Non-parametric and Parametric Time-Frequency Analysis of Heart Rate Variability during Arousals from Sleep

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Abstract

Arousal from sleep is a normal physiologic event during normal sleep, which produces a tachycardia-bradycardia pattern on the heart rate variability (HRV) signal, which testifies the involvement of the autonomic nervous system related to a central nervous system event. Repetitive arousals may be associated to excessive sleep fragmentation (for example in respiratory pathologies such as Obstructive Sleep Apnea) and to a bad quality of sleep. In this work we studied the HRV signal in the time-frequency domain during isolated and repetitive arousals. During isolated arousal episode, time and frequency domain parameters showed the behavior associated to vagal withdraw and sympathetic activation. Multivariate time-variant AR model was used to evaluate interaction between HRV and respiration during repetitive arousals. We found an increased synchronization between HRV and respiration and an entrainment between LF oscillation and respiration at the frequency of micro-arousals.

1. Introduction

Arousal from Sleep is a common and physiologic event during the night, and usually the subject is not aware of this. An excessive number of arousals, however, produces sleep fragmentation with a variety of consequences as daytime sleepiness [1-2] and impaired mental performances; in addition, in recent years, a bad quality of sleep has also been related to many relevant pathologies (cardiac pathologies, diabetes, etc.). An arousal is scored, in sleep clinics by specialized personal, from the EEG signal. Arousal consists in an abrupt shift in EEG frequency, which may include theta, alpha and/or frequencies greater than 16 Hz but not spindles, the definition of arousal more widely used is given by the American Sleep Disorders Association [3]. Repeated arousals generally take place as a defense of a noxius respiratory disease as Obstructive and Central Sleep Apnoea. Moreover, arousal presents a typical rhythm in heart rate. This pattern consists in a sudden rise of heart rate, as a result of vagal tone abrupt withdrawal and an increase in heart sympathetic outflow [4].

Spectral decomposition techniques represent non invasive powerful tools to analyze the regulation of the Autonomic Nervous System from heart rate variability signal. These allow us to investigate the Sympathetic and Parasympathetic balance in different conditions and pathologies. It is worthy known that Heart Rate Variability (HRV) presents fluctuations between 0.15 – 0.5 Hz which are in synchrony with respiration and are directly correlated with the vagal flow, while oscillation between 0.02 – 0.15, not related to respiration, represent mainly the sympathetic modulation [5]. An Arousal episode produces a transitory reflex of the sympathetic activation which is reflected as an abrupt change in the heart rate. This non stationarity in the series makes necessary the use of advanced spectral techniques as Time-Frequency Distributions, Time-Varying Autoregressive Models and Wavelet decomposition in order to reach a satisfactory estimation of the spectral parameters of HRV, and to obtain a better physiological interpretation. On one hand, the Time-Frequency approach is based on the estimation of the time dependent autocorrelation function. These techniques achieve high time and frequency resolution: there exist large families of different distributions, each of them characterized by a function called kernel (smoothing windows used to eliminate the interference terms generated by the quadratic nature of the distribution) [6]. On the other hand, the Time-Varying approach attempts to find the parameters of an autoregressive model which better fits the series inside a moving observation window [7]. In addition, this approach allows evaluating the interaction between different systems as the influence of respiration in the Heart Rate. Most of the works developed until now, have analysed the arousal events applying basic methods

such as Fourier Transform [4].

The aim of this study is to characterize the autonomic involvement during spontaneous arousal from sleep (Time-Frequency Analysis), and its interaction with the respiratory system (Multivariable Time-Variant Analysis).

2. Methods

2.1. Protocol

Five ECG and EEG recordings were obtained from five obese subjects who underwent polysomnography for suspected obstructive sleep apnea. Age was 48 ± 5 years (mean ± SD) and body mass index was 36 ± 2 Kg/m^2. The data were obtained using a polymnosograph Heritage Digital PSG Grass Telefactor with a sample frequency of 100 Hz.

Expert clinical personal, scored the sleep and detected the arousals based on the American Sleep Disorders Association standardized criteria [8]. The arousal events were selected sufficiently far from any apneic influence and free of spurious signals. Isolated arousals (at least 150 second between two consecutive arousals), and sequences of repetitive arousals, also classified as cyclic alternating pattern (CAP) sleep, were selected.

Intervals of 150 sec as baseline and the same interval as recovery after arousal were considered. R-R intervals were measured from the ECG signal using parabolic interpolation in order to overcome the limitations of the low sampling rate. The time series were corrected if misdetections and extra-systoles happened.

