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Relation Between Heart Beat Fluctuations and Cyclic Alternating Pattern During Sleep in Insomnia Patients.

R. de León-Lomelí, J.S. Murguía, I. Chouvarda, *IEEE Member*, MO Mendez, *IEEE Member*, E. González-Galván, A. Alba, *EMBS Member*, G. Milioli, A. Grassi, MG. Terzano, L. Parrino.

Abstract— **Insomnia is a condition that affects the nervous and muscular system. Thirty percent of the population between 18 and 60 years suffers from insomnia. The effects of this disorder involve problems such as poor school or job performance and traffic accidents. In addition, patients with insomnia present changes in the cardiac function during sleep. Furthermore, the structure of electroencephalographic A-phases, which builds up the Cyclic Alternating Pattern during sleep, is related to the insomnia events. Therefore, the relationship between these brain activations (A-phases) and the autonomic nervous system would be of interest, revealing the interplay of central and autonomic activity during insomnia. With this goal, a study of the relationship between A-phases and heart rate fluctuations is presented. Polysomnography recording of five healthy subjects, five sleep misperception patients and five patients with psychophysiological insomnia were used in the study. Detrended Fluctuation Analysis (DFA) was used in order to evaluate the heart rate dynamics and this was correlated with the number of A-phases. The results suggest that pathological patients present changes in the dynamics of the heart rate. This is reflected in the modification of A-phases dynamics, which seems to modify of heart rate dynamics.**

I. INTRODUCTION

Insomnia is a condition where the subject experiences an inability to sleep, which prevent the human body from resting, and therefore affects the nervous and muscular system. The effects of this disorder often involve problems such as poor school or job performance, traffic accidents and also are related with cardiac fails [1]. In this paper we consider two types of primary insomnia: psychophysiological insomnia and paradoxical insomnia which are compared with subjects without sleep disorders [2].

Previous studies showed that insomnia has a relationship with CAP (Cyclic Alternating Pattern) [3]. CAP is a periodic activity reflected in the EEG during non-REM sleep, and is characterized by sequences of transient electrocortical events, called A-phases, deviating from the baseline of the EEG activity, and occurs repeatedly in 2 to 60 seconds interval. Increased CAP (generally, also the number of A-phases increase) itself may indicate unstable sleep and / or sleep disturbance, and can also be used to identify patterns associated with some sleep disorders. A-phases are identified as A1, A2 and A3, and are closely related to the stages of sleep wakefulness and NREM [2].

A-phases are classified in three groups based on the observed frequency information:

i. A1-phase. It is characterized by bursts and k-complexes of Delta waves (0.5 Hz - 4 Hz).

ii. A2-phase. It has rapid EEG waves that cover between 20% and 50% of the A-phase duration.

iii. A3-phase. It is characterized by Alpha (8 Hz - 12 Hz) and Beta waves (12 Hz - 30 Hz), which cover more than 50% of the A-phase duration [3].

Moreover, the dynamics of the heart rate could be characterized by the Heart Rate Variability (HRV), computed as the time between the detection of consecutive R peaks, obtained from an electrocardiogram signal [4]. Previous analysis focused on the HRV signals in apnea patients and other pathologies, finding a correlation grade between them, using DFA as analysis method.

However the correlation between A-phases and heart dynamics in sleep stages has not been analyzed before. And even there is little information about the interaction of the time series in HRV and EEG sleep periods [4] [5] [6].

The main goal of this study is to investigate potential correlation between the A-phases and the HRV signals and to understand the effect of insomnia in them. DFA analysis of HRV is applied and its changes with sleep macro and icro structure are discussed.

II. METHODS AND MATERIALS

A. Mathematical analysis

In 1994 C. K. Peng et al. [7] proposed a method, referred to as Detrended Fluctuation Analysis (DFA) that enables the

detection of long-range correlations in non-stationary time series. This method uses a coefficient (α) to determine the complexity of the signals. A typical example is the R-R series.

Let $y(t_i)$ be a time series, where $t_i = i\Delta t$ and $i = 1, ..., N$ with a sample rate Δt. The DFA algorithm is computed as follows [8]:

I. Determine the profile

$$x(t_i) = \sum_{j=1}^{i} \left[y(t_j) - \bar{y} \right], \quad i = 1, ..., N, \tag{1}$$

of the time series, which is the cumulative sum of the time series from which the series mean value is subtracted.

