Time-Variant Spectral Analysis of the Heart Rate Variability during Sleep in Healthy and Obstructive Sleep Apnoea Subjects

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Abstract

A time-variant autoregressive approach was used in order to evaluate the spectral parameters of the heart rate variability (HRV), through the all sleep stages, in both normal subjects and patients with severe obstructive sleep apnoea. Recordings coming from five normal and five pathologic subjects were analyzed in the study. The parameters of the autoregressive model were fixed for the entire night recordings: model order = 8 and forgetting factor = 0.98. The classical spectral indexes of the Heart Rate Variability were normalized respect to the total power. The results in this study showed, in normal subjects, an increment in the HFn components in NREM, while pathologic subjects presented a reduced activity in this component in all the time, which suggest a low activation of the vagal nerve. Furthermore, in both groups of subjects, VLFn reached high levels during REM and wake than NREM. In conclusion, this method could offer an alternative approach, with high resolution and efficient computation in the spectral decompotition, in order to develop a classification of sleep stage and apnoea detectors from the HRV.

1. Introduction

Previous studies have reported that heart rate variability presents characteristic fluctuations in each sleep stage through the whole night [1-6]. In normal subjects, the heart rate shows a diminution during NREM (non rapid eye movement) as compared with awake, while REM is characterized by higher heart rate and a large instability than NREM. These variations in heart rate fluctuation have been explained using invasive and direct measurement of burst rate of the muscle sympathetic nerve activity [1]. The results showed a depression or decreasing in the activation of the sympathetic activity during NREM and an instability and increasing in REM. The subjects who suffer obstructive sleep apnoea (OSA) are at high risk of hypertension, myocardial ischemia, stroke and a series of consequences during the daily life due to the low sleep quality produced by the repetitive apnoeas and arousals during the sleep time. OSA is a cardio-respiratory sleep disorder characterized by breath cessation at least for 10 seconds and commonly accompanied by arousal from sleep. An arousal takes place at the final of the apnoea, helping to recover the respiration. Obstructive sleep apnoea presents complex autonomic and hemodynamic responses which consist in the consequences of apnoea, hypercapnia, hypoxia, arousal and the Mueller maneuver (inspiration against closed glottis) [6-7]. The OSA diagnosis is not of easy access to the general population. This has elevated clinical cost and is performed in specialised hospitals with sleep laboratory. Overnight Polysomnography represents the gold standard for sleep apnoea diagnosis. electroencephalogram, electromyogram, pulse oximetry, electrooculogram, electrocardiogram, air flow, and respiratory efforts are recorded and analysed, by specialised personal, during the polysomnography. In addition, an OSA event elicits a unique heart rate rhythm of brady-tachycardia. The physiological basis for the rhythm is that, during obstructive events, inspiratory efforts are made against an occluded upper airway, producing vagal stimulation and bradycardia. An event terminates with arousal, increasing sympathetic discharge, thus producing a tachycardia. Different attempts in order to find an easier and more economic diagnosis of OSA have been carried out with interesting methodologies and good results [8], these approaches specially used the electrocardiogram due to its very simple recording procedure and its high levels of signal to noise ratio.

Sleep staging was defined primarily from the EEG, with rules developed by Rechtschaffen and Kales [9]. This procedure is part of the polysomnophy scoring and the whole night recording is divided in blocks of 30 seconds with six possible stages: Wake, stage 1 (transition), stage 2 (light sleep), stage 3-4 (deep sleep) and REM stage. Additionally, sleep staging can be reorganized in thee groups: Wake, NREM (Stages 1-4) and REM. The classification of the sleep stages is of fundamental importance since sleep quality and OSA are evaluated on the basis of them.

