Biomedical Signal Processing and Control 40 (2018) 111–116

Contents lists available at ScienceDirect

Biomedical Signal Processing and Control

journal homepage: www.elsevier.com/locate/bspc

Time-varying analysis of the heart rate variability during A-phases of sleep: Healthy and pathologic conditions

Guadalupe Dorantes-Méndez[a,*], Martin O. Mendez[a], Alfonso Alba[a], Liborio Parrino[b], Giulia Milioli[b]

[a] Facultad de Ciencias, Universidad Autónoma de San Luis Potosí, San Luis Potosí, Mexico
[b] Sleep Disorders Centre, Department of Neurology, University of Parma, Parma, Italy

ARTICLE INFO

Article history:
Received 19 April 2017
Received in revised form 7 August 2017
Accepted 10 September 2017

Keywords:
Cyclic alternating pattern
Heart rate variability
Time-varying analysis
Nocturnal front lobe epilepsy

ABSTRACT

In the present study, a comparison of the heart rate variability (HRV) behavior between healthy subjects and Nocturnal Front Lobe Epilepsy (NFLE) patients was carried out during the A-phases of sleep. The A-phases are short cortical events that interrupt the basal oscillation of the sleep stages and form the cyclic alternating pattern phenomenon. HRV was assessed by means of standard temporal measures and frequency measures based on time-varying autoregressive (TVAR) models. The analysis of HRV, in relation to the A-phases occurrence, was performed selecting two segments: one before the onset of the A-phase and one during the A-phase time. The results showed a significant increment in the heart rate during the A-phases in both, healthy subjects and NFLE patients. In addition, a major participation of the sympathetic nervous system was found in both healthy and pathologic conditions based on the sympatho-vagal index (LF/HF) during A-phases. The intensity of the shift towards sympathetic activity is related of A-phase type, where the largest shift is found in A3 phases. However, the NFLE patients present a weaker autonomic response during A-phases. The results suggest that the autonomic cardiac response related with the surveillance mechanism of NFLE patients is affected.

1. Introduction

In the past few years, the analysis and assessment of sleep have become an important procedure in clinical practice. This is due to the large evidence about the relationship between sleep quality reduction and the decrease in capabilities as concentration, memorization and reaction. In addition, a reduced sleep quality for an extensive period of time may cause negative physiologic effects, such as hypertension, metabolic syndrome and myocardial hypertrophy [1].

Sleep quality is evaluated by means of polysomnography, which consists in recording different biological signals across the whole night, including the electroencephalogram (EEG), electrooculogram (EOG) and electromyogram (EMG). If necessary, other signals can also be acquired, for instance: oxygen saturation, electrocardiogram (ECG) and respiration signals. From these signals, the clinician defines sleep stages and pathological events such as apneas.

During sleep, the EEG signal exhibits short time recurrent events called A-phases which are part of the Cyclic Alternating Pattern phenomenon [1–3]. A-phases occur repeatedly at intervals between 2 s and 60 s, with an approximate average duration of 7 s. These are classified into three subtypes, on the basis of:

- A1-phase: EEG synchrony is the predominant activity. This phase is characterized by slow frequencies (0.5 Hz–4 Hz), K-complex sequences, vertex sharp transients and polyphasic bursts with less than 20% of rapid activity.
- A2-phase: The EEG activity is a mixture of slow and fast rhythms (8 Hz–30 Hz) with 20–50% of A-phase occupied by fast rhythms.
- A3-phase: It is characterized by Alpha (8 Hz–12 Hz) and Beta waves (12 Hz–30 Hz), which cover more than the 50% of the A-phase duration.

If the duration between two consecutive A-phases is less than 60 s, this time period is called B-phase. A CAP cycle is defined as succession of an A-phase and a B-phase. Two or more consecutive CAP cycles compose CAP sequences which are used to compute the CAP rate.

In general, A1-phases are more frequently observed during the first sleep cycles or during deep sleep, while A2-phases and A3-phases usually appear before the onset of REM sleep in healthy subjects [4]. In addition, the A3-phases are connected to a well known cortical phenomenon named arousal which is a marker of

* Corresponding author.
E-mail address: guadalupe.dorantes@uaslp.mx (G. Dorantes-Méndez).

http://dx.doi.org/10.1016/j.bspc.2017.09.010
1746-8094/

sleep disruption. Thus, a high occurrence represents a detrimental and harmful feature for sleep [5].

Despite the substantial literature regarding A-phases and the CAP phenomenon, only a few studies deal with the relationship between A-phases and the different physiological systems. Extending and expanding these studies is essential to understand the CAP phenomenon from a multi-systemic point of view. Ferri et al. evaluated the heart rate (HR) response during CAP and non-CAP periods and concluded that non-CAP is characterized by basal rhythms of the sleep stage [6]. The other related work was presented by Kondo et al. [7] where they analyzed the cardiovascular response during A-phases in healthy subjects. They observed changes in HR, blood pressure and peripheral vasoconstriction, related to the A-phase. In addition, some studies have evaluated the cardiorespiratory response according to short EEG events such as Delta bursts, K-complexes and microarousals [8] or comparing the response with orienting and startle stimuli [9]. These studies agree with the increase in HR as a short EEG event response. An additional analysis in time domain was performed by González et al. [10], where the increase in HR was found around 4 s after the onset of A-phases. However, the instantaneous evolution of spectral components of the heart activity in pathological conditions is needed to evaluate the response of the autonomic nervous system (ANS) in different circumstances and to understand in a better way the role of ANS during A-phases.

