TIME-FREQUENCY ANALYSIS OF THE HEART RATE VARIABILITY IN AROUSAL FROM SLEEP

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Abstract: Time-frequency Born-Jordan Distribution was applied to evaluate the dynamics of the HRV during arousals from sleep. An arousal is an abrupt and spontaneous change in the normal cerebral rhythms during sleep. This one is related with sleep fragmentation, which causes sleepiness, low concentration, traffic accident during the day, however it acts as a defence to pathologies as Obstructive Sleep Apnoea (OSA) during sleep. Five pair of EEG and ECG records from obese subjects with OSA and during therapy (3 CPAP and 2 APAP) were used in the study. The autonomic response showed an increment in the heart rate during the first 12 seconds after the arousal ($p<0.5$), which is followed by a bradycardia. Consistently, the Low frequency component presented a decrement also in the initial time of the event, and it was proceeded for an increment in the Low frequency component ($P<0.5$), which remained over the baseline value about 20 seconds after to the rise up. Also the Total Power, Low to High frequency ratio and Very Low frequency component had a similar behaviour that the Low frequency component. In conclusion the autonomic response to an arousal is similar for normal and ill subjects even though they are under therapy.

Keywords— **Obstructive sleep apnea, Born-Jordan distribution, Arousal, Heart rate variability, Sympatovagal balance.**

Introduction

The dominant symptom seen in a respiratory sleep clinic is excessive daytime sleepiness which is often due to sleep fragmentation secondary to repetitive arousal from sleep as a defense to a noxious nocturnal stimulus. A number of sleep disorders such as Obstructive Sleep Apnea, Cheyne-Stokes Respiration are commonly associated with frequent sleep arousals [1-7]. The typical way for detecting an arousal event is using either the central or occipital derivation of the EEG. The Arousal obeys a specific pattern which consists in *an abrupt shift in EEG frequency, which may include theta, alpha and/or frequencies greater than 16 Hz but not spindles* [8]. Additionally to the changes that arousal produces in the regular behavior of the brain waves during sleep, this one also produce alterations in the function of the Autonomic Nervous System (ANS) which are visible and characteristic in the normal rhythm of heart rate. These modifications in heart rate during an arousal event show a classical pattern that consists in a sudden rise of heart rate immediately after what an episode is present, as a result of vagal tone abrupt withdrawal, and an increase in heart sympathetic outflow [3]. Subsequently to the tachycardia the system tries to recover its basal stage producing a bradycardia.

For some years the analysis of the Heart Rate Variability (HRV) with application of the spectral decomposition methods has been used as a non invasive method in order to evaluate and to diagnose different pathologies, taking how variable only the cardiovascular system. From the spectral decomposition of the HRV, it was found out that frequencies in the range of 0.15 – 0.5 Hz (High Frequencies Component) describe the activity of the parasympathetic branch of the ANS that innerve and control the heart rate, while the ones between 0.04 - 0.15 Hz (Low Frequency Component) represent preponderantly the sympathetic activity [9-11]. Most of the conventional approaches for spectral decomposition as Fourier Transform and Batch Analysis require that the signal satisfies the condition of stationarity in the interval of analysis. However, arousal events invoke transient episodes of the reflex sympathetic activation. This abrupt changes in the sympathetic activity can be peripherally detected from variations of the heart rate variability. For attending the last problem of non stationarity in the signal, there exists a number of approaches that can overcome this inconvenient. The most commonly used in biomedical applications are time-varying autoregressive analysis, wavelets decomposition and time-frequency analysis [12-17]. Different studies have used time-frequency approaches in diverse diseases and maneuvers that produce transient episodes in the signal. The results obtained using this kind of approaches had showed satisfactory and useful results for understanding the response of the human body under these pathologies and maneuvers, contributing at the development of diagnosis and new knowledge to the clinical and research fields. Besides, there are only few works referring to the application of these advance spectral

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approaches for quantifying the dynamic evolution of the cardiovascular parameters during arousal events [2,18]. The Born-Jordan Distribution presents a large quantity of proprieties essentials for a fine evaluation of the spectral evolution in the time of the dynamic of the HRV signal during non-stationary episodes, how are the induced by the arousal from sleep in the heart rate. Some of the most important proprieties are frequency-shift and time-shift invariance, be real-valued and positive, have time and frequency marginals, energy conservation, and finite time and finite frequency support.

