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Alterations in Sleep Electroencephalography and Heart Rate Variability During the Obstructive Sleep Apnoea and Hypopnoea

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1. Introduction

Sleep is a vital physiological function and high quality sleep is essential for maintaining the good health. Sleep disorders however are amongst the most common disorders suffered by humans and it is rare for most people to regularly enjoy the amount of quality sleep they need. The behavioural and social causes of sleep disorders are typically the result of modern lifestyle, which are usually linked to Obstructive Sleep Apnoea Hypopnea Syndrome (OSAHS). Healthcare professionals and sleep researchers are currently looking for ways to improve the clinical diagnosis of OSAH sufferers. OSAH means "cessation of breath" [Vgontzas, 1999]. Due to this cessation of breath, the sufferer might experience related

changes in the electrical activity of the *brain and heart* [Roche, et al., 1999; Cvetkovic et al., 2009; Dingli, et al., 2003; Jurysta, et al., 2006; Task Force of the European Society of Cardiology and the North American Society of Pacing and Electrophysiology, 1996]. This activity recorded from electroencephalographic (EEG) and electrocardiographic (ECG) signals might differ in patients suffering from sleep apnoea. The analysis and tools used in sleep scoring and detection till now are based on the conventional sleep staging from whole night polysomnography (PSG) introduced by Rechtschaffen and Kales [Rechtschaffen, et al., 1968] which covere only a limited part of sleep-related EEG phenomena. A considerable number of computerised scoring systems have been introduced to attain a more standardised system of sleep EEG evaluation. In sleep research, the analysis of sleep microstructure has been recognised. The sleep EEG, in particular during the OSAH episodes often contains linear and non-linear information as well as stochastic components (noise). The separation and evaluation of these signal components remains a problem not entirely solved. Hence, new approaches to the detection and evaluation of sleep EEG transients during the OSAH episodes are required. The application of non-linear time series analysis method to sleep EEG was carried in the framework of the chaos hypothesis and characterized as the Lyapunov exponent [Fell, et al., 1993; Fell, et al., 1996; Übeyli, 2006]. Positive Lyapunov exponents have indicated that the EEG may result from a low-dimensional chaotic process. Lyapunov exponents can serve as clinically useful parameters. Estimation of the Lyapunov exponents is computationally more demanding, but estimates of these parameters are more readily interpreted with respect to the presence of chaos, as positive Lyapunov exponents are the hallmark of chaos [Haykin & Li, 1995; Abarbanel, et al., 1991]. Eigenvector methods are used for estimating frequencies and powers of signals from noise-corrupted measurements. These methods are based on an eigen-decomposition of the correlation matrix of the noise–corrupted signal. Even when the signal-to-noise ratio (SNR) is low, the eigenvector methods produce frequency spectra of high resolution. These methods are best suited to signals that can be assumed to be composed of several specific sinusoids buried in noise [Schmidt, 1986; Akay, et al., 1990; Übeyli, 2008; Übeyli, et al., 2007; Cvetkovic et al., 2009]. In this study, the eigenvector's multiple signal classification (MUSIC) method, of the linear time series characteristic, was used for estimating frequencies and powers of EEG signals from noise-corrupted measurements.

The use of Heart Rate Variability (HRV) and EEG signals for detecting cardiovascular disease and sleep disorder has been proposed to overcome the drawback of PSG method. The HRV parameters derived from frequency domain analysis of ECG R-R Intervals (RRI) have been used to assess an Autonomic Nervous System (ANS) which play an important role in the control of cardiac activity like heart rate and rhythms. The Low Frequency (LF) and High Frequency (HF) bands are used to reflect the activation of ANS subsystem; the sympathetic and parasympathetic, respectively. Whereas, the HRV's Very Low Frequency (VLF) is believed to reflect thermoregulation mechanism. The LF and HF ratio (LF/HF) is normally used as the marker of sympathovagal balances [Task Force of the European Society of Cardiology and the North American Society of Pacing and Electrophysiology, 1996]. Previous studies [Vaughn, et al., 1995; Bonnet, et al., 1997; Vanoli, et al., 1995; Jurysta, et al., 2003] have suggested that HRV vary with sleep stages; the LF component is dominant during Wake stage and gradually decreases in Non-Rapid Eye Movement (NREM) and peaks again in Rapid Eye Movement (REM) stage. An opposite trend was reported for the

HF component. Few studies have investigated the relationship between specific EEG frequency bands with the HRV parameters in healthy patients and in the sleep apnoea hypopnoea sufferers [Ako, et al., 2003; Yang, et al., 2002; Brandenberger, et al., 2001; Ehrhart, et al., 2000].

The aim of this study is two-fold. Firstly, it is set to investigate any possible changes in the human EEG activity due to OSAH occurrences by applying the non-linear and linear time series methods. Secondly, it is set to assess the correlation between EEG frequency bands and HRV in normal and sleep apnoea human clinical patients at different sleep stages. The parameters obtained from this correlation can be used to distinguish the healthy and patients suffering from sleep apnoea and hypopnoea syndromes. The first part of this study consisted of investigating the EEG activity throughout all sleep stages for one patient only. The second part of the study involved a much larger sample size of healthy and unhealthy patients to investigate the changes and possible correlation of EEG and HRV activity.

