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New insight into arrhythmia onset using HRV and BPV analysis

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Abstract — **In this paper Heart Rate Variability (HRV) and Blood Pressure Variability (BPV) were analyzed before the onset of cardiac arrhythmia in order to derive markers for short-term forecasting. The (a) coherence between systolic blood pressure (SBP) and cardiac oscillations in low-frequency (LF) and high-frequency (HF) band; (b) fluctuations of phase; (c) HRV and BPV as a LF power and HF power in frequency and time-frequency domain; (d) transfer function analysis of cardiovascular signals were analyzed. Arrhythmia was preceded by: a) lower coherence; b) increase in fluctuations of phase between signals; c) higher spectral energy associated with respiratory frequency in blood pressure signal; d) raise of sympathetic outflow to the heart; e) decreased HRV. Cardiac arrhythmia was characterized mainly by an increase in LF power of blood pressure, cardiac signal and transfer function. During self-termination of arrhythmia a larger increased in total BPV and HRV was recorded. These results suggest that important information about both neuronal cardiovascular control and risk for spontaneous arrhythmia can be provided by combined analysis of frequency, phase, and time-frequency analysis of blood pressure and cardiac oscillation.**

Keywords - cross-spectral algorithm, wavelet analysis, arrhythmia, blood pressure and heart rate variability, wavelet coherence

I. Introduction

In the last decades, several studies have suggested the role of the autonomic nervous system (ANS) both in the genesis and maintenance some of arrhythmias [1-4]. Time and frequency domain analysis of heart rate variability (HRV) has been proven effective in describing alterations of ANS control mechanisms and in identifying patients with increased cardiac and arrhythmic mortality [4-9].

Studies on HRV analysis have shown a relationship between sympathovagal dysfunction and the occurrence of atrial fibrillation (AF) [3-7] or ventricular tachycardia (VT) [8-9], suggesting a potential role of HRV as an earlier marker of disease. However, studies analyzing variability of the length of individual heart cycles in implantable cardioverter defibrillators (ICD) stored data led to different results [10-12].

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Moreover, inappropriate or unnecessary ICD discharges remain an important clinical problem as they cause pain, psycho-social and sometimes proarrhythmic effects [13]. The discrepancies might be caused by different methods for HRV analysis, but also by the study design - the majority of the methods describing the ANS control mechanisms or cardiac function using only cardiac electrical signals analysis.

Evidences showing that monitoring arterial pressure and heart rate may allow for early diagnosis of arrhythmia long before manifestation of its clinical symptoms are now emerging [14-16]. These multivariable studies adjusted for age, hypertension requiring treatment, and mean arterial pressure have suggested also that pulse pressure can predict future development of AF. The purpose of this study was to evaluate the relationship between blood pressure and cardiac electrical activity of the heart, by cross spectral algorithm, HRV and blood pressure variability (BPV) through spectral analysis, before, during, and after a self-terminating cardiac arrhythmia.

In this study, our team has developed a rabbit model for electrophysiological research related with ANS role on atrial fibrillation inducibility. In this model, atrial fibrillation has been provoked by a 50Hz pacing of atria, or by vagal and sympathetic electrical stimulation. During experimental work, one rabbit (from 22) developed a cardiac arrhythmia for about 7 minutes, before experimental procedure for ANS stimulation and high frequency pacing. The present work discuss the ability and importance of wavelet analysis, cross-spectral and transfer function algorithm to follow the short-term cardiovascular function changes before, during, and after self-terminating cardiac arrhythmia in this rabbit.

II. Methods

A. Study design

The details of animal model preparation to study the mechanism of atrial fibrillation (AF) are published elsewhere [5]. Briefly, the New Zealand white rabbit was anaesthetized, paralyzed, and artificially ventilated. After a medial thoracotomy, a bipolar electrode was placed on the right cervical vagus nerve for parasympathetic electrical stimulation whereas a concentric bipolar electrode was inserted in the intermediolateral cell column of the spinal cord, at T1 level, for sympathetic stimulation. A set of recording electrodes was also placed on the atrial epicardium and in the area surrounding the pulmonary veins. Blood

pressure, ECG and atrial electrograms were recorded throughout the experiment.