In this study we applied a time-frequency approach called Born-Jordan Distribution in order to quantify the dynamic changes in the Heart Rate Variability that are produced by the arousal from sleep outside of any pathological event (spontaneous arousals). A next step will be to take into account arousals how defence to noxious respiratory pathologies, as the Obstructive sleep Apnoea, in order to investigate in a deeper way the changes induced in the pathology by the observed phenomena.

Materials and Methods

Five ECG and EEG pair records were obtained from five sleeping obese subjects, ages between 30 to 58 years and body mass index 36 ± 2 Kg/m^2. All the subjects were diagnosed with Obstructive Sleep Apnea disease and recorded during the therapy. Two of the subjects used during the registration the Automatic Positive Airway Pressure (APAP) therapy device and the other ones Continuous Positive Airway Pressure (CPAP) therapy device. The data was obtained using a polymnosograph Heritage Digital PSG Grass Telefactor with a frequency sample of 100 Hz during 7 hours night record.

A. Protocol

Arousals were detected from the EEG by experts using the American Sleep Disorders Association standardized criteria [8]. Each arousal event record was selected free of noise, indifferently from REM and non-REM sleep macrostructure stage, and sufficiently distant from the influence of an apneic episode. It was taken an interval of 2 min 30 sec as baseline and the same interval as recovery after arousal. By means of an algorithm that we implemented, the R-R intervals were measured from the ECG records. The time series were verified and corrected where misdetections and extra-systoles happened.

B. Spectral Estimation

Resulting RR sequence was resampled at 4 Hz by cubic spline interpolation and detrended by smoothness priors. Born-Jordan time-frequency distribution was used to obtain the evolution of the signal power at different frequencies and times. This one is part of time-frequency Cohen's Class distributions, which have the characteristic of being time and frequency invariant. Born-Jordan Distribution is evaluated as [12, 13, 16]:

$$BJD_x(t,f)=\int_{\tau}\left[\int_{t'}\varphi(t-t',\tau)x(t'+\frac{\tau}{2})x^*(t'-\frac{\tau}{2})dt'\right]e^{-j2\pi f\tau}d\tau \quad (1)$$

Where :

$BJD_x(t,f)$ = Time-frequency distribution of the signal
$\varphi(t-t',\tau)$ = Born-Jordan kernel
x = Signal

And the kernel in defined as:

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

Therefore, it was computed the time evolution of the classical heart rate variability indexes: total power, from 0.003 to 0.6 Hz (P_T); low frequency component, from 0.04 to 0.15 Hz (LF); very low frequency component, from 0.003 to 0.04 Hz (VLF); high frequency component, from 0.15 to 0.6 Hz (HF); and low to high frequency components ratio (LF/HF). All spectral indexes were computed in absolute units; high frequency component was also expressed in percentage units (HF_r=HF/P_T).

C. Data Analysis

The data were synchronized with the occurrence of an most closest abrupt decrement in RR series and a sudden rise up in the Total Power to the arousal mark. From it, an ensemble average was obtained for each index. It was computed a reference value in each index as the mean of the 60 seconds former at the synchronization point.

All the indexes values were given as mean ± standard deviation. Segments of 60 seconds from data and spectral indexes were analyzed. One way ANOVA tests for repeated measures were performed to compare the indexes in the time respect to the reference value. Bonferroni's post-hoc analyses were performed to estimate significant statistic differences ($P<0.05$).