2. Data Description

Subjects
For the first part of this study, one human patient (age: 32, sex: male, weight: 96kg, height: 1.76m), diagnosed with the Apnoea Hypopnoea Index (AHI) of 5.1, was recruited for an overnight PSG recording at St. Lukes Hospital (Sydney, NSW, Australia). The second part of the study consisted of 8 healthy (5 males and 3 females) and 11 sleep apnoea patients (9 males and 2 females). Descriptive clinical features and sleep parameters of healthy and sleep disorder patients are presented in Table 1.

	Healthy	Sleep Apnoea
Age (years)	48.13 ± 10.52	50.64 ± 11.39
BMI (kg/m^2)	27.01 ± 2.94	32.92 ± 5.30
AHI	2.75 ± 1.22	48.97 ± 27.52
Total sleep time (min)	379.83 ± 59.57	393.83 ± 33.01
Sleep latency (min)	26.45 ± 30.59	23.25 ± 23.89
REM latency (min)	211.36 ± 89.81	161.52 ± 39.13
Sleep efficiency (%)	82.70 ± 8.03	87.89 ± 8.31
Wake (%)	16.35 ± 8.31	11.32 ± 8.21
Stage 1 (%)	7.5 ± 6.10	6.47 ± 3.34
Stage 2 (%)	45.83 ± 5.42	52.57 ± 11.22
Stage 3 (%)	12.51 ± 3.32	10.30 ± 7.82
Stage 4 (%)	1.84 ± 3.61	2.52 ± 4.36
REM (%)	15.01 ± 7.48	16.03 ± 5.03

Table 1. Patient clinical features and sleep scoring parameters.

Experimental Protocol
An eight-hour standard clinical sleep PSG was recorded with sampling frequency of 256 Hz using Bio-Logic System and Adults Sleepscan Vision Analysis (Bio-Logic Corp, USA). Surface electrodes were placed on the scalp's surface (C3, C4 and O2; 10-20 system) and referenced to bridged left and right mastoid to record the EEG activity. Two channels were

used to record the eye movements, with one electrode placed 1 cm above and slightly lateral to the outer canthus of one eye and the second electrode recording the potentials from an electrode 1 cm below and slightly lateral to the outer canthus of the other eye. The other electrodes recorded the EMG from the muscle areas on and beneath the chin, ECG (using lead-II across the chest area), nasal and oral airflow, snoring sounds, breathing effort (measured at the chest and abdomen), oxymetry, actigraphy recording body positioning and leg movements (right and left anterior tibialis).

The respiratory signals of apnoea and hypopnoea events were evaluated using American Academy of Sleep Medicine (AASM) Criteria [American Academy of Sleep Medicine Task Force, 1999] and visually scored by the sleep technician from 30 second epochs. The one patient sleep analysis reported 64.5% sleep efficiency and 91.8% in sleep maintenance with 132 min spent in wake (W) stage, 30 min in stage 1 (S1), 125 in stage 2 (S2), 17 min in stage 3 (S3), 49 min in stage 4 (S4), 26 min in stage REM, 220 min non-REM and 3 min in movement time [Cvetkovic, et al., 2007]. The hypopnoea segments used in this investigation were only visually detected in S2.

3. Signal Processing Methods

Nonlinear Measures

The Lyapunov exponents are a quantitative measure for distinguishing among the various types of orbits based upon their sensitive dependence on the initial conditions, and are used to determine the stability of any steady-state behaviour, including chaotic solutions. The reason why chaotic systems show a periodic dynamics is that phase space trajectories that have nearly identical initial states will separate from each other at an exponentially increasing rate captured by the so called Lyapunov exponent [Haykin et al., 1995; Abarbanel, et al., 1991]. This is defined as follows. Consider two (usually the nearest) neighbouring points in phase space at time 0 and at time *t*, distances of the points in the *i-th* direction being $\|\delta x_i(0)\|$ and $\|\delta x_i(t)\|$, respectively. The Lyapunov exponent is then defined by the average growth rate λ_i of the initial distance,

$$\frac{\|\delta x_i(t)\|}{\|\delta x_i(0)\|} = 2^{\lambda_i t} (t \to \infty) \text{ or} \tag{1}$$

$$\lambda_i = \lim_{t\to\infty} \frac{1}{t} \log_2 \frac{\|\delta x_i(t)\|}{\|\delta x_i(0)\|} \tag{2}$$

The existence of a positive Lyapunov exponent indicates chaos. This shows that any neighbouring points with infinitesimal differences at the initial state are abruptly separate from each other in the *i -th* direction. In other words, even if the initial states are close, the final states are much different. This phenomenon is sometimes called sensitive dependence on initial conditions. Numerous methods for calculating the Lyapunov exponents have been developed in the past decade. Generally, the Lyapunov exponents can be estimated either from the equations of motion of the dynamic system (if it is known), or from the observed time series. The latter is what is of interest due to its direct relation to the work in this chapter. The idea is based on the well-known technique of state space reconstruction with delay coordinates to build a system with Lyapunov exponents identical to that of the original system from which our measurements have been observed. Generally, Lyapunov

exponents can be extracted from observed signals in two different ways. The first is based on the idea of following the time-evolution of nearby points in the state space. This method provides an estimation of the largest Lyapunov exponent only. The second method is based on the estimation of local Jacobi matrices and is capable of estimating all the Lyapunov exponents. Vectors of all the Lyapunov exponents for particular systems are often called their Lyapunov spectra [Haykin et al., 1995; Abarbanel, et al., 1991].