On other hand, earlier researches with spectral analysis suggest a strong correlation between the heart rate (HR) and autonomic nervous system. Wide band of the spectral components of heart rate includes frequencies from 0.003 Hz until 0.5 Hz. This range is divided in three principal components: range between 0.003 – 0.04 Hz (very low frequency component, VLF) takes account of long-term regulation mechanisms and specially during OSA could represents apnea repetition, 0.04 – 0.15 Hz (low frequency component, LF) characterizes sympathetic activation but under certain conditions could be influenced by respiration and consequently be influenced by a possible participation of the vagal nerve. The range between 0.15 – 0.5 Hz (high frequency component, HF) corresponds to parasympathetic flow and it is highly synchronous with respiration and vagally controlled [10].

From the former antecedents, the aim of this study is to analyze overnight polysomnography recordings using a simple and efficient approach of spectral decomposition called time-varying autoregressive model to asses, in a beat to beat basis, the spectral parameters of the heart rate variability through the different sleep stages in normal and severe OSA subjects.

2. Methods

2.1. Protocol

Twelve whole night polysomnography recordings of five healthy and five severe OSA subjects were include in the study. Age range, for healthy subjects was 38±6 years, weight range of 75±10 Kg and AHI of zero. While OSA subjects were 50±5 years old, weight 100±20 Kg and 71±9 as AHI. Recordings included oxygen saturation, body position, two encephalograph derivations (C4/A1 and O1/A2), chin electromyogram, left and right electrooculograms, airflow, thoracic and abdominal efforts, electrocardiogram, snoring and oxygen saturation. Signal were acquired in Philips Hospital, Marburg, Germany with a polygraph (Schwarzer polygraph, Neurocard, Munchen, Germany) digitalized at different frequencies. Sampling rate of ECG was 200 Hz. Stage 1, 2, 3, 4 and REM sleep stages were evaluated according to the standard criteria Rechtschaffen and Kales [9] by expert technicians. In the study were only used the hypnogram and the ECG signal.

2.2. Spectral analysis

From the raw ECG signals, the R peaks were searched and computed the RR intervals. Ectopic beats and misdetection were corrected by visual inspection. Thereafter, from the RR series the time-variant spectra was calculated by an autoregressive model with eight coefficients over the night recordings for all the subjects. The recursive least square algorithm (RLS) was used to estimate autoregressive parameters updating. The forgetting factor was 0.98 (time window with 50 beats). From the estimate time-varying autoregressive parameters the power spectrum was computed for each time series [11]. Thereafter, the following classical indexes of the HRV were computed from the power spectra: VLF component (0.005 – 0.04) LF component (0.04 – 0.15 Hz); HF component (0.15 – 0.6 Hz); and low to high frequency components ratio (LF/HF). All spectral indexes were normalized by total power.

2.3. Data analysis

Mean series each 10 seconds, from all the indexes, was calculated. Wake, light (stage 2), deep (stage 3-4), and REM sleep stages were used in statistical analysis. Repeated measures anova (Bonferroni's post-hoc analyses were performed to estimate significant statistic differences ($P<0.05$)), in normal subjects through the different sleep stages while anova one way was applied to the pathologic subjects since some recordings did not have deep sleep. Two samples t-test was employed in order to compared statistically ($P<0.05$) the different sleep stage between groups.

3. Results

Table 1. Mean and Standard Error of the spectral indexes of heart rate variability during the different sleep stages in both normal and pathologic subjects.

Index	Normal				Obstructive Sleep Apnoea			
	Wake	Light	Deep	Rem	Wake	Light	Deep	Rem
RR (s)	0.976±0.05	1.008±0.06	0.986±0.06	0.942±0.05	0.875±0.02	0.949±0.03	0.899±0.04	0.975±0.03
VLFn	0.367±0.03	0.169±0.02	0.111±0.02	0.259±0.04	0.382±0.01	0.267±0.01*	0.230±0.01*	0.428±0.04*
LFn	0.428±0.01	0.503±0.45	0.393±0.02	0.499±0.02	0.515±0.01*	0.637±0.01*	0.583±0.02*	0.521±0.41
HFn	0.203±0.03	0.327±0.03	0.494±0.03	0.241±0.04	0.102±0.01*	0.095±0.03*	0.186±0.03*	0.515±0.00*
LF/HF	5.020±1.05	2.802±0.66	1.399±0.36	3.347±0.54	20.33±7.81*	10.39±1.43*	6.097±2.45*	14.06±1.17*

RR = time interval between consecutive R peaks of the electrocardiogram, LFn = low frequency component, HFn = high frequency component, LF/HF low to high frequency ratio. * represents significant difference between corresponding sleep stages of the groups. The gray color denotes the statistic difference between REM and the other sleep stages for each group. $P < 0.05$.