Results

The results of the analysis of RR sequences and the time evolution of the spectral indexes obtained by the application of the Born-Jordan Distribution are shown in Figure 1 as mean ± standard deviation.

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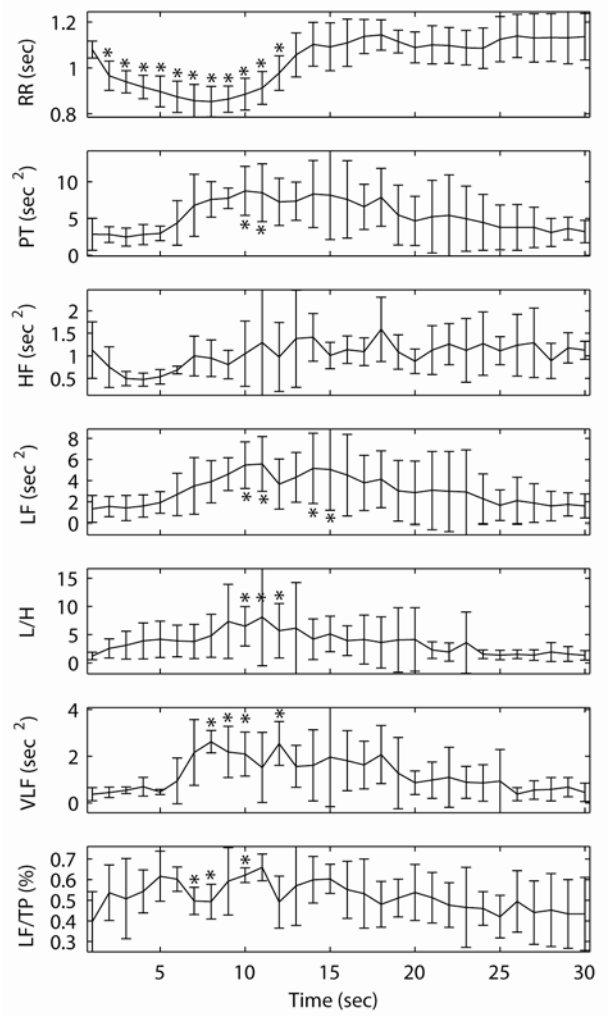

Figure 1: Mean ± Standard Deviation of the spectral indexes obtained by Born-Jordan distribution during an arousal from sleep episode. From the top to the bottom, RR intervals, PT (Total power), HF (High frequency component), LF (Low frequency component), L/H (Low to High frequency ratio), VLF (Very low frequency ratio) and LP/TP (Low frequency component between Total power). The fist point in the plots represent the baseline or point of reference which was calculated as the mean of the former 60 seconds to the abrupt decrement in the RR intervals after an arousal episode. TP, HF, LF and VLF were multiplied by 1000.

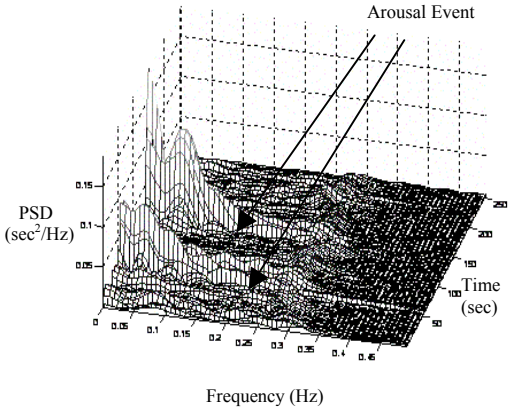

Figure 2: An typical example of the time evolution of the Power Spectral Density of R-R intervals obtained by Born-Jordan Analysis during arousal from sleep episodes.

The RR intervals showed a incessant decrement immediately after to the reference point (arousal episode) until around six seconds after, such decrement had values that were statistically significant . Then these ones presented a continuo recovery, which overpass its baseline, the values remained different statistically until the second 12.