Linear Measures

Eigenvector methods are used for estimating frequencies and powers of signals from noise-corrupted measurements. A number of eigenvector methods have been applied by authors [Akay, et al., 1990; Übeyli, 2008; Übeyli, et al., 2007; Cvetkovic et al., 2009], such as Pisarenko, Multiple Signal Classification (MUSIC) and Minimum-Norm. The polynomial $A(f)$ which contains zeros on the unit circle can then be used to estimate the power spectral density (PSD):

$$A(f) = \sum_{k=0}^{m} a_k e^{-j2\pi fk} \tag{3}$$

where $A(f)$ represents the desired polynomial, a_k represents coefficients of the desired polynomial, and m represents the order of the eigenfilter, $A(f)$.

The polynomial can also be expressed in terms of the autocorrelation matrix R of the input signal. Assuming that the noise is white:

$$R = E\left\{x(n)^* \cdot x(n)^T\right\} = SPS^{\#} + \sigma v^2 I \tag{4}$$

where $x(n)$ is observed signal, S represents the signal direction matrix of dimension $(m+1)\times L$ and L is the dimension of the signal subspace, R is the autocorrelation matrix of dimension $(m+1)\times(m+1)$, P is the signal power matrix of dimension $(L)\times(L)$, σv^2 represents the noise power, * represents the complex conjugate, I is the identity matrix, # represents the complex conjugate transposed, T shows the matrix transposed. S, the signal direction matrix is expressed as:

$S = \left[Sw_1 \quad Sw_2 \quad \cdots \quad Sw_L\right]$

where w_1, w_2, $\cdots$, w_L represent the signal frequencies:

$Sw_i = \left[1 \quad e^{jwi} \quad e^{j2wi} \quad \cdots \quad e^{jmwi}\right]^T \qquad i = 1,2,\cdots,L$.

In practical applications, it is common to construct the estimated autocorrelation matrix $\hat{R}$ from the autocorrelation lags:

$$\hat{R}(k) = \frac{1}{N}\sum_{n=0}^{N-1-k} x(n+k)\cdot x(n) \qquad k = 0,1,\cdots,m \tag{5}$$

where k is the autocorrelation lag index and N is the number of the signal samples.
Then, the estimated autocorrelation matrix becomes:

$$\hat{R}(k) = \begin{bmatrix} \hat{R}(0) & \hat{R}(1) & \hat{R}(2) & \cdots & \hat{R}(m) \\ \hat{R}(1) & \hat{R}(0) & \hat{R}(1) & \cdots & \hat{R}(m-1) \\ \hat{R}(2) & \hat{R}(1) & \hat{R}(0) & \cdots & \hat{R}(m-2) \\ \vdots & \vdots & \vdots & \ddots & \vdots \\ \hat{R}(m) & \hat{R}(m-1) & \cdots & \cdots & \hat{R}(0) \end{bmatrix} \tag{6}$$

Multiplying by the eigenvector of the autocorrelation matrix a, equation (4) can be rewritten as:

$$\hat{R}a = SPS^{\#}a + \sigma v^2 a \tag{7}$$

where a represents the eigenvector of the estimated autocorrelation matrix $\hat{R}$ and a is expressed as:

$$\left[a_0, \quad a_1, \quad \cdots, \quad a_m\right]^T .$$

In principle, under the assumption of white noise all noise subspace eigenvalues should be equal:

$$\lambda_1 = \lambda_2 = \cdots = \lambda_K = \sigma v^2$$

where λ_i represents the noise subspace eigenvalues, $i = 1,2,\cdots,K$ and K represents the dimension of the noise subspace.

The MUSIC method has been applied in this particular analysis, which is a noise subspace frequency estimator and eliminates the effects of spurious zeros by using the averaged spectra of all of the eigenvectors corresponding to the noise subspace. The resultant PSD is determined from:

$$P_{MUSIC}(f) = \frac{1}{\frac{1}{K}\sum_{i=0}^{K-1} \left|A_i(f)\right|^2} \tag{8}$$

where K represents the dimension of noise subspace, $A_i(f)$ represents the desired polynomial that corresponds to all the eigenvectors of the noise subspace [Schmidt, 1986; Akay, et al., 1990; Übeyli, 2008; Übeyli and Cvetkovic, 2007; Cvetkovic et al., 2007, 2009].

EEG and HRV Signal Processing and Analysis

The EEG, EOG and ECG data was processed and analysed using Matlab software (Mathworks, USA). The EEG-EOG correction was applied based on the regression analysis, together with source noise removal using the 50 Hz notch filter. The EEG data was processed in 30 sec segments.

A five-minute ECG data window of free movement artefacts for each sleep stage was visually selected for the HRV analysis for each patient. Signal processing algorithm implemented in Matlab, identified a QRS complex for extraction of RR Intervals (RRI) which was based on Hilbert transformation [Benitez, et al., 2001]. RRI was re-sampled at 4 Hz using Berger algorithm [Berger, et al., 1986]. Further non-parametric spectral analysis based on Fast Fourier Transform (FFT) with no windowing function was performed according to Task Force [Task Force of the European Society of Cardiology and the North American

Society of Pacing and Electrophysiology, 1996]. The absolute and normalised spectral power within each frequency band was computed using trapezoidal integration of the area under spectral curve. The HRV frequency bands are as follows: very low frequency (VLF: ≤ 0.04 Hz), low frequency (LF: 0.04-0.15 Hz) and high frequency (HF: 0.15-0.4 Hz). The normalised value was calculated as LFnu=LF/(Total power – VLF) and HFnu= HF/(Total power – VLF).