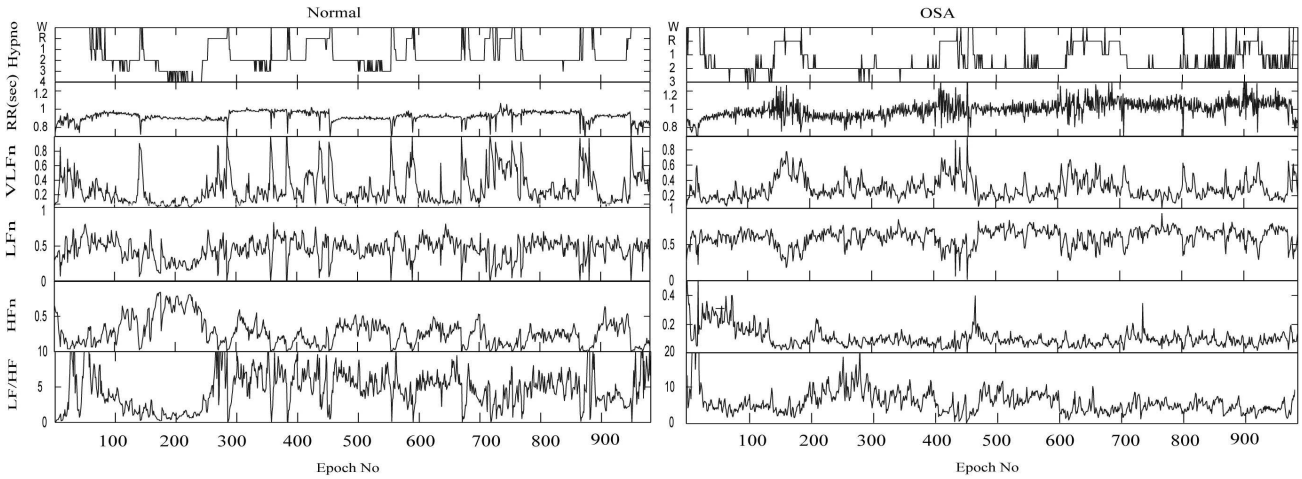

Figure 1. Time evolution of spectral indexes of the heart rate variability in healthy and severe obstructive apnoea subjects. The time-variant spectra was obtained by an autoregressive model. From the top to the bottom: Hypnogram, RR intervals, VLFn (very low frequency), LFn (low frequency), HFn (High frequency) and LF/HF (low to high ratio). All the spectral indexes were normalised by the mean of the whole record of each index.

Overnight recordings coming from five healthy and five pathologic subjects with severe obstructive sleep apnoea were analysed. Table 1 presents the mean and Standard Error of the HRV indexes used in the study. The statistics was carried out between REM and the others sleep stages for each group. In normal subjects, the RR intervals presented high values in light and deep than REM and wake, being significant only in light respect to REM. VLFn was lower during deep, light and wake than REM (P>0.5). LFn and LF/HF presented a smaller value during deep and light than wake and REM. The significant difference was found respect to REM in deep sleep stage. HFn presented a increase level (P>0.5) during deep sleep. Interesting results are the statistic difference, in VLFn, between light-deep and REM in OSA patients. On the other hand most of the spectral indexes presented statistic difference in the sleep stages between both groups. VLFn, LFn and LF/HF were higher in OSA subjects than normal ones while HFn presented lower values. Fig 1 depicts the hypnogram, in the row 1, of the normal subjects in the first column and of pathologic ones in the second column. All the spectral indexes were normalised respect to the total power. In normal subject, RR intervals elicit large and fast changes when REM or Wake stages are present, and a stable evolution during NREM sleep. VLFn component presented oscillation of high activity during REM and Wake and almost null level when NREM sleep stage occurs. In the third row, it is depicted the LFn component, which shows low levels when Deep, REM and Wake stages took place. Thereafter, HFn component presented the maximum value during deep sleep and levels very close to zero during REM and Wake. Finally the HF/LF ratio showed a temporal evolution similar to LFn. When OSA occurs all the cardio-respiratory and hemodynamic behaviour of the human body are altered, then a different temporal evolution of the classical spectral indexes through overnight are mutated. From the second column in Fig. 1, it is appreciable that in terms of sleep hypnogram is relatively normal in spite of the subject never arrives to the deep sleep. RR intervals present a performance very close to a normal subject but with large oscillations in all the sleep stages. Mainly during REM these oscillation presented enormous changes. VLFn component again shows higher levels in REM than during NREM while the LFn component presents opposite changes. The big difference with the normal subjects is the very low levels in the HFn.