II. Divide the integrated time series $x(t_i)$ into windows of length **n**, corresponding to a time scale $\tau = n\Delta t$.

III. Calculate the local trend for each window by a least-squares polynomial fit of the integrated series. The interpolated curve $x_{pol,m}(t_i, \tau)$ represents the local trend at each window, where **m** is the degree of the polynomial function.

IV. Compute the local fluctuation sequence associated to each window, which is given by

$$z_m(t_i, \tau) = x(t_i) - x_{pol,m}(t_i, \tau) \tag{2}$$

For $i = 1, ..., N$.

V. Calculate the fluctuation function $F_m(\tau)$ defined as

$$F_m(\tau) = \sqrt{\left(\frac{1}{N}\right) \sum_{j=1}^{N} z_m(t_j, \tau)^2} \tag{3}$$

which corresponds to the root mean square of the sequence $z_m(t_i, \tau)$.

Repeat the above procedure for a wide range of segments of length **n**. According to the author recommendations (Penzel [7]), the size of windows should be between $n_{min} \cong 5$ and $n_{max} \cong N/4$.

In order to determine if the analyzed signal presents a scaling behavior, the fluctuation function $F_m(\tau)$ should reveal a power law scaling

$$F_m(\tau) \sim \tau^{\alpha_m}, \tag{4}$$

where the scaling exponent α_m can be estimated as the slope of the line in a $\log(F_m(\tau))$ versus $\log(\tau)$ plot, and it quantifies the correlation properties of the time series. Here, we employ a linear polynomial in the detrending procedure, thus m=1, and for convenience we denote $\alpha_1 = \alpha$.

The value of $\alpha=1/2$ corresponds to an uncorrelated signal, and it presents a white noise behavior. On the other hand, if $0<\alpha<1/2$ the signal presents an anticorrelated behavior (alternation between small and large values); if $1/2<\alpha<1$, we have correlated signals, where large values in the series are more probably to appear after large values, and vice versa. The particular values $\alpha=1$ and $\alpha=3/2$ correspond to $1/f$ noise and Brownian motion, respectively.

An interesting phenomenon that some signals may display is the crossover, when the log-log graph of $F_m(\tau)$ presents two slopes $\alpha1$ and $\alpha2$. Some references indicate that this occurs in 75% of cases and only the first slope helps to determine the level of signal correlation and so the level of patient pathology [7] [8]. This paper focuses on the analysis of the signals of patients with insomnia problems based only on the result of $\alpha1$.

As an example, Fig. 1 illustrates the application of the DFA procedure to a frame of HRV data at an insomnia patient. This Figure only shows the procedure for the case of a window size of 37 points.

B. Data analysis

The study was carried out on three different groups of patients: (a) normal sleepers (Nor group), (b) psychophysiological insomnia group (PsI group), and (c) sleep misperception group (Mis group). The three groups considered five subjects, two males and three females, where one sleep polysomnographic recording per subject was provided by the Parma University Sleep Disorders Center [2]. In the Nor group the subjects were healthy with a mean age of 36 years and no sleep complaints. The subjects in the PsI group suffered psychophysiological insomnia, with a mean age of 41.5 years. On the other hand, in the Mis group the subjects have paradoxical insomnia, also known as sleep state misperception, with a mean age of 36.2 years.
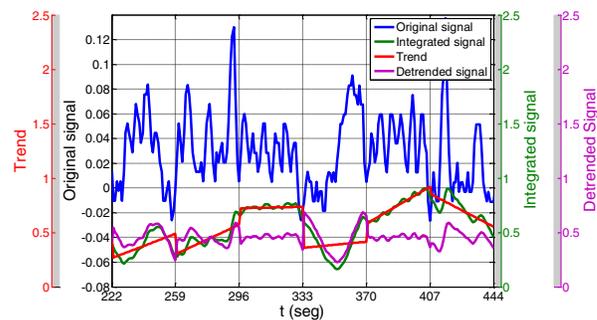

Figure 1. Detrended fluctuation analysis example with a box size of 37 points.