From the raw EEG signals, the same five-minute segments used for processing ECG signals were applied for spectral analysis. For the present analysis, EEGs' C3-A2 derivation was used due to our earlier study which has shown significant changes of EEG activity in an apnoea-hypopnoea patient [Cvetkovic et al., 2009]. The power spectral of 10x30-second epochs for each segment was computed using FFT with no windowing points. The estimated power is grouped into five EEG frequency bands: delta (0.5-4.5 Hz), theta (5-8.5 Hz), alpha (9-12.5 Hz), sigma (13-16.5 Hz) and beta (17-30 Hz). Initially, an absolute power was computed followed by the relative power which was derived by dividing the power within each band by the total power (0.5-30 Hz). For further analysis, the relative powers were averaged every five-minutes.

4. Results

Average Lyapunov Exponent Method
Multiple Wilcoxon (matched-pairs) signed-ranks non parametric tests were performed to analyse the pre and during-hypopnoea average Lyapunov exponents for individual EEG electrodes (C3, C4 and O2), using SPSS 17 (SPSS Inc., USA). For the average Lyapunov exponent results, a significant decrease (z=-2.934, p<0.0003) was revealed from pre-hypopnoea (mean=5.806, SD=0.434) to during-hypopnoea (mean=5.425, SD=0.539) at C3, as shown in Table 3 and Figure 1A) and 1B). It was evident for C3 electrode that throughout the 11 epochs, the average Lyapunov exponent values were significantly lower during the hypopoea in comparison to pre-hypopnoea. The other significant decrease (z=-2.312, p<0.021) from pre-hypopnoea (mean=5.664, SD=0.468) to during-hypopnoea (mean=5.445, SD=0.492) was evident at O2 electrode (see Table 3 and Figure 1B). Similar for C3 electrode, at O2, the average Lyapunov exponent values were lower during-hypopnoea (throughout the 11 epochs except for epoch 10). A *post hoc* analysis with alpha rate correction of p<0.017 was calculated using Bonferroni test for multiple average Lyapunov exponent values. According to this alpha rate correction, the only significant difference recognised was at C3 electrode of (p<0.0003).

MUSIC Method
For the MUSIC results, a significant increase (z=-2.045, p<0.041) was revealed from pre-hypopnoea (mean=0.005, SD=0.004) to during-hypopnoea (mean=0.009, SD=0.009) at O2 and sigma EEG band, as shown in Table 2 and Figure 2A). Throughout the 11 epochs, the average MUSIC values were significantly higher during the hypopoea in comparison to pre-hypopnoea (except for epochs 2 and 6) (Figure 2A)). The similar significant increase (z=-2.233, p<0.026) from pre-hypopnoea (mean=0.004, SD=0.002) to during-hypopnoea (mean=0.005, SD=0.003) was evident at the same O2 electrode and beta EEG band (see Table 2 and Figure 2B)).

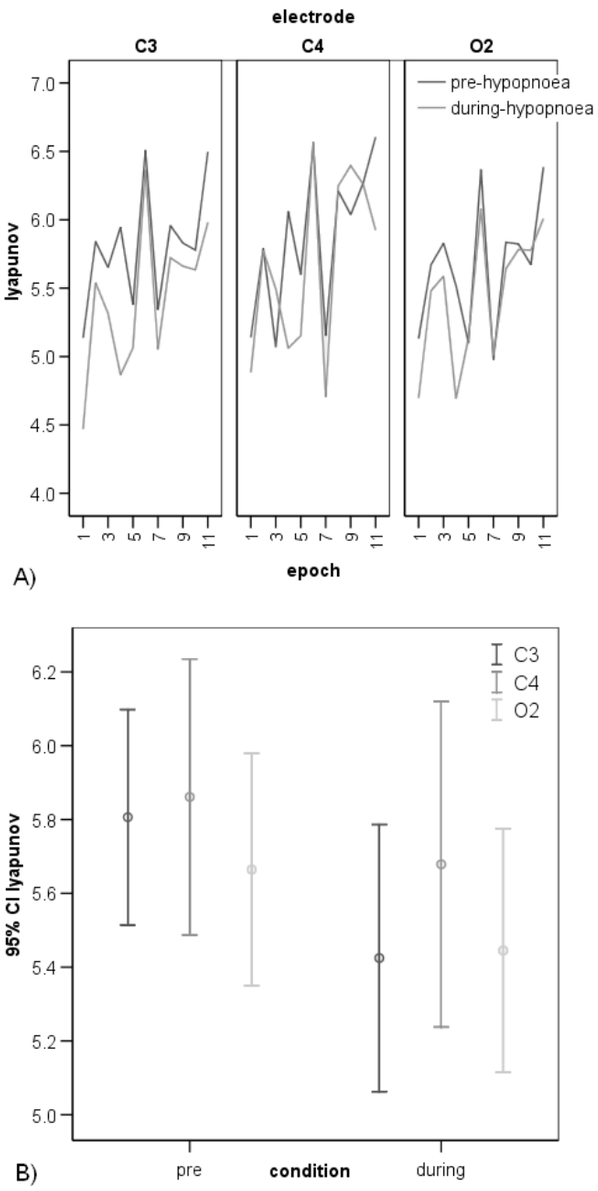

Fig. 1. The comparison of A) pre and during hypopnoea average Lyapunov exponents (y-axis) vs. 1-11 epoch (x-axis) for each EEG electrode (C3, C4 and O2) is represented. B) The confidence intervals of Lyapunov exponents (y-axis) vs. pre and during-hypopnoea conditions (x-axis) for each EEG electrode (C3, C4 and O2) is illustrated.

