Sympatho-Vagal Activity Described by the Complex and Deterministic Behavior of Heart Rate Variability

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Abstract

This study aims to present new variables to improve the characterization of the autonomous nervous system function by analyzing the heart rate variability. These new variables are the effective energies (Efe), defined from the Hartley-Shannon theorem, in the three frequency bands Efe_{VLF}, Efe_{LF} and Efe_{HF} (VLF, 0-0.04 Hz; LF, 0.04-0.15 Hz; HF, 0.15-0.45 Hz). The effective energy is obtained using a complexity measure of the RR signal (Shannon entropy, SH) and the instantaneous frequency, *defined from the time-frequency representation (TFR). Two groups of subjects have been studied: 53 patients with idiopathic dilated cardiomyopathy (IDC) and 64 healthy people considered as the control group (NRM). The effective energies obtained in the VLF, LF and HF presented statistical significant differences ($p<0.005$) characterizing IDC patients. The instantaneous frequency contained in the VLF band was lower in IDC patients than in the control group. The main complexity differences given by the analyzed entropies were obtained in the LF and HF bands.*

1. Introduction

Different studies have shown that the heart rate variability (HRV) can reflect the activity of the autonomous nervous system. The influence of the autonomous nervous system in the cardiac diseases has been largely analyzed using classical measurements of the time-domain and frequency-domain analysis [1,2]. Recent studies, based on the spectral density analysis, show that patients with myocardial infarction that suffered malignant ventricular tachycardia present a substantial decrease of the components in the low and the high frequency bands (0.04-0.45 Hz) of the HRV [3]. The application of this knowledge with the non-linear dynamics analysis of the cardiac system can be useful in the stratification of the sudden death risk [4-6].

In this study, new variables are proposed to improve the characterization of the autonomous nervous system function by analyzing the HRV. These new variables are the effective energies (Efe), defined from the Hartley-Shannon theorem, in the three frequency bands Efe_{VLF}, Efe_{LF} and Efe_{HF} (VLF, 0-0.04 Hz; LF, 0.04-0.15 Hz; HF, 0.15-0.45 Hz). The effective energy is obtained using a complexity measure of the RR signal (Shannon entropy, SH) and the instantaneous frequency, defined from the time-frequency representation (TFR).

The results have been statistically analyzed by means of a discriminate analysis and a univariable analysis of the variance (ANOVA), with the objective of finding indexes able to characterize pathological processes in cardiac illnesses. In all variables was considered a significant level of $p<0.05$.

2. Material and methods

2.1. Analyzed patients

In this work we have analyzed 24-h Holter ECG digital recordings from the IDEAL database [7], with 3 orthogonal leads sampled at a frequency of 200 Hz. Two groups of subjects have been studied: Group IDC, 53 patients with idiopathic dilated cardiomyopathy (age 50±14); Group NRM (control group), 64 healthy people (age 36±16).

2.2. Methodology

The RR series were obtained beat-to-beat using software developed by our group [8], selecting the lead with the highest signal-to-noise ratio. Only night segments of RR were considered from 0:00 h to 5:00 h, corresponding to 17000 beats approximately.

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An adaptive filtering was applied to the RR signals, using the LMS algorithm, in order to eliminate the artifacts. The RR sequences were interpolated using cubic splines and sampled at 1 Hz.

2.2.1. Time-frequency representation

Sequences of 400 seconds of the RR signal were considered each 15 minutes. From each RR sequence of 400 s, time frequency distribution (TF_{xx}) was obtained.

Choi-Williams distribution (TF_{xx}) was selected for the analysis, which general expression [9] is:

$$TF_{XX}(t,f) = \iint \psi\ (t-t',f-f')W_{x,x}(t',f')dt'df' \qquad (1)$$

where $W_{x,x}(t,f)$ is the Wigner distribution, $\Psi(t,f)$ the Choi-Williams exponential, x(t) the analyzed signal and x^* (t) its conjugate. The optimal parameter value σ_c was estimated as 0.15.

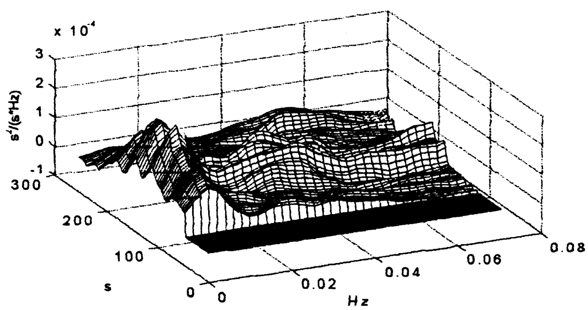

Figure 1. Spectrum of the RR signal in the VLF band for a given time.