ECG and blood pressure were acquired at 1kHz (*PowerLab, AD Instruments*). Data were analyzed before, during and after the arrhythmia in the following way: 1 minute of baseline in the beginning of recording, 2 minutes before arrhythmia onset, 2 minute during the arrhythmia and 2 minute after the termination of arrhythmia. Intervals between changes in cardiac electrical activity were detected using dynamically varying thresholds in order to identify R wave or AF or ventricular tachycardia (VT) I wave. Frequency and time-frequency analysis of HRV and BPV power spectra were estimated for R-R or I-I intervals and systolic blood pressure signals. The subtraction of a linear trend from the data was realized using a multiresolution wavelet decomposition algorithm. The signals were decomposed using db10 mother wavelets and reconstructed without coefficient of decomposition corresponding to band frequencies between 0-0.05 Hz. The fast Fourier transform (FFT), continuous wavelet decomposition (CWT) and complex wavelet transform were used to estimate the power spectra.

B. Cross spectrum

Cross-spectrum were calculated between the blood pressure variables (SAP) and the R-R or I-I intervals.

The power spectrum for blood pressure signal x_n and cardiac signal y_n was calculated as:

$$P_{xx}(f) = \left|X_x(f)\right|^2 \text{ and } P_{yy}(f) = \left|Y_y(f)\right|^2 \quad (1)$$

The cross spectrum of x_n against y_n is defined as:

$$P_{x,y}(f) = X_x^*(f) Y_y(f) \quad (2)$$

where the * denotes complex conjugate. We calculate the

$$P_{x,y}(f) = L(f) - iQ(f) \quad (3)$$

with $L(f)$ the cross spectrum and $Q(f)$ the quadrature spectrum. The smoothed squared –coherence estimator is:

$$k^2(f) = \frac{\overline{(L(f))}^2 + (\overline{Q}(f))^2}{\overline{P_{xx}}(f)\overline{P_{yy}}(f)} \quad (4)$$

where the bar denotes smoothing (triangular in our case).

The cross spectrum between two signals consists of two parts: the coherence spectrum and the phase spectrum. The coherence spectrum having value between 0 and 1, is a measure of the correlation between the variations of two signals at the frequency f.

The smoothed estimator of the phase spectrum was calculated as:

$$\phi(f) = \arctan\left(-\frac{\overline{Q}(f)}{\overline{L}(f)}\right) \quad (5)$$

The phase spectrum $\phi(f)$ indicates at each frequency f the phase difference (lead or lag) between the signals. All phase spectra we present have been scaled in the region -180° to +180°. A negative value of $\phi(f)$ implies that the pressure variation leads the interval variation at this frequency; for a positive phase the reverse holds. If the coherence is low for a certain frequency, the phase at this frequency cannot be estimated reliably. In the phase spectra, lines between successive values were suppressed if the difference was larger than 180° because in these cases the phase has passed the -180° border to reappear at +180°, or vice versa. If no such method is used, confusing vertical lines may appear in the phase spectra.

When the observation is based entirely on frequency analysis, information on dynamically varying or "short time" dependence between the signals or the temporal structure of coherence, which is useful in the study of cardiovascular dynamics, is not obtained. Wavelets combine high temporal resolution with good frequency resolution and offer a reasonable balance between these parameters. The continuous wavelet transform (CWT) can decompose a signal into a set of finite basis functions. Wavelet coefficients $W_x(a,\tau)$ are produced through the convolution of a mother wavelet function $\psi(t)$ with the analyzed signal x_n where a and τ denote the scale and translation parameters. Daubechies mother wavelet was applied to SAP, R-R or I-I intervals in order to estimate time-frequency changes in blood pressure and cardiac signals before, during and after arrhythmia using CWT. The CWT has edge artifacts because the wavelet is not completely localized in time. In order to eliminate outliers the normalization was applied.