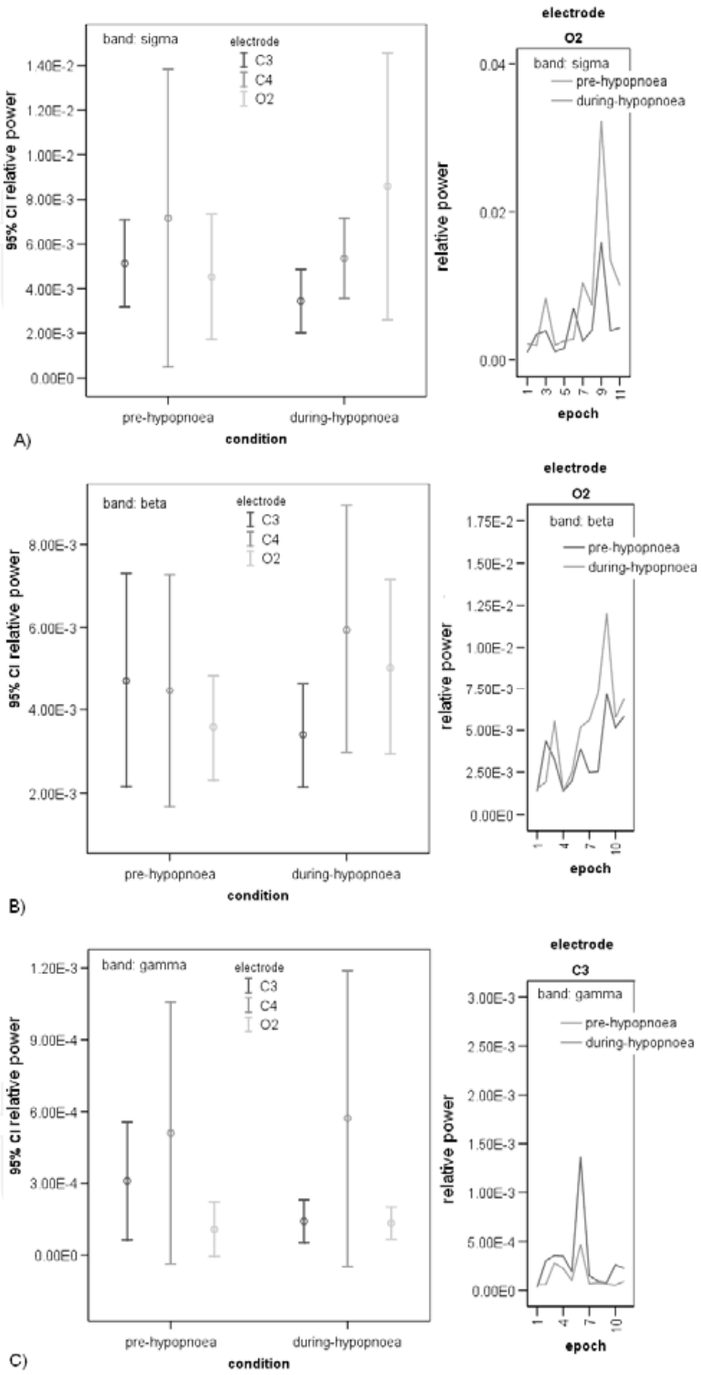

Fig. 2. The comparison of pre and during hypopnoea relative MUSIC powers (y-axis) vs. 1-11 epoch (x-axis) for specified EEG electrode is represented together with the confidence intervals of relative MUSIC powers (y-axis) vs. pre and during-hypopnoea conditions (x-axis) for each EEG electrode (C3, C4 and O2) at A) sigma, B) beta and C) gamma bands.

A significant decrease was revealed at gamma EEG band at C3 electrode (z=-2.667, p<0.008) from pre-hypopnoea (mean=0.0003, SD=0.0003) to during-hypopnoea (mean=0.0001, SD=0.0001) (see Table 2 and Figure 2B)). Epoch 1 only showed a slight inconstancy in this significant decrease throughout all the epochs. According to a *post hoc* analysis with the Bonferroni test alpha rate correction of p<0.0028, calculated for multiple average MUSIC values, none of the significant differences were recognized as actually being significant. Therefore, no significant finding could be concluded from the MUSIC method.

Linear MUSIC	Z Asymp. Sig. (p)	delta	theta	alpha	sigma	beta	gamma
C3	*Z*	-1.156	-1.156	-0.356	-1.511	-0.711	**-2.667**
	p	0.248	0.248	0.722	0.131	0.477	**0.008**
C4	*Z*	-0.622	-1.156	-0.178	-0.711	-1.334	-1.067
	p	0.534	0.248	0.859	0.477	0.182	0.286
O2	*Z*	-0.445	-1.067	-0.089	-2.045	-2.233	-1.778
	p	0.657	0.286	0.929	0.041	0.026	0.075

Table 2. Wilcoxon (matched-pairs) signed-ranks test analysis of pre and during-hypopnoea average MUSIC values for individual EEG electrodes (C3, C4 and O2) and bands (delta, theta, alpha, sigma, beta and gamma).