4. Discussion and conclusions

A whole night spectral analysis of the HRV in five normal and five subjects with severe obstructive sleep apnoea recordings was carried out. A simple time-varying autoregressive approach was applied in order to obtain the classical indexes of the HRV. Our results suggest that the autoregressive models have great capacity and applicability in the analysis of the whole night recordings, to study or to develop instruments for diagnosis inside the sleep disorder field. Similar patterns in VLFn and LFn, through the different sleep stages, are found in normal and OSA pathologic subjects. An increment during REM in VLFn and a decrement in LFn. In normal subjects, the high level in HFn have an important sense since it represents the predominant influence and modulation of respiration in the ANS. However, when the OSA takes place, it is difficult to find this typical influence due to the apnoea-breath pattern and the repetition of the apnoeic events is more significant. A variety of studies have published about the correlation between the sleep stages (evaluated from EEG) and the HR. The results of these

studies, in normal subjects, are in agreements with them [2-4]. HF component presented high levels during NREM while low levels are presented in wake and REM sleep stages. Most of the methods take segments of the RR intervals, evaluating the Fourier transform and in this way completing the overnight recording [8,12]. Contrarily, this approach has the advantage of being time variant and it could arrive to have a resolution so high as a beat. Other approaches could be also useful in order to evaluate the sleep stages in OSA with high resolution, two important approaches are Wavelets and Time-Frequency distributions [13]. It is important to comment the power that could represent the Autoregressive models, since it could be possible a) to evaluate with some accuracy the sleep stages, b) to determine if the subject suffer of sleep fragmentation and finally c) to give a good approximation of the periods at apnoea and periods at normal respiration. The computational efficiency is also an attractive feature. Future work will consist in implement together with this simple approach a patter recognition method in order to achieve the objectives commented former.

A criticism in the study could be concerned to the model order and forgetting factor. We decided to use a model order and forgetting factor in base to the following criterions: a model order in the range between 8-16 is adequate to fit the HRV signal, however a test to define the best model order to specific characteristics of a time series is required. Nevertheless, the signal features across the sleep stages, movements, apneas, arousal and the infinity of the various physiologic and pathologic events make a very difficult task the definition of the best model order, and the selection is taken in base to others necessities. The computation time is one of the more important factors. A second point in the selection was addressing in this way. For a complex signal is required a higher model order which is able to fit the signal. However, in signal with low complexity, the minimum order is the best. When the model order is higher than the optimum one, there produces overfiting and negative power is found in the spectrum. Therefore, in this special problem the minimum order give us excellent results, fitting correctly when the complexity of the signal is low or mild and reaching a good fitting when the complexity increase.

In conclusion time-variant parametric models offer fine characteristic in the spectral decomposition of the Heart Rate Variability signal in different circumstances. Furthermore, although the VLFn and LFn presented similar time evolution in normal as well as pathologic subjects, the mechanism involved works in a different way. Autoregressive models plus an adequate pattern recognition could offer an easy way and economic approach in order to detect sleep stages and obstructive sleep apnea diagnosis.

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