Topographic EEG brain mapping before, during and after Obstructive Sleep Apnea episodes

David Belo[1], Ana Luísa Coito[1], Teresa Paiva[2], and J. Miguel Sanches[1]

[1]Institute for Systems and Robotics / Instituto Superior Técnico
[2] Centro de Electroencefalografia e Neurofisiologia Clínica / Faculdade de Medicina da Universidade de Lisboa
* djbelo@isr.ist.utl.pt,anacoito20@gmail.com,tpaiva@ispa.pt, jmrs@ist.utl.pt

Abstract. Obstructive Sleep Apnea Syndrome (OSAS) is a very common sleep disorder that is associated with several neurocognitive impairments. The present study aims to assess the electroencephalographic (EEG) power before, during and after obstructive apnea episodes, in four frequency bands: delta (δ), theta (θ), alpha (α) and beta (β). For that propose, continuous wavelet transform was applied to the EEG signals obtained with polysomnography, and topographic EEG brain mapping (EBM) to visualize the power differences across the whole brain. The results demonstrate that there is a significant decrease in the EEG δ power during OSAS that does not totally recover immediately after the episode. Furthermore, a power decrease in a specific brain region was noticed for all EEG frequency ranges.

Keywords: Obstructive Sleep Apnea, Electroencephalogram, Spectral Analysis,Continuous Wavelet transform, Brain Mapping

Obstructive Sleep Apnea Syndrome (OSAS) is a very common sleep disorder affecting 4% of men and 2% of women [1] and is sometimes undiagnosed. It is is characterized by recurrent apneas during sleep, which are caused by the partial or complete collapse of the upper airway, resulting in repetitive hypoxemic and hypercapnic episodes, and interruptions of the normal sleep pattern.

OSAS contribute to the development of not only respiratory and cardiovascular disorders but also neurocognitive impairments. Indeed, neuropsychological investigations of patients with OSAS have shown impairments in functions as memory, attention and executive control [2]. The pathophysiological mechanisms underlying the morbidity of OSAS are not completely understood, which make the research on the OSAS an important issue.

It is known that intermittent hypoxia, as it occurs in OSAS, is associated with cortical neuronal cell death (gray matter loss) in cognitively relevant brain regions and consequent cortico-hippocampal damage [3]. Moreover, it was found

* Partially supported by project the FCT (ISR/IST plurianual funding) through the PIDDAC Program funds and FCT project "Detection of Brain Microstates in Fibromyalgia" (PTDC/SAU-BEB/104948/2008)

out that during an apnea episode there is a decrease of oxyhemoglobin, increase of deoxyhemoglobin and an increase of cerebral blood flow, however the latter cannot compensate for reduced arterial oxygen saturation and cerebral tissue hypoxia may occur during OSA [4].

Neurophysiological assessment through the electroencephalographic (EEG) signal provides an objective method for detecting changes in cortical activity. The EEG signal shows patterns of electrical activity, each one characterized by a typical frequency band and amplitude. The normal human EEG shows activity over the range of 1-30 Hz with amplitudes in the range of 20-100 μV [5]. The lowest amplitude waves and highest frequency, 18-30 Hz, are named beta (β) rhythm. Alpha (α) rhythm lies between 8-12 Hz with amplitude of 50 μV. Larger regular waves of frequency range 4-7 Hz called theta (θ) rhythm have been recognized along with a slow wave of less than 4 Hz called the delta (δ) rhythm [5]. The EEG spectral analysis was found to be a very useful tool to assess the EEG power in the four stated EEG frequency ranges [5].

In the current study, obstructive sleep apnea (OSA) episodes were carefully selected and segmented in three parts, the OSA event (*dur*), a certain period immediately preceding (*pre*) and a time interval after (*post*) the event in order to assess the dynamic EEG power changes. The analysis of the EEG signal in the four bands is performed by using the continuous wavelet transform (CWT) and topographic EEG brain mapping (EBM) for visualization of the power in the whole brain.

As far as the authors know this is the first study where data segmentation in *pre*, *dur* and *post* was performed in adult OSAS patients to study the EEG power changes. The studies that analyzed the EEG power during apnea are usually focused in the detection of non-visible arousals (related to autonomic activation). Furthermore, EBM is introduced as a powerful tool to visualize spectral changes during OSA episodes across the brain in a local basis.

This is the second study applying EBM to assess spectral power changes during OSA. The first one dates back to 1993 and had a poor resolution [6]. We consider a promising method for studying neurophysiological aspects of brain function during OSA since it allows the assess of the local power distribution across the whole brain and, thus, to visualize which specific region is affected during an apneic event. The relevance of this paper is held in the correlation of some known neurocognitive impairments occurring in OSAS patients with their affected brain areas, establishing a new door to a better understanding of the effects of this sleep disorder in the human being.