Non-linear	Z Asymp. Sig. (p)	Lyapunov
C3	*Z*	***-2.934***
	p	***0.003***
C4	*Z*	-1.156
	p	0.248
O2	*Z*	-2.312
	p	0.021

Table 3. Wilcoxon (matched-pairs) signed-ranks test analysis of pre and during-hypopnoea average Lyapunov exponents for individual EEG electrodes (C3, C4 and O2).

Statistical Correlation Between EEG and HRV Results

The Mann-Whitney, a non-parametric test was used to asses the differences of HRV parameters and EEG frequency bands with sleep stages *between the healthy and the sleep apnoea* patients. To study the relationship between HRV parameters and EEG frequency bands in different sleep stages, Pearson's correlation was applied in both groups. An alpha level of 0.05 was used for statistical test using SPSS 17 (SPSS Inc., USA) software.

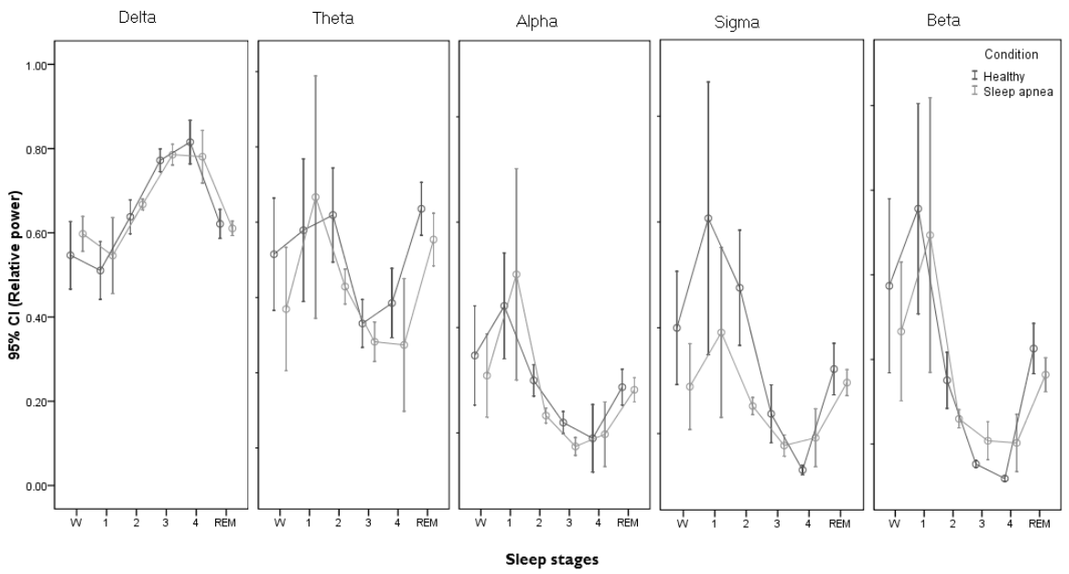

Fig. 3. Comparison of mean relative power and 95% confidence intervals (CI) of five EEG frequency bands (delta, theta, alpha, sigma and beta) versus sleep stages in the healthy and sleep apnoea groups.

Figure 3 shows that only delta EEG increased from Wake to Stage 4 and decreased in REM. Other EEG frequency bands indicated an increase from Wake to Stage 1, further decreased throughout sleep Stages 1-4 and increased again in REM. In sleep apnoea group, the relative power of theta EEG was lower compared to the healthy group during Wake ($z=1.98$, $p=0.048$), Stage 2 ($z=-2.63$, $p=0.008$) and Stage 4 ($z=-2.15$, $p=0.032$) (Figure 3). In addition to Stage 2 ($z=-4.19$, $p<0.001$), the relative power in alpha EEG of sleep apnoea group was lower in Stage 3 ($z=-4.26$, $p<0.001$). Likewise, the difference of relative power in sigma EEG for the sleep apnoea and the healthy groups were observed in Wake ($z=-2.22$, $p=0.026$), Stage 2 ($z=-5.13$, $p<0.001$) and Stage 3 ($z=-2.37$, $p=0.018$). Conversely, the relative power of beta EEG in the sleep apnoea group was higher than the healthy group during Stage 3 and lower during Stage 2 ($z=-2.95$, $p=0.003$) and REM ($z=-2.58$, $p=0.01$).

In the healthy group, the LFnu and LF/HF ratio continuously decreased from Wake to Stage 4 and peaked during REM while HFnu had the converse effect (Figure 4). In the sleep apnoea group, the LFnu was higher than the healthy group during Stage 3 ($z=-3.11$, $p=0.002$). Despite the fact that the sleep apnoea group had similar trends in HFnu component, its activity was slightly lower during Stage 3 ($z=-2.42$, $p=0.016$). The sleep apnoea group also revealed a higher LF/HF activity during Stage 2 ($z=-2.13$, $p=0.033$) and Stage 3 ($z=-2.93$, $p=0.003$) in comparison to the healthy group (Figure 4).

