2, etc) belonging to the HF band as defined for spectral analysis [12]. We computed the corresponding powers LF_{RR}, HF_{RR}, LF_{SAP}, HF_{SAP} as the sum of variances of LF and HF modes respectively. The modes with characteristic frequencies lower than LF2 were considered as VLF modes.

C. Traditional methods to estimate baroreflex gain

C.1. Baroreflex Sequence Analysis

This method is based on the search for sequences characterized by the contemporaneous increase (positive sequence) or decrease (negative sequence) of RR interval and SAP. The lag τ between RR interval and SAP samples is chosen as the lag producing the maximum in the normalized RR-SAP cross-correlation function. Both positive and negative sequences are referred to as baroreflex sequences if they match the following prerequisites:

1. the total of RR variations is > 5 ms,
2. the total of SAP variations is > 1 mmHg,
3. the length of the sequences is 4 beats (3 variations).

For each sequence the slope of the regression line in the ($SAP_{i-\tau}$, RR_i) plane is calculated. All the slopes with correlation coefficient >0.85 are averaged, and this average, represented by α_{BS} is considered as a measure of the baroreflex gain [5]. The reliability of α_{BS} depends on the number of baroreflex sequences detected in the series.

C.2. Power Spectral Analysis

The method relies on the calculation of the power spectrum of the RR and SAP series and on the evaluation of the power inside two bands, the LF and HF bands. Two indexes estimating the baroreflex gain are calculated [6] as

$$\alpha_{PS(LF)} = \sqrt{LF_{RR}/LF_{SAP}} \qquad (1)$$

$$\alpha_{PS(HF)} = \sqrt{HF_{RR} / HF_{SAP}} \quad (2)$$

where LF_{RR}, LF_{SAP}, HF_{RR} and HF_{SAP} represent the power in LF and HF bands detected on RR interval and SAP series, respectively. These indexes are reliable if the coherence function (K^2) sampled at LF and HF is greater than 0.5, thus meaning that the RR and SAP signals are significantly correlated at that specific frequency.

D. EMD-based methods to estimate baroreflex gain

D.1. EMD-based baroreflex sequence analysis

We applied the EMD to RR and SAP series and assessed the baroreflex gain by means of baroreflex sequence analysis applied to the LF and HF modes (EMD-$\alpha_{BS(LF)}$ and EMD-$\alpha_{BS(HF)}$), to the combination of them (EMD-$\alpha_{BS(LF+HF)}$), and to the VLF modes (EMD-$\alpha_{BS(VLF)}$).

D.2. EMD-based spectral analysis

We applied the EMD to the RR and SAP series, then EMD-based LF_{RR}, LF_{SAP}, HF_{RR} and HF_{SAP} were calculated and EMD-$\alpha_{PS(LF)}$ and EMD-$\alpha_{PS(HF)}$ were derived.

E. Statistical Analysis

The results are expressed as median and first-third quartile range.

One-way ANOVA for repeated measures was utilized, whenever possible, to evaluate the differences in the measured variables elicited by the different experimental steps with respect to the relevant baseline parameter. When the normality test failed, Friedman Analysis of Variance on ranks (Dunnett's test) was used.

*, indicate $p<0.05$ significativity compared to rest.

#, indicate $p<0.05$ significativity between experimental steps.

III. RESULTS

The baroreflex sensitivity computed by standard spectral indexes $\alpha_{PS(LF)}$ and $\alpha_{PS(HF)}$ as well as by sequence analysis index α_{BS} was significantly decreased only at Exe3, compared to rest (Fig. 1(a,d,g) respectively). EMD filtering enabled a clearer estimation of the progressive baroreflex gain decrease during exercise, by showing significant changes otherwise missed by standard methods. In particular, EMD-based $\alpha_{PS(LF)}$ showed a significant decrease at Exe2 and Exe3 compared to rest while EMD-based $\alpha_{PS(HF)}$ was found significantly and progressively decreased with all the exercise phases compared to rest (Fig. 1(b,e) respectively). Moreover, the intensity of exercise had a remarkable effect on the EMD-based $\alpha_{PS(LF)}$ and $\alpha_{PS(HF)}$ as shown by the significant difference occurred between Exe1 and Exe3.

Interesting results were also obtained by using EMD-based α_{BS} index. Baroreflex sequence method was applied to not only to the LF and HF modes combined together, but also to the LF or HF modes taken separately and to the combination of the remaining modes in the VLF band. In particular, EMD-$\alpha_{BS(LF+HF)}$, EMD-$\alpha_{BS(LF)}$ and EMD-$\alpha_{BS(HF)}$ were all found significantly reduced with Exe2 and Exe3 compared to rest (Fig. 1(h,c,f) respectively). The intensity of exercise had a marked effect on the EMD-based $\alpha_{BS(LF+HF)}$, $\alpha_{BS(LF)}$ and $\alpha_{BS(HF),}$ as shown by the significant difference between Exe1 and Exe3. The combined modes at VLF exhibited some baroreflex sequences but their gain did not decrease during exercise (Fig. 1(i)).

IV. DISCUSSION

The good performances of EMD-based approaches can be explained in terms of their ability of accounting for nonstationarities present in RR and SAP series.