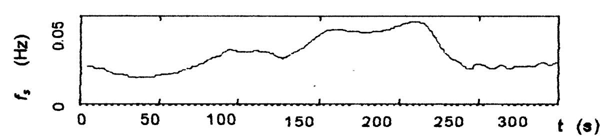

Figure 2. Instantaneous frequency of a RR sequence in the VLF band.

The instantaneous frequency function (figure 1) can be defined as the average frequency of the spectrum for a given time

$$f_s(t) = \frac{\int f \cdot TF_{xx}(t,f)df}{\int TF_{xx}(t,f)df} \qquad (2)$$

and it has been calculated in each one of the bands (VLF, LF, HF). Also, the energy at each band has been calculated by means of the integral of the time-frequency distribution, and normalized by the total energy. For each subject, new functions were obtained as the mean of all instantaneous frequency functions in each spectral band (figure 2), and the mean value of these instantaneous frequency functions (f_{VLF}, f_{LF}, f_{HF}) calculated. The mean value of the energy in each band (e_{VLF}, e_{LF}, e_{HF}) was determined by a similar way.

2.2.2. Estimated entropies

For this analysis the time-series RR was previously filtered in the following frequency-bands, VLF, LF and HF by means of a 200-order FIR filtering. Shannon and Rényi entropies were applied to windows of 400 seconds considered every 15 minutes of each RR signal without filtering (TF) and of the signal filtered in the VLF, LF and HF bands. The entropies were calculated from a three-dimension phase-space constructed considering different lags τ (2, 10 and 20 seconds). Figure 3 shows an example of a three-dimension phase-space with a lag τ = 10s.

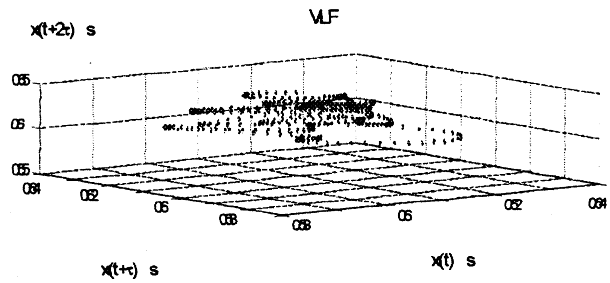

Figure 3. Phase-space, considering a lag τ=10s, of a window of 400 s of the RR signal in the VLF band.

The probability density function P(i) was calculated on the phase-space, considering each of its coordinate quantified in N=16 levels, equivalent to quantify the phase-space in N^3=4096 levels. The quantification was done using the complete signal. For each patient, the minimum and maximum values of the signal were calculated, considering the signal without filtering band and filtered in each band. In this way, for each subject and for each frequency band all 400s-windowed signals have the same range. Finally, in each window and in each one of the different frequency bands and lags τ the entropies of Rényi, for the orders q=0.25 and 2, and of Shannon were calculated.

Rényi: $$H = \frac{1}{1-q}\log_{10}\left(\sum_{i=1}^{N^3} P^q(i)\right) \qquad (3)$$

Shannon: $$H = -\sum_{i=1}^{N^3} P(i)\cdot \log_{10}(P(i)) \qquad (4)$$

Figure 4 shows the evolution of the entropies for a RR signal of the IDC group. The averaged values of the temporal evolutions of the entropies were calculated, obtaining for each lag the Rényi entropy variables of order 0.25 ($Re25\_2_x$, $Re25\_10_x$, $Re25\_20_x$), the Rényi entropy of order 2 ($Re2\_2_x$, $Re2\_10_x$, $Re2\_20_x$) and the Shannon entropy variables (SH_2_x, SH_10_x, SH_20_x). The sub-index x denotes the frequency band TF, VLF, LF, or HF.

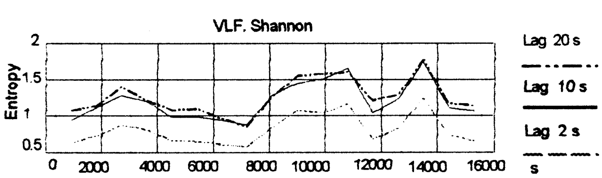

Figure 4. Evolution of the Shannon entropies, for the lags 2, 10 and 20 s, calculated for a RR signal in the VLF band.

2.2.3. Relationship between effective energy, bandwidth and entropy

The object of this section is to establish a relation between entropy, bandwidth and energy in order to obtain new variables to improve the characterization of the autonomous nervous system. We consider the transmission of the RR signal through a channel, and the Hartley-Shannon theorem [10] can be applied:

$$C = B\log_2\left(1+\frac{S}{N}\right) \qquad (5)$$

where C is the capacity of the communication channel, B is the bandwidth of the channel, S is the power of the signal and N is the noise power.