On the other hand, the Total Power, the Low to High frequency ratio and both the Low and Very Low frequency components were constant until around the seventh second. Therefore, these ones showed an increment with a parabolic behaviour, which return the reference value until around 20 seconds after to the rise, and they were significant different around to the seconds 8 to 15 subsequent to arousal event. In addition, High Frequency component presented a decrement immediately after to the arousal, followed by a non regular behaviour in its time evolution, whereas non significant different was founded.

Figure 2 depicts an typical example of the time evolution of the Power Spectral Density of an RR sequence obtained by Born-Jordan Distribution during two arousal from sleep events. Immediately after to the arousal episode, it appeared with great intensity spectral components in range of the very low frequencies and low frequencies. On the contrary, the wave components in the interval of high frequencies, showed a reduction together with a frequency shift toward the low frequency components just after to the arousal episode. Therefore, all the spectral components came back to the normal values after a period no more that 30 seconds.

Discussion

The time evolution of the classical spectral indexes of HRV during arousal from sleep, in obese subjects diagnosed with obstructive sleep apnoea and during APAP and CPAP therapies, were computed by applying the Born-Jordan Time-Frequency Distribution. Ours preliminary results were: A reduction in the High frequency component and RR intervals after to the arousal episode. The increment of Total power, Low and Very low frequency components such as the Low to High frequency ratio after around 6 seconds of the arousal event, the rise up in these indexes was superior to the baseline value for about 20 seconds. Ours results are similar with the other ones published by other authors [2,18], event though, the arousal episodes were taken in obese subjects with obstructive sleep apnoea under therapy. The suddenly and progressive decrement in the RR intervals is produced by a diminution of the value in the high frequency component. In other words, there is a withdrawal in the vagal tone since this one is completely represented by the high frequency component of the HRV. In addition, the frequency shift of this component suggests a decouple between the respiratory and cardiovascular system. This situation produce some complications which provokes a low sleep quality and could be a fine indicator of the arousal episode if it is studied together to other mechanisms how is the respiratory system. In addition, Blasi et. al. [2] used a time-varying autoregressive model in normal

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subjects, with evoked arousals applying acoustic impulses, and they showed that the withdrawal of the vagal tone is accompanied with changes in the respiration. They suggested that the changes in the parasympathetic flow are secondary to the variations in the respiration. Ours results are similar to them but due to the different methodology and approach are present some variations. Contrarily to them, we utilized spontaneous arousals and obese subjects with OSA diagnosis during CPAP and APAP therapies. Additionally, they synchronized the data with respect to the stimulus. In addition, the response of the ANS must be diverse, for the reason that persons with OSA have altered their cardiovascular response. Furthermore, C. Mantaras et. al. [18] studied the dynamic of the HRV after arousal from sleep applied also a time-varying autoregressive analysis in normal and pathologic subjects with OSA respectively. Differently to them, they synchronized the indexes taking as reference point the minimum value of the RR intervals. The great variance in the data could be because of we took arousal event from subjects with different therapies and indifferently REM and non-REM sleep stage. The future goal is applied this approach in a bivarited way in order to study deeper the cardio-respiratory interaction during arousal form sleep, hence as during apnea events, in REM-nonREM sleep structure and CPAP-APAP therapies with the intention to studied the cardio-respiratory changes produced by the arousals.

Conclusions

The time frequency Born-Jordan Distribution is a fine tool to evaluate the non stationarity dynamic of the heart rate variability which are produced during arousal form sleep. Future studies include the analysis of the response of the cardiovascular system during arousal during the different therapies APAP and CPAP. A bivariate analysis between the respiratory and cardiovascular system will be also the next goal in order to study the chronobiological changes among the different systems in REM-nonREM sleep structure, CPAP-APAP therapies and apnea-non apnea condition after an arousal episodes.

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