C. Preprocessing for Heart Rate Extraction

The ECG was processed using the Pan Tompkins algorithm to obtain the R-R time series and a beat to beat visual checking corroborates the correct R peak detection. The R-R time series were segmented in 10 minutes long windows and grouped in: (a) light sleep (stages 1 and 2), (b) deep sleep (stages 3 and 4) and (c) REM stage. The time intervals less than 10 minutes were eliminated from the analysis.

D. Heart Rate DFA analysis

The former data was analyzed by the DFA method. For each analyzed frame, the number of the different A-phases (A1, A2 and A3) per hour was calculated.

The segments extracted from whole night data were classified in three groups: light sleep, deep sleep and REM. This favors finding information about the signal dynamic. In this work, all the frames at each stage in all night register were analyzed, and a mean was calculated. Also the results per patient group were averaged.

III. RESULTS

Fig. 2 shows the DFA analysis during light sleep for the three subject groups. At this stage, a previous work [4] establishes an alpha value of 1.00±0.21 in healthy patients (Nor). The values obtained in this work were 1.0616 for healthy patients, 1.1369 for PsI patients and 1.0772 for Mis patients. Scale sizes selected are from n>5 to n<45, to focus on the small scale signal properties.

Fig. 3 shows the analysis results during deep sleep. The alpha value in Nor patients is clearly different as compared to the value corresponding to patients with sleep pathologies. The alpha of healthy patients was 0.9830, which is a value within the 0.82±0.19 range, established by [4] for people with no sleep problems. In the case of PsI patients, the calculated value of alpha is 1.1111, while in the case of patients belonging to the Mis group, the alpha value is 1.107.
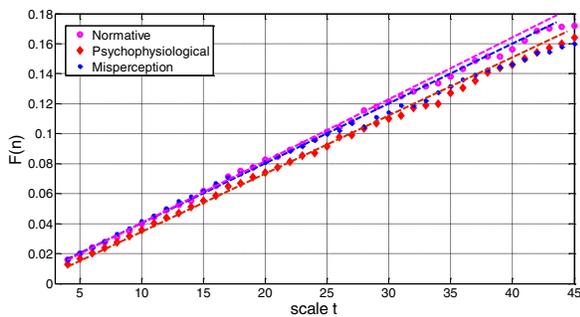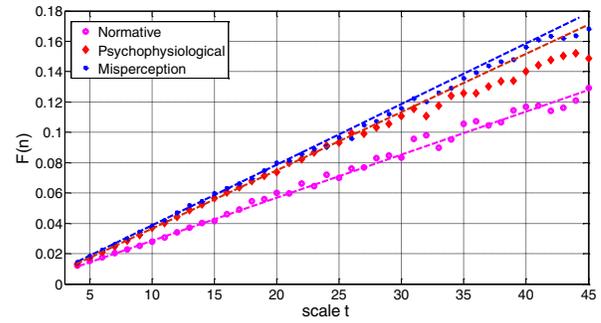

Figure 3. Result of DFA analysis during DEEP sleep.

Fig. 4 shows boxplots of the DFA results for each sleep stage and each group of patients. The difference between the patients is noticeable; however according to the alpha values, all of the signals display *1/f* behavior. The Misperception group presents the largest variance of the three, whereas normal subjects show a similar behavior with little variance. In NREM sleep normal subjects tend to present lower alpha, with the opposite in REM sleep. These findings may relate to the fact that normally, in deep sleep, there is a raised parasympathetic activity, which could be related with a lower DFA, while in insomnia sympathovagal balance, may be modified, and hyperarousal could keep high sympathetic tone. In insomnia the DFA differences among sleep stages are less evident, suggesting a high somatic arousal.

Table I shows the mean number of A-phases and the mean alpha measure. For the A-phases (A1, A2 and A3), the mean by hour was calculated for each type of patient, separating in light sleep and deep sleep. The percentage represents the contribution at each sleep stages from the A-phases. So, Nor patients in light sleep had an 50.69% of A1, 26.99% of A2 and 22.31% of A3-phases.