As the transmission of the signal through the channel implies to codify previously this signal, we take into account that this codification is the algorithm applied in the calculation of the entropy.

A sampled RR signal, with certain entropy, crosses a system with bandwidth B and at the output the following variables are measured: entropy H_x, instantaneous frequency f_x and energy e_x. In fact, they are the obtained values of the RR signal after having been processed and filtered in the VLF, LF and HF frequency bands. As the entropy at the input will not be the same that the entropy at the output, then this system can be associated with a channel capacity. This is valid when the noise is gaussian, and we consider the hypothesis that the channel introduces this type of noise. We will have three systems or channels, determined by their band widths, VLF (0-0.04 Hz), LF (0.04-0.15 Hz) and HF (0.15-0.45 Hz) that represents the filtering applied to the RR signal in each one of these bands.

The channel capacity C can be measured by the entropy rate $R=rH_x$ where r is the speed of transmission of pulses. The bandwidth B of the channel could be substituted by the instantaneous frequency, since it is the frequency where the energy of a signal is located in a given time. Then the following equation is obtained from equation (5)

$$rH_x = nf_x.\log_2\left(1+\frac{S}{N}\right) \qquad (6)$$

where n is the number of pulses in that the main pulse is coded. As the relationship between powers is the same that between energies, for a given interval of time, the signal to noise ratio will be measured as the ratio between energies. In this way, the energy e_x measured at the output of the system is the combined signal:

$$e_x = Efe_x + N \qquad (7)$$

where Efe_x can be called the effective energy of the signal. Its meaning could be considered as the minimum energy of the signal in this band, in presence of noise, containing the information H_x. From equations (6) and (7), and considering the minimum sampling frequency of the signal for the band in study r=2B, the following equation is obtained:

$$Efe_x = e_x\left(1-2^{\frac{-2BH_x}{nf_x}}\right) \qquad (8)$$

where the sub-index x denotes the VLF, LF and HF frequency bands. Also, this expression could be considered as a transformation of the energy variable in function of the entropy signal.

For all the subjects of both groups, the variables described in equation (8) have been calculated. The entropy variables have been calculated with a lag $\tau=10$. This expression will tend to concentrate the energy values for high and dispersed values of H_x. In this way, the effective energy can also be seen as a function that homogenizes the variance of the energy variable.

3. Results

Classic analysis of the RR signals was done in the time-domain comparing IDC and NRM groups. The averaged values of the RR signal (Group IDC, 917.5±152.5; Group NRM, 959.5±159) do not discriminate between the two analyzed groups, and the standard deviation (Group IDC, 83±38.5; Group NRM, 98±35.5) presents a significance level of p=0.028.

Table 1 presents the variables obtained applying time-frequency representation that shows the highest statistical significant level, when comparing IDC patients and healthy subjects (group NRM).

Table 1. Instantaneous frequencies in the very low (VLF) and high (HF) frequency bands.

Variable	IDC ($m \pm \sigma$)	NRM ($m \pm \sigma$)	p-value
f_{VLF}	0.0245±0.0036	0.0282±0.0027	<0.0001
f_{HF}	0.2639±0.0217	0.2473±0.0167	<0.0001

Characterizing IDC and NRM groups, the statistical analysis showed a statistical significance p <0.0005 for all the entropy variables, except for those calculated in the VLF band. Figure 5 shows graphically these results for the three bands, considering the Shannon entropy. The entropies in the total band TF follow the same tendencies that the sub-bands.

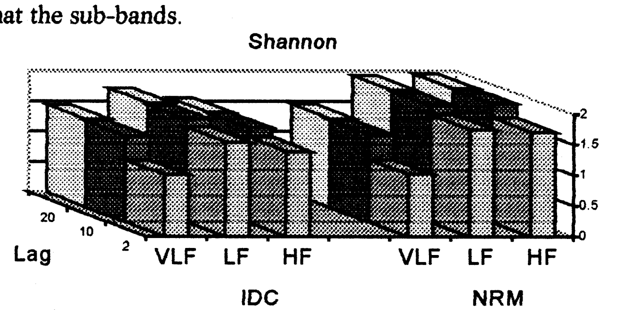

Figure 5. Shannon entropies of two groups of subjects (IDC and NRM) considering different frequency bands and lags.

Table 2 presents the effective energy variables obtained applying the Hartley-Shannon theorem that present the highest statistical significant level, when comparing IDC patients and healthy subjects (group NRM).

Table 2. Mean ± sd of the effective energy variables.