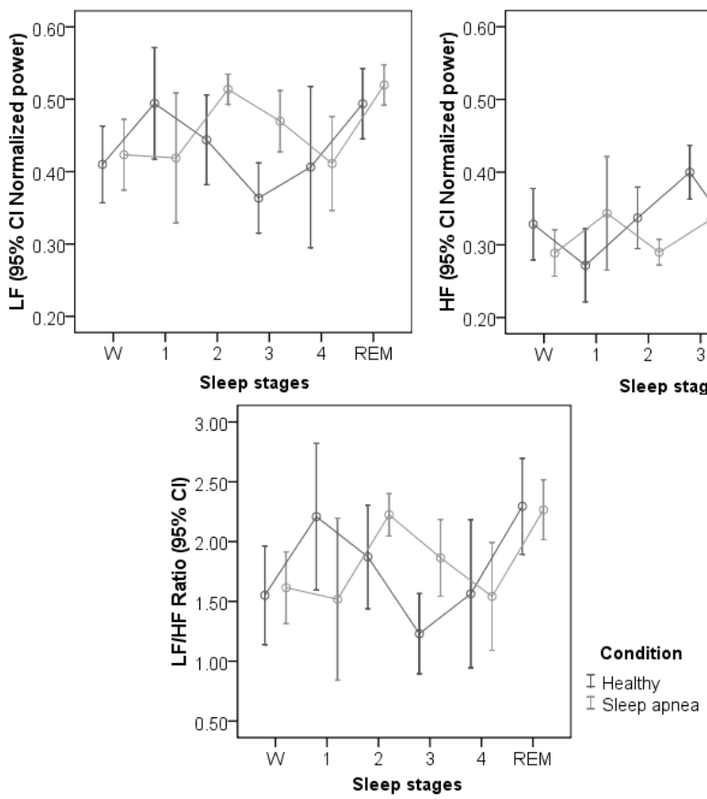

Fig. 4. Mean and 95% confidence intervals (CI) normalized power of low frequency (LF), high frequency (HF) and the ratio between LF and HF of HRV versus sleep stages in normal and patients with sleep apnoea.

The relation between the five frequency bands of EEG and HRV parameters for each sleep stage in both groups were summarized in Table 4. In the healthy groups, delta EEG negatively correlated with LF/HF and LFnu during sleep Stage 3, 4 and REM and positively correlated with HFnu in Stage 3 and 4. In contrast to healthy group, the LF/HF, LFnu and HFnu in sleep apnoea group correlated with delta EEG only in Stage 3. Theta EEG only correlated with LFnu (Stage 1) in the healthy group and with HFnu (Stage 1-2) in the sleep apnoea group. Correlation between HRV parameters and alpha EEG did not exist in the sleep apnoea group however it was only correlated with LFnu for the healthy group. Interestingly, for sleep apnoea group, sigma and beta EEG showed positive correlation with HFnu and negative correlation in LF/HF and LFnu both in Stage 2 and REM. Similar correlation trends for sigma and beta EEG bands was observed but only in LFnu and HFnu in the healthy group.

A post hoc analysis with Bonferroni alpha rate correction of $p<0.002$ revealed that in the healthy group, only delta EEG was negatively correlated with LF/HF during Stage 4. Whereas a positive correlation was observed in the sleep apnoea patients. Sigma and beta EEG also showed a significant difference for LF/HF and LFnu during Stage 2 and REM respectively in the sleep apnoea group.

		delta		theta		alpha		sigma		beta	
		H	S	H	S	H	S	H	S	H	S
LF/HF	W	0.10	0.12	0.08	-0.13	-0.05	-0.08	-0.11	-0.09	-0.18	-0.12
	S1	0.02	0.09	0.29	-0.19	0.02	-0.25	-0.14	-0.05	-0.30	0.23
	S2	0.09	-0.04	-0.20	-0.12	-0.32*	-0.14	-0.25	-0.31**	-0.15	-0.33**
	S3	-0.36*	0.29*	-0.06	0.12	0.05	-0.07	-0.22	-0.04	-0.18	-0.17
	S4	-0.88**	0.14	-0.17	0.01	0.21	-0.06	0.28	-0.09	0.25	-0.08
	REM	-0.29*	-0.04	-0.06	0.05	0.11	-0.15	-0.18	-0.32*	-0.16	-0.31*
LFnu	W	0.21	0.23	0.22	-0.01	-0.04	-0.24	0.01	0.03	-0.13	-0.04
	S1	-0.07	-0.09	0.48*	-0.13	0.26	-0.17	0.02	0.13	-0.16	0.26
	S2	0.03	-0.05	-0.09	-0.06	-0.20	-0.13	-0.37*	-0.33*	-0.09	-0.43*
	S3	-0.25	0.39**	-0.11	0.20	0.06	-0.18	-0.29*	-0.13	-0.29*	-0.25
	S4	-0.79*	0.22	-0.41	-0.10	0.63*	-0.18	0.20	-0.24	0.15	-0.24
	REM	-0.30*	-0.01	-0.02	0.08	0.14	-0.19	-0.10	-0.32**	-0.08	-0.32**
HFnu	W	-0.18	-0.12	0.06	0.08	0.29*	0.21	0.17	0.03	0.14	-0.03
	S1	-0.25	-0.22	-0.07	0.47*	0.21	0.25	0.28	0.15	0.41*	0.07
	S2	-0.14	0.13	0.11	0.26*	0.20	0.13	0.31*	0.29*	0.15	0.35*
	S3	0.39*	-0.27*	0.01	-0.08	-0.04	0.04	0.09	-0.01	0.19	0.09
	S4	0.74*	-0.01	0.07	-0.20	-0.18	-0.16	-0.20	-0.17	-0.15	-0.16
	REM	0.20	0.05	0.05	-0.11	-0.18	0.05	0.15	0.24*	0.16	0.21*

Table 4. Correlation coefficients between EEG frequency bands and HRV parameters throughout different sleep stages in the healthy (H) and sleep apnoea (S) groups.
*alpha level at $p<0.05$, ** alpha rate correction at $p<0.001$.