2.2. Spectral analysis

Isolated Arousals

Resulting RR signals were detrended and resampled at 2 Hz by cubic spline interpolation. Thereafter, the Hilbert transform was applied to the series. Born-Jordan distribution was used to obtain the signal power in the time-frequency domain. This distribution is defined as follows [15, 19]:

$$BJD_x(t,f)=\int_{\tau}\left[\int_{t'}\varphi(t-t',\tau)x(t'+\frac{\tau}{2})x^*(t'-\frac{\tau}{2})dt'\right]e^{-j2\pi f\tau}d\tau$$

where $BJD_x(t,f)$ is Time-frequency distribution of the signal x(t), while the kernel $\phi(t,\tau)$ in defined as:

$$\varphi(t,\tau)=\begin{cases}\dfrac{1}{|\tau|}, & |t/\tau|<1/2\\ 0, & |t/\tau|>1/2\end{cases}$$

From each spectral estimation, coming from Time-Frequency approach we computed the spectral indexes of HRV along time: total power (TP) 0.04 - 0.5 Hz; low frequency component (LF) 0.04 – 0.15 Hz; high frequency component (HF) 0.15 – 0.5 Hz; and low to high frequency components ratio (LF/HF).

Repetitive Arousals

To evaluate correlation level between tachogram and respirogram signals a bivariate time-variant parametric analysis was applied. We estimated the quadratic coherence function defined as:

$$K^2(f)=\frac{G_{12}{}^2(f)}{P_{11}(f)\cdot P_{22}(f)}$$

$0\le K^2(f)\le 1$, where $G_{12}(f)$ is the magnitude of the cross-spectrum of the signals, and $P_{11}(f)$, $P_{22}(f)$ are the corresponding autospectra. Furthermore, total power of tachogram coherent with respiration, or the variability directly related to respiration (respiratory sinus arrhythmia, RSA), was evaluated through the bivariate time-variant model in which respiration is considered an external input acting on HRV. The forgetting factor of the recursive algorithm was set at 0.98 and the model order was equal to 12 [7].

2.3. Data analysis

The data were synchronized with the occurrence of the minimum of RR series, obtaining an ensemble average for each group of subjects. All values in each time series were baseline corrected with respect to the mean value of the last 60 beats before the onset of the arousal. Data are expressed in normalized values as percent change from baseline. The spectral indexes were also synchronized, and the same procedure was applied.

Segments of 30 beats from normalized data were analyzed. Segments were taken from 5 beats before to 25 after minimal RR during the arousal. One way ANOVA tests for repeated measures were performed to compare the RR intervals at each beat. Bonferroni's post-hoc analyses were performed to evaluate significant statistic differences ($P<0.05$).

3. Results

Spectral parameters of Heart Rate Variability during Arousals from Sleep were analyzed. Figure 1 presents mean and SE of time evolution of the spectral indexes of HRV for ten arousals from sleep. The values are represented as the percentage change with respect to the baseline. RR intervals present the expected behavior: a fast decrement which reaches its minimum value around seven seconds after the initial increment in the cerebral

Beta activity, after that a recovery phase begins over-passing the baseline and returning to the base line 25 seconds later. The second subplot shows the Beta activity, significant differences from baseline are found from 7 to 15 second. HF component has a decrement immediately when an arousal happens during the first 3 seconds, then a constant increment which arrives at the maximum value close to the final of the arousal. However, no significant differences were found. LF component presents a strong increment arriving at its maximum close to the same time in which the RR value is minimum and going back to the base line value 25 seconds later. Significant difference respects to base line are from 7 to 14 second and 4 to 16 seconds. VLF component and LF/HF ratio showed an analogous performance as the LF component.

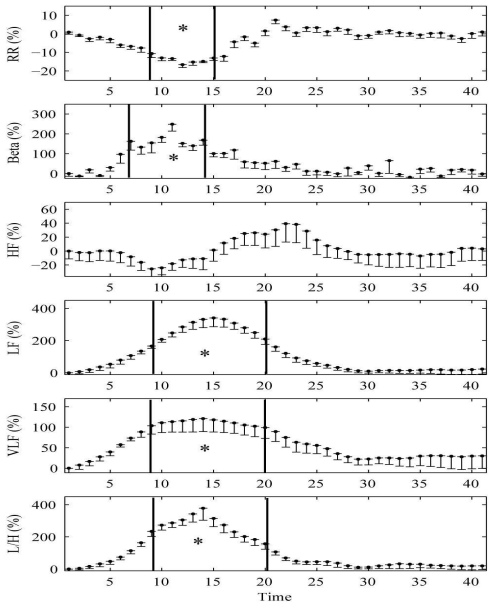

Figure 1. Grandaverage (across arousals of all the subjects) time evolution of indexes of the heart rate variability Form the top to the bottom: RR intervals, cerebral Beta activity, HF (High frequency component), LF (Low frequency component), VLF (Very low frequency component) and LF/HF (Low to high frequency ratio). Values are mean ± SE. * indicates significant difference time points (P < 0.05 vs baseline).