Variable	IDC ($m \pm \sigma$)	NRM ($m \pm \sigma$)	p-value
Efe_{VLF} ,(n=1)	0.596±0.145	0.526±0.122	0.005
Efe_{LF} ,(n=1)	0.113±0.031	0.156±0.036	<0.0001
Efe_{HF} ,(n=6)	0.230±0.134	0.310±0.164	0.005

A linear discriminate function has been constructed considering the following variables: Effective energy (Efe_x), instantaneous frequency (f_x), Shannon entropy (SH_x), and Rényi (Re_x) entropies of order 0.25 and 2, obtaining the following discriminate function:

$$D = -2.527 + 18.774\, Efe_{LF} - 3.913\, Re25\_2_{HF} + 4.991\, Re2\_2_{HF}$$

with a good compromise between the number of included variables and the sensitivity and specificity results.

Table 3. Results of the classification between subjects of the IDC and NRM groups using the leaving-one-out technique.

Groups	Well classified	Badly classified	%
IDC	44	9	83
NRM	52	12	81.3

This new variable D permits to stratify IDC group from NRM group with $p < 0.0005$. Using the cross-validation leaving-one-out technique, the obtained classification is shown in table 3.

In case that the discriminate analysis has been developed without considering the proposed effective energy variables, the obtained discriminate function is:

$$D = -4.285 + 2.716\, Re25\_2_{LF} - 5.252\, Re25\_2_{HF} + 6.140\, Re2\_2_{HF}$$

and the results obtained using the leaving-one-out technique are presented in the Table 4.

Table 4. Results of the classification between subjects of the IDC and NRM groups without considering the proposed effective energy variables.

Groups	Well classified	Badly classified	%
IDC	39	14	73.6
NRM	50	14	78.1

4. Conclusions

This study shows that the heart rate variability can provide valuable information when it is analyzed by means of non-linear dynamics methods and by means of instantaneous frequency calculated from time-frequency representation. Instantaneous frequencies in the very low frequency and high frequency bands have shown to be statistically significant. The entropies have shown that they are not sensitive to the lag, used to construct the phase-space, higher than 10 seconds. Moreover, comparing the behavior of the entropies between the groups and between the different frequency bands they have presented statistically significant differences. In this way, entropies are always higher in healthy subjects than in IDC patients and in these patients the entropies in the LF band are always significantly higher than in the HF band, when the average information of the signals in the VLF band is similar for both groups.

On the other hand, the effective energies, build from Hartley-Shannon theorem and calculated using entropy and instantaneous frequency measures, have permitted to construct a discriminate function containing the components Efe_{LF}, $Re25\_2_{HF}$ and $Re2\_2_{HF}$, ($p<0.0005$), with 83 % of IDC patients and 81.3 % of NRM subjects well classified.

Acknowledgements

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References

[1] Bianchi AM, Mainardi LT, Meloni C, Chierchia S, Cerutti C. Continuous monitoring of the sympatho-vagal balance through spectral analysis. IEEE Engineering in Medicine and Biology 1997;16:64-73.

[2] Bigger JT, Fleiss JL, Steinman RC, Rolnitzky LM, Kleiger RE, Rottman JN. Correlations among time and frequency domain measures of heart period variability two weeks after acute myocardial infarction. Ambulatory Journal of Cardiology 1992;69:891-8.

[3] Làng E, Caminal P, Horváth G, Jané R, Vallverdú M, Slezsák I, Bayés de Luna A. Spectral analysis of heart period variance (HPV) – a tool to stratify risk following myocardial infarction. Journal of Medical Engineering & Technology 1998;22:248-56.

[4] Kurths J, Voss A, Witt A, Saparin P, Kleiner HJ, Wessel M. Quantitative analysis of heart rate variability. Chaos 1995;5:88-94.

[5] Lombardi F, Sandrome G, Mortara A, Torcillo D, La Rovere MT, Signorini MG, Cerutti S, Malliani A. Linear and no linear dynamics of heart rate variability after acute myocardial infarction with normal and reduced left ventricular ejection fraction. Am J Cardiol 1996;77:1283-88.

[6] Zebrowski JJ, Poplawska W, Baranowski R. Entropy, pattern entropy and related methods for the analysis of data on the interval between heart beats from 24 hours electrocardiograms. Physical Review E 1998;50:4187-205.

[7] IDEAL Database. Intercity Digital ECG Alliance. University of Rochester Medical Center 1997.

[8] Laguna P, Jané R, Caminal P. Automatic detection of wave boundaries in multilead ECG signals: Validation with the DSE database. Computer and Biomedical Research 1994;27:45-60.

[9] Cohen L. Time-frequency analysis. Prentice Hall Signal Processing Series, 1995

[10] Lathi BP. Introduction to the communication theory systems. Limusa S.A., 1974

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