Despite its efficient computational algorithm, the wavelet transform suffers from three main drawbacks. The discrete and CWT is shift sensitive because input signals shifts generate unpredictable change in wavelet coefficients. The discrete and CWT suffer from poor directionality and lacks the phase information that accurately describes non-stationary signals behavior. To overcome these drawbacks, the complex wavelet transform was applied. In this study, complex wavelet transform was used for feature extraction from cardiovascular signals analyzed for intervals of 60s. We used the complex Morlet wavelet, given by:

$$\psi_0(t) = \pi^{-1/4} e^{i\omega_0 t} e^{-1/2 t^2} \quad (6)$$

where ω_0 is the wavelet central pulsation.

The Gaussian's second order exponential decay of the Morlet function gives a good time and frequency localization. We choose the complex WT (cMWT) as it provide the signal amplitude and phase simultaneously and permits investigation on the coherence/synchronization between two signals. The cross wavelet transform of two time series x_n and y_n is defined as:

$$W_{xy}(a,\tau) = W_x(a,\tau) W_y^*(a,\tau) \quad (7)$$

where * denote complex conjugation.

The complex argument *arg* (W^{xy}) can be interpreted as the local relative phase between x_n and y_n in the time

frequency space. The plot of $|W_{xy}(a,\tau)|^2$ is called cross scalogram. It provides a mean to indicate coincident events over frequency, for each time in the signals x_n and y_n. High frequency oscillation of the signals (HF; 0.25-1.0 Hz) are represented between scales 1-8, low frequency (LF; 0.1-0.25 Hz) and very low oscillation (VLF; 0.0-0.1 Hz) are represented at scales 8-32, and 32-64, respectively.

Cross wavelet power reveals areas with high common power. Following Torrence and Compo (1998) [17], we define the wavelet coherence of two time series as:

$$(C(a,\tau))^2 = \frac{|W_{xy}(a,\tau)|^2}{W_{xx}(a,\tau)W_{yy}(a,\tau)} \quad (8)$$

with the cross scalogram defined as:

$$W_{xy}(a,\tau) = \frac{1}{a}\int_{-\Delta t}^{+\Delta t} W_x(a,\tau+t)W_y^*(a,\tau+t)dt \quad (9)$$

When using this definition the coherence is bounded between $0 \le ((C(a,\tau))^2 \le 1$.

If the two series are physically related, we would expect a consistent or slowly varying phase lag that can be tested against mechanistic models of the physical process.

III. Results and Discussion

In this study we have shown that the arrhythmic heart activity signals have time–dependent properties since they reflect complex pattern of electrical activation wave.

Using power spectrum, information on average signal behavior over a long time interval could be observed. Wavelets transform added information on the distribution of signal energy in the time-frequency domain. By using wavelets transform rapidly transient oscillation can be clearly detected at the correct latencies and frequencies. An increase power in FFT spectrum of BPV signal, in HF band (862.805 *versus* 305.093 $mmHg^2/Hz$) occurred before arrhythmia while BPV LF component increased during arrhythmia and recovery of sinusal rhythm (Table 1).

Before arrhythmia event and important decrease in HRV (from 0.0913 to 0.0017 ms^2/Hz, Table 2) and increase in LF/HF ratio was observed in frequency domain analysis of the cardiovascular signals.

Table 1. Blood Pressure Variability before and during arrhythmia.

	BPV				
	LF	LFn	HF	HFn	TV
	$mmHg^2/Hz$		$mmHg^2/Hz$		$mmHg^2/Hz$
Baseline	21,9E+0	45,3E-3	461,5E+0	954,7E-3	483,4E+0
Before_1 A	21,2E+0	64,8E-3	305,1E+0	935,2E-3	326,2E+0
Before_2 A	24,8E+0	27,9E-3	862,8E+0	972,1E-3	887,6E+0
Arrhythmia_1	11,3E+3	795,8E-3	2,9E+3	204,2E-3	14,3E+3
Arrhythmia_2	17,6E+3	930,6E-3	1,3E+3	69,4E-3	19,0E+3
Recovery_1	10,9E+3	770,9E-3	3,2E+3	226,1E-3	14,2E+3
Recovery_2	2,4E+3	454,8E-3	2,9E+3	545,2E-3	5,3E+3