In figure 2, on the left, it is shown the squared coherence function computed between RR intervals and respiration (right) in the time-frequency plane. Top subplot was obtained for normal sleep, and bottom for periodic arousals (CAP sleep). It is possible to observe an increase in K^2 in the LF and VLF frequency range during CAP sleep, indicating that HRV and respiration synchronize also at the frequency of repetition of the periodic arousals. In such a situation the sympatho-vagal balance cannot be evaluated through the classical parameter in the frequency domain (i.e. the LF/HF ratio), which could be misleading. The total power of the HRV signal was then divided into power related to respiration (RSA, Respiratory Sinus Arrhythmia) and power not related to respiration (NRSA) Percentage of RSA are shown in figure 3 for the two different sleep conditions. Significant differences (P<0.05) were found between absence of arousals (no arousals) and periodic arousals (CAP) analyzed, showing an increased interaction between RR intervals and respiration in periodic arousals case.

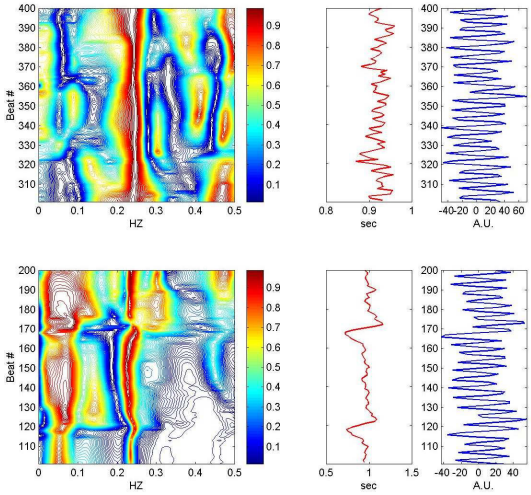

Figure 2: Squared coherence function for RR intervals and respiration. Top figure shows K^2 (left) for normal sleep; RR intervals and respiration was showed at right. Bottom figure was obtained for CAP sleep, K^2 (left), RR intervals and respiration (right).

4. Discussion and conclusions

This work presents a study of the autonomic changes controlling HRV during Spontaneous Arousals from Sleep. Time-Frequency approach was used in order to obtain the time evolution of spectral parameters of the non stationary HRV. Furthermore, Multivariate Time-Variant Model was applied to the RR intervals and respiratory signal in order to characterize their interaction during spontaneous periodic Arousals. Our main findings are: a) An increment in VLF, LF and LF/HF took place at the same time as Beta activity, while RR intervals showed a decrement and HF remained stable. Thereafter, almost at the same time that Beta activity reached the maximum level, RR intervals and HF presented their minimum values. Then during the recovery of Beta activity, RR intervals and HF, VLF, LF and LF/HF ratio arrived at the

highest value. Finally, the Beta activity came back to the normal level, a bradycardia was present and an increment in HF appeared. All at once, LF and LF/HF were very close to the normal point.

Blasi et al. [9] reported a delay in the LF response when an inducted Arousal is produced. This divergence could be explained by nature of the arousals (spontaneous in the present work and induced in [9]) and by the interactions and activations of other mechanism involved. b) Bivariate time-variant AR model allowed us to estimate appropriately power spectra of RR intervals and respiration, and their quadratic coherence function. In this way, we could evaluate differences in the influence of RSA during two situations, absence of arousals and periodical arousals (CAP), finding an increased synchronization between HRV and respiration in CAP.

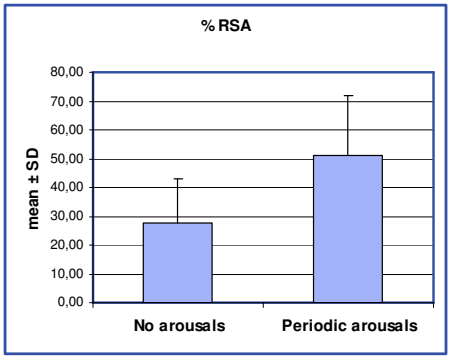

Figure 3: Influences of RSA in absence of arousals (no arousals) vs periodic arousals (CAP). Values are mean ± SD. The differences are significant ($P<0.05$)

In conclusion Time-Frequency approaches showed to be a fine tool to evaluate the spectral parameter of the HRV during non stationary conditions. Furthermore, the results suggest a major participation of sympathetic nervous system during arousals and parasympathetic activity after arousal. With respect to bivariate time-variant AR model, it is a powerful tool to evaluate interaction between HRV and respiration.

Acknowledgements

This paper was supported by the My Heart Project IST 507816 of the European Community and by CONACYT-México.

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