Basically, the ANS is composed of two branches whose respective roles are accelerating or decelerating the function of organs as pancreas, heart and lungs. These branches are called sympathetic and parasympathetic nerves. By means of the beat-to-beat time series (computed from the R peaks) the heart rate fluctuations can be analyzed and these fluctuations are commonly called heart rate variability (HRV). It is well known that its frequency content in the range 0.15 Hz–0.5 Hz (high frequency, HF) is directly related with the parasympathetic activity, while the frequency components in the range 0.04 Hz–0.15 Hz (low frequency, LF) is considered to be a measure of both vagal and sympathetic influences [11]. However, during the presence of A-phases, the statistical properties of the RR intervals and its spectral analysis requires techniques with high temporal resolution to adequately assess the behavior of the ANS. Time-varying autoregressive (TVAR) models are among the most popular techniques to evaluate the spectral components in non-stationary signals in a sample-by-sample manner. The TVAR model presents interesting advantages such as: easy adaptability to transient events, low computational cost and it does not require prior tuning of the frequency bands to explore.

This work focuses on the study of the relationship between A-phases and the ANS, measured through sample-by-sample spectral components of the RR intervals signal. It also explores the connection between the A-phases and ANS during healthy and pathologic condition. Nocturnal Front Lobe Epilepsy (NFLE) was selected, since NFLE is characterized by a percentage ratio of A-phases similar to the percentage found in healthy subjects, and in particular, these patients do not complain of morning tiredness and/or excessive sleepiness [12]. On the other hand, NFLE is a central system pathology, and is therefore not associated with exogenous stimuli that may directly affect the autonomic system.

2. Methods

2.1. Subjects and data collection

Data were collected during Polysomnographic studies from 10 healthy subjects (6 female) with a mean age of 33.2 ± 4.7 years, acquired as the control group and data from 10 patients (3 female) with a mean age of 26.2 ± 9.5 years diagnosed with NFLE. Data acquisitions were held at the Sleep Disorders Center at the University of Parma, Italy using international standard procedures [2]. Exclusion criteria to healthy subjects were neurological disorders, cardiovascular disease and use of drugs that affect the ANS.

Sleep staging (hypnogram) and CAP A-phases were scored by experts based on standard guidelines [2,13]. A-phase annotations were performed by a different expert for each subject, and subsequently reviewed and corrected by a team of sleep experts from the Sleep Disorders Center of the Ospedale Maggiore of Parma in Italy. ECG and EEG signals were acquired during a whole night of sleep, approximately 8 h long, with a sample frequency of 128 Hz. A total of 1713 A-phases were evaluated in 10 healthy subjects and 2294 A-phases for the 10 NFLE patients. RR intervals were automatically detected from ECG by the Pan-Tompkins algorithm and correction of artifacts and ectopic beats was performed by experts. The RR intervals selected correspond to the stage 2 of NREM sleep since the three subtypes of A-phases are present during this stage, whereas deep sleep (sleep stages 3–4) is largely dominated by A1-phases.

2.2. Time varying autoregressive model (TVAR)

The beat-by-beat signal was linearly detrended and resampled by cubic spline interpolation to 4 Hz. The frequency of RR intervals is approximately 1 Hz. Therefore, the selection of 4 Hz is appropriate in order to have evenly sampled data and to perform time – varying analysis. Note that since the RR-interval signal was in fact upsampled, the high frequency content remained unaffected and no aliasing artifacts were produced. Each RR intervals time series is described by a TVAR model as follows:

$$y(n) = \sum_{i=1}^{M} a(i,n)\, y(n-i) + v(n), \tag{1}$$

where M is the model order, $a(i,n)$ represents the TVAR coefficients and $v(n)$ is a white noise error term [14]. The coefficients of the TVAR model were obtained by an adaptive filtering prediction scheme based on the recursive least squares (RLS) algorithm [15]. The RLS algorithm minimizes the cost function:

$$\xi(n) = \sum_{i=1}^{n} \beta(n,i)\, |e(i)|^2 \tag{2}$$

where $e(i) = d(i) - y(i)$ is the model prediction error, defined as the difference between the desired response $d(i)$ and the FIR filter output $y(i)$, and $\beta(n,i)$ is the weighting factor whose role is to ensure that data in the past are forgotten in order to follow the model changes. In addition, the forgetting factor can be defined as an exponential weighting factor: $\beta(n,i) = \lambda^{n-i}$, where $\lambda = 1$ corresponds to infinite memory [15].

The RLS algorithm consists in the following steps, for each instant of time:

$$\mathbf{k}(n) = \frac{\lambda^{-1}\mathbf{P}(n-1)\,\mathbf{u}(n)}{1 + \lambda^{-1}\mathbf{u}^{\mathrm{H}}\mathbf{P}(n-1)\,\mathbf{u}(\boldsymbol{n})}$$

$$\xi(n) = \mathrm{d}(n) - \hat{\mathbf{w}}^{\mathrm{H}}(n-1)\,\mathbf{u}(n) \tag{3}$$

$$\hat{\mathbf{w}}(n) = \hat{\mathbf{w}}(n-1) + \mathbf{k}(n)\,\xi^{*}(n)$$
$$\mathbf{P}(n) = \lambda^{-1}\mathbf{P}(n-1) - \lambda^{-1}\mathbf{k}(n)\,\mathbf{u}^{\mathrm{H}}(n)\,\mathbf{P}(n-1)$$

where $\mathbf{P}(n)$ is the inverse correlation matrix, $\mathbf{k}(n)$ is the gain vector, $\mathbf{u}(n)$ is the tap input vector and $\mathbf{w}(n)$ is the tap weight vector, considering $y(i) = \mathbf{w}^{\mathrm{H}}(i)\,\mathbf{u}(i)$.

The forgetting factor selected was 0.98, while the model order was selected according to the Akaike criterion and was fixed at eight, although different tests were performed with an order in the range of 6–12 with similar results.