LF- Low Frequency component (0.10-0.25 Hz); LFn – normalized LF; HF – High Frequency component (0.25-1.00 Hz); HFn – normalized HF; TV – Total Variability

Normalized LFn values increased from 0.045 to 0.557. High increase of variability of cardiac signal was observed before self-terminating arrhythmia with higher increase in LF/HF ratio. As cardiac oscillations at low frequency are associated with sympathetic outflow [6], these results suggest a different pattern of sympathetic heart control before initiation and before ending of arrhythmia events. Figure 1. describes the coherence and phase spectrum of cardiovascular signals recorded before initiation of arrhythmia. Coherence function is more than 0.5 over a wide frequency range (0.15-1.0 Hz) in baseline condition, suggesting that the relationship between oscillation in blood pressure and cardiac signals is relatively linear.

Table 2. Heart Rate Variability before and during arrhythmia.

	HRV				
	LF	LFn	HF	HFn	TV
	ms^2/Hz		ms^2/Hz		ms^2/Hz
Baseline	4,18E-3	46,7E-3	87,22E-3	955,3E-3	91,3E-3
Before_1 A	1,3E-3	46,7E-3	27,4E-3	955,3E-3	28,7E-3
Before_2 A	944,6E-6	556,6E-3	751,5E-6	443,4E-3	1,7E-3
Arrhythmia_1	900,0E-3	272,1E-3	2,4E+0	727,9E-3	3,3E+0
Arrhythmia_2	90,9E+0	948,2E-3	5,0E+0	51,8E-3	95,9E+0
Recovery_1	1,3E+0	936,1E-3	88,4E-3	63,9E-3	1,4E+0
Recovery_2	622,8E-3	193,6E-3	2,6E+0	806,4E-3	3,2E+0

LF- Low Frequency component (0.10-0.25 Hz); LFn – normalized LF; HF – High Frequency component (0.25-1.00 Hz); HFn – normalized HF; TV – Total Variability

Before arrhythmia onset, a lower coherence at frequency around 0.15-0.2 Hz and different pattern in phase spectrum was observed. As in feedback systems, phase determines the stability between two systems and characterizes the delay between the input and the output signals. Lower fluctuations of phase in baseline signals suggest that fewer waves circulate in the cardiovascular system. On the other hand, a less organized system is described graphically by more fluctuation of phase, without a distinct harmonic pattern, suggesting a larger number of wavelets. The zero crossing phase oscillation in LF and HF band was used for quantification of stability of the cardiovascular system. An increase in TF was observed during arrhythmia both in LF and HF band, while recovery of sinusal rhythm was characterized by 10 time lower TF in LF band showing an increase of the baroreflex control on heart (Table 3).

Table 3. Transfer Function and Phase at central frequency in the LF and HF bands.

	LF			HF		
	TF	F	Phase	TF	F	Phase
	mmHg/ms	Hz	°	mmHg/ms	Hz	°
Baseline	25,1E-3	0,109	17,93	1,8E-3	0,489	-25,99
Before_1 A	32,0E-3	0,109	75,20	707,5E-3	0,625	43,66
Before_2 A	854,0E-6	0,190	-1,24	714,3E-6	0,440	5,83
Arrhythmia_1	1,1E+0	0,108	1,82	814,5E-3	0,924	-41,48
Arrhythmia_2	1,3E+0	0,164	-51,63	2,1E+0	0,383	44,00
Recovery_1	99,8E-3	0,109	-69,19	59,8E-3	0,382	-49,07
Recovery_2	886,7E-3	0,109	63,46	443,2E-3	0,600	56,70

TF-transfer function; F- central frequency, LF – low frequency component, HF- High Frequency component.