The strict definition of the inferior and the superior limits of the frequency bands peculiar to the spectral method for the baroreflex estimate, cannot account for the unavoidable intra or inter-individual variability that naturally occurs. Indeed, the frequency of LF and HF rhythms might undergo changes during the recording and these modifications might be even relevant (e.g. HF rhythms could enter into the LF band, or LF oscillations could become very slow and escape the LF band, especially when vasomotor control overcomes baroreflex regulation). In addition, the frequencies of the LF and HF rhythms might vary between subjects according to the individual metabolic demands and response to internal and external stimuli. The application of EMD-based approach allows the rigid definition of the limits of the frequency bands typical of the spectral method to be overcome. Indeed, the decomposition of the series into modes or components does not impose a strict association between modes and the LF and HF bands, thus being suitable to follow changes of frequency in the rhythms.

The application of EMD approach improves also the baroreflex sequence method. This result can be again explained in terms of the ability of EMD to deal with non stationarities. Indeed, nonstationarities, by reducing the number of baroreflex sequences and the correlation between RR and SAP samples, increase the variance of the estimate of the baroreflex gain, thus preventing to observe significant differences among experimental conditions.

It is worth noting that the application of baroreflex sequence method to the VLF modes allowed the detection of some baroreflex sequences whose gain did not decrease during exercise, thus suggesting a non-baroreflex origin of the detected sequences.

V. CONCLUSIONS

The changes of the baroreflex gain during a mild exercise protocol were more adequately assessed by using EMD procedures than using the traditional techniques. This result might be explained in terms of a stronger ability of EMD in dealing with nonstationarities present in the heart period variability [13].

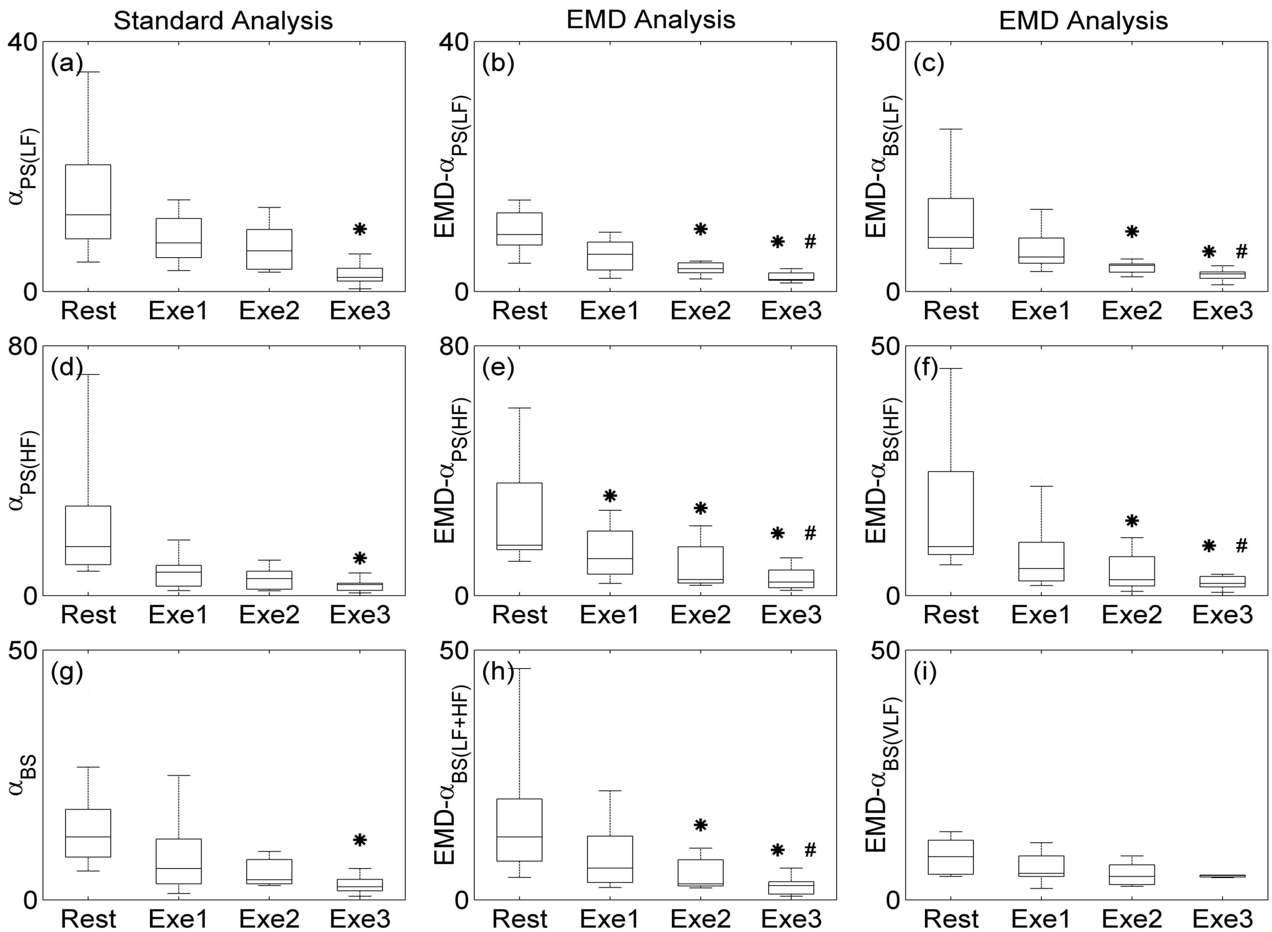

Fig. 1 The box-and-whisker plots summarize the results relevant to the standard (a,d) and EMD-based (b,e) spectral analysis as well as to the standard (g) and EMD-based (c,f,h,i) sequence analysis for the baroreflex gain estimation performed on the incremental bicycle exercise protocol at rest, during Exe1, Exe2 and Exe3.

The symbol * indicates $p<0.05$ vs Rest; #: $p<0.05$ vs Exe1.

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