5. Discussion & Conclusion

The evaluation of sleep EEG transients from low-dimensional chaotic process during the OSAH episodes was conducted using the established non-linear time series analysis method, the positive Lyapunov exponent [Fell, et al., 1993; Fell, et al., 1996]. Whereas, the eigenvector's multiple signal classification (MUSIC) method, of the linear time series characteristic, was used for estimating frequencies and powers of EEG signals [Übeyli and Cvetkovic, 2007; Übeyli, 2008; Cvetkovic et al., 2007, 2009]. Previous studies investigated the analysis of the EEG signals using Lyapunov exponents, which were used as inputs of the multilayer perceptron neural networks (MLPNNs) [Übeyli, 2006], and multiclass support vector machine (SVM) [Übeyli, 2008]. Similar research demonstrated the performances of Lyapunov exponents and eigenvector methods in representing the EEG signals [Andrzejak, et al., 2001]. The power levels of the power spectral density estimates (PSDs) obtained by the eigenvector methods can be used to represent the features of the PPG, ECG, EEG signals [Übeyli and Cvetkovic, 2007].

The statistical results from this first part of our one-patient EEG sleep study needed to consider the Bonferroni test alpha rate correction which depended on the number of factors involved in the multiple tests. The reason MUSIC method revealed corrected non-significant findings was due to six EEG bands and three electrodes (18 factors). Whereas, for the Lyapunov alpha correction, only three factors were considered. As the result, the corrected alpha rate was much lower ($p<0.017$) and the only 'true' significant finding was revealed at the left central region (C3). Therefore, the results from this first part of study indicated

significant changes in the human EEG activity due to OSAH occurrences by applying the non-linear series methods at C3 electrode.

The results from the second part of this study confirmed the existence of association between the HRV parameters and delta EEG frequency band in normal patients which varies with sleep stages as reported in previous studies [Jurysta, et al., 2003; Ako, et al., 2003; Yang, et al., 2002; Brandenberger, et al., 2001]. The power extracted from HRV and EEG bands was computed using spectral analysis based on Fast Fourier Transform (FFT). Our results showed that in healthy group, delta EEG which often prevails in deep sleep was inversely correlated with LFnu and LF/HF and positively correlated with HFnu suggesting a decrease in sympathetic activity and an increase in parasympathetic activity. The present study also found an increase in LFnu and LF/HF particularly during Stage 2 in sleep apnoea patients compared with the healthy. This finding was in line with study by [Roche, et al., 1999; Cvetkovic, et al., 2009] which suggested an increase in sympathetic and parasympathetic activity around apnoea-hypopnoea episodes which occurred mostly during NREM sleep. As reported by [Svanborg, et al., 1996], increased during NREM apnoea. Our results revealed that delta EEG and LFnu positively correlated, observed in sleep apnoea group during Stage 3. In addition, beta and sigma also showed a negative association with the LFnu and LF/HF parameters. This association observed during Stage 2 and REM may be due to predominance of cardiac sympathetic during apnoea-hypopnoea episodes.

In conclusion, our study elucidates a significant correlation between HRV activity and EEG frequency bands particularly in delta, beta and sigma in sleep apnoea group. Further studies using non-linear methods for EEG and ECG feature extraction are necessary to verify this association.

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Recent Advances in Biomedical Engineering

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The field of biomedical engineering has expanded markedly in the past ten years. This growth is supported by advances in biological science, which have created new opportunities for development of tools for diagnosis and therapy for human disease. The discipline focuses both on development of new biomaterials, analytical methodologies and on the application of concepts drawn from engineering, computing, mathematics, chemical and physical sciences to advance biomedical knowledge while improving the effectiveness and delivery of clinical medicine. Biomedical engineering now encompasses a range of fields of specialization including bioinstrumentation, bioimaging, biomechanics, biomaterials, and biomolecular engineering. Biomedical engineering covers recent advances in the growing field of biomedical technology, instrumentation, and administration. Contributions focus on theoretical and practical problems associated with the development of medical technology; the introduction of new engineering methods into public health; hospitals and patient care; the improvement of diagnosis and therapy; and biomedical information storage and retrieval. The book is directed at engineering students in their final year of undergraduate studies or in their graduate studies. Most undergraduate students majoring in biomedical engineering are faced with a decision, early in their program of study, regarding the field in which they would like to specialize. Each chosen specialty has a specific set of course requirements and is supplemented by wise selection of elective and supporting coursework. Also, many young students of biomedical engineering use independent research projects as a source of inspiration and preparation but have difficulty identifying research areas that are right for them. Therefore, a second goal of this book is to link knowledge of basic science and engineering to fields of specialization and current research. The editor would like to thank the authors, who have committed so much effort to the publication of this work.

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