Wavelet based coherence allow better detection and characterization over time of the dynamical changes in cardiovascular system (see figure 2). The cross scalogram and phase spectra obtained are open to physiological interpretation documenting the possible input perturbations that drive the cardiovascular system. Where the coherence falls, as can be observed at scale associated with VLF, output fluctuations reflect the influence of system non-linearities, loss of time invariance or other system inputs signals. Less organized phase spectrum of cardiovascular signals recorded during arrhythmia is observed both in frequency and time-frequency domain representation (Figs. 2 and 3).

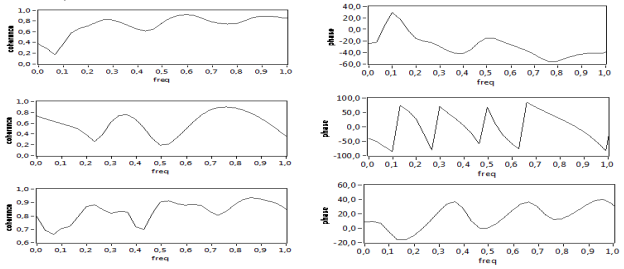

Figure 1. Coherence and phase representation of cross spectrum between SAP and cardiac signal recorded before initiation of arrhythmia in the frequency domain. From top to bottom can be observed decrease in coherence and increase variation of phase spectrum.

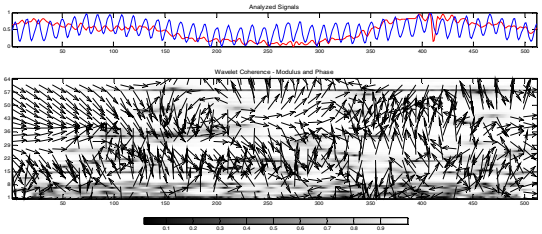

Figure 2. Wavelet coherence and phase of blood pressure and cardiac signal recorded in baseline condition. The arrows are phase angle and direction.

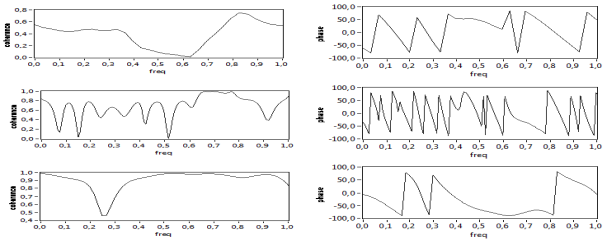

Figure 3. Coherence and phase representation of cross spectrum between SAP and cardiac signal, in the frequency domain, recorded during arrhythmia (first two line of graphics) and during self-terminating arrhythmia. From top to bottom can be observed increase in coherence and lower variation of phase spectrum.

In wavelet coherence and phase spectrum, rapidly changes in phase mainly at low and very low frequency was observed (Fig.3), suggesting influence of various inputs signals other than those associated with the ANS system. Self-termination of arrhythmia was characterized by an increasing in coherence and lower fluctuation of phase, suggesting that higher sympathetic outflow to the heart could lead (negative phase angle in LF band) the self-termination arrhythmia process.

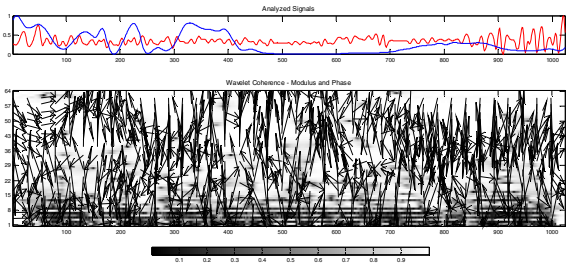

Figure 4. Wavelet coherence and phase of blood pressure and cardiac signal recorded during initiation of arrhythmia. Rapidly changes in phase angle and directionality in LF and VLF bands can be observed.

IV. Conclusion

This work shows the power of the cross spectrum and time-frequency analysis in the study of features of arrhythmia. As far as we know, this is the first study that used the analysis of BPV and transfer function for arrhythmia characterization and forecasting. Our results show that BPV and cardiovascular coupling characterization may be used to predict the onset of arrhythmic episodes. In addition, using the proposed algorithm, valuable information on mechanisms of certain cardiac arrhythmia with reference to respiration and blood pressure changes can be better understood.

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