For the A-phases in light stage, an increase in A2-phases and A3-phases can be observed and a decrease in A1-phases for both insomnia groups, with respect to the normal subjects. In deep sleep stage the number of A-phases does not follow the same tendencies, however show clear differences between healthy and insomnia patients.
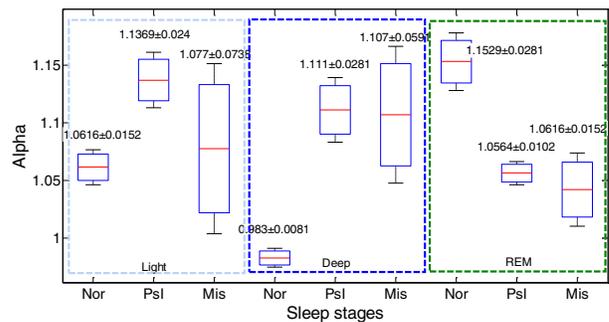

Figure 2. DFA analysis of HRV signal for patients with insomnia and normal subjects during light sleep.

Figure 4. Boxplots of the DFA results (αvalues) for each group of patients (Nor, PsI, Mis) during each sleep stage (light, deep, REM).

TABLE I. A-Phases Behavior and the Alpha1 Value Obtained in Each Case.

Parameter	Group	Sleep stage			Mean
		Light	*Deep*	*REM*	
A1-phases	Nor	31.5	73.72		105.22 [a]
	%	50.69	90.37		73.22
	PsI	26.54	84.95		111.49 [a]
	%	35.01	89.24		65.21
	Mis	24.27	89.56		113.83 [a]
	%	34.77	97.67		70.49
A2-phases	Nor	16.77	6.888		23.65 [a]
	%	26.99	8.443		16.46
	PsI	21.85	8.08		29.93 [a]
	%	28.83	8.489		17.50
	Mis	17.07	1.114		18.18 [a]
	%	24.46	1.21		11.26
A3-phases	Nor	13.86	0.965		14.82 [a]
	%	22.31	1.183		10.31
	PsI	27.39	2.155		29.54 [a]
	%	36.14	2.264		17.28
	Mis	28.45	1.017		29.46 [a]
	%	40.75	1.11		18.24
α1	Nor	1.061	0.983	1.152	1.065
	Psi	1.136	1.1111	1.056	1.101
	Mis	1.077	1.1	1.04	1.072

*Note: number of A-phases in both stages.

IV. DISCUSSION

An analysis of the HRV dynamics during sleep and its correlation with the CAP was presented. DFA was used in order to evaluate the HRV fluctuations at different scales, in order to assess the correlation among the scales. Our main findings are: (a) it seems that exist an increase in the number of A3-phases during the pathologic conditions with respect to the normal subjects. This arousal increase may be related with an observed increase in the HRV alpha value (> 1) during deep sleep, and (b) the variance in the HRV alpha value appears higher in the misperception patients as compared to the normal subjects and psychophysiological insomnia patients.

It is well known that A3-phases (commonly referred to as Arousals from sleep) produce a clear tachy-bradycardia pattern that could often be observed in the HRV. Thus, the transition of the HRV correlation (as measured by the DFA alpha values) from 1/f behavior towards Brownian motion, could be produced by the dynamics imposed by the A3-phases in pathologic conditions.

In addition, even if the mean alpha value for misperception and psychophysiological insomnia is similar, the variance is considerably higher for misperception patients. This could suggest that the HRV dynamics do not have a specific pattern imposed only by A3-phases, and thus mechanisms behind the two types of insomnia may differ. Values obtained in this study were consistent with those obtained by Penzel [7] for normal patients. Insomnia patients results were compared with the obtained for patients with sleep apnea, and were very similar, which is an indication of a trend in the HRV behavior in people with sleep disorders.

It was observed that the degree of apnea pathology affects the level of correlation of the cardiac signals, and the central system behavior reflected as CAP.

Results were concordant with obtained in previous analysis [2]. In this, the A3- phases in insomniac patients show the same increasing behavior in the light sleep.

The main limitation of this study was the number of patients, thus a future step include increasing the population in the study in order to improve our results and increase the reliability of our findings. In addition, another improvement to the current work is the correlation of the A-phases with respect to the classical HRV parameters, in order to have a better point of reference.

V. CONCLUSION

This study presents an analysis of the cardiac activity during sleep A-phases, using DFA analysis. In DFA the signal can be characterized according to the relationship between frequency and power. The results suggest that the increase in the number of A3-phases may have an impact on the dynamics of the HRV which shifts toward Brownian motion.

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