1 METHODS

A total of 15 male individuals with OSAS, mean aged 55 $\pm$ 6.10 (mean $\pm$ standard deviation, SD) and with a mean body mass index (BMI) 28.74 $\pm$ 5.26 $Kg.m^{-2}$, participated in this study. They underwent overnight polysomnographic (PSG) assessment through a computerized PSG system (*Somnologica 5.0.1*, *Embla*) during approximately 8 hours.

EEG electrodes were positioned according to the International 10-20 System and 21 recordings were acquired, at a sampling frequency of 100 Hz, from the following leads: Fp1, Fp2, Fpz, F3, F4, F7, F8, Fz, C3, C4, Cz, P3, P4, Pz, O1, O2, Oz, T3, T4, T5 and T6, in reference to linked ears (A1 and A2). Electrocardiogram, thorax and abdominal efforts, airflow, oxygen saturation (SpO_2) and electromyographic channels were also recorded.

Each recording was visually examined and sleep stages were scored manually at 30 seconds intervals, according to the criteria of the *American Academy of Sleep Medicine* [7].

An oxygen desaturation event was detected when the oxygen saturation fell by at least 4%.

1.1 Dataset

A sleep apnea event was detected when a 10 second interval of the airflow signal dropped below 20% of the reference amplitude. Only episodes that obeyed to some criteria were considered: obstructive apnea-type events occurring in NREM-2 sleep stage, lasting up to 60 seconds and be preceded and followed by at least 30 seconds of continuous breathing, since it was intended to analyze data not only during an OSA (*dur*) but also before (*pre*) and after (*post*) the event. Each *pre* and *post* have a duration of 30 seconds.

The final dataset included 171 isolated OSA episodes, without artifacts, extracted from the 15 mentioned patients. In total, 10773 epochs (171 episodes×3 periods×21 channels) were analyzed. The mean duration of these episodes is 14.54 ± 6.43 s.

1.2 Signal Processing

The recordings were exported to European Data Format (EDF) files in order to be analyzed in Matlab 7.5.0, in which all the signal processing was performed.

First of all, a noise reduction step was taking into account. The moving average of each EEG signal was removed using time windows of 4s. A median filter of order $n = 10$ was also applied to the signals.

In order to obtain the power in δ, θ, α and β frequency bands, the continuous wavelet transform (CWT) method was then applied to each EEG epoch.

The wavelet transform has been considered over the recent years as a powerful time-frequency analysis for the manipulation of complex nonstationary signals, such as physiological signals [8]. This technique decomposes a signal into a set of basic functions called wavelets, which are obtained by dilations, contractions and shifts of a unique function: the mother wavelet [8], that in the case of the present study was the Morlet function, defined as:

$$\psi(t) = \frac{1}{\sqrt[4]{\pi}} \left(e^{iw_0 t} - e^{-\frac{w_0^2}{2}} \right) e^{-\frac{t^2}{2}} \tag{1}$$

where w_0 is the central frequency of the mother wavelet (frequency at the center of a Gaussian curve), the term in brackets is known as the correction term (it corrects the nonzero mean of the complex sinusoid of the first term)

For a practical implementation, CWT is computed over a discretized time-frequency grid, which involves an approximation of the transform integral. [8].

1.3 Power Calculation

After processing the EEG signal (x), the mean energy (E_p) for each apnea epoch ($p = pre, dur, post$), episode ($i = 1, ..., M$), channel (c), frequency band (ω_b), and was calculated by the following equation:

$$E_p(c, i, \omega_b) = \frac{1}{N} \sum_{n=1}^{N} \left[\sum_{s=1}^{S} |x(c, n) * W(n, \omega_s)|^2 \right], \forall\, \omega_s \in \omega_b \tag{2}$$

where n represents the sample ($n = 1, ..., N$) and s the wavelet scale. W(n,ω_s) represents the scaled version of the Morlet wavelet with the central frequency of ω_s. The integral of the power of the frequency band ω_b is the combination of S equal spaced wavelets in the frequency domain.

Finally, the relative energy of each EEG channel and frequency band is calculated by the following equation:

$$e_p(c, \omega_b) = \frac{1}{M} \sum_{i=1}^{M} \left[\frac{E_p(c, i, \omega_b)}{E_{pre}(c, i, \omega_b)} \right] - 1 \tag{3}$$

1.4 Brain Mapping and Statistical Analysis

The EBM were made by the aproximation of the head to a semi-sphere [9]. This simplification allows spherical interpolation of the vector $B_p^{\omega_b} = [e_p(1, \omega_b), e_p(2, \omega_b), ..., e_p(21, \omega_b)]^T$ for the mean values. The same processing was made for the standard deviation. The EBM was computed using EEGLAB's function topoplot() with $B_p^{\omega_b}$ as the input vector. EEGLAB is a software toolbox for Matlab (more information is freely available from http://www.sccn.ucsd.edu/eeglab/) [10].

Powers corresponding to *dur* and *post* for each EEG frequency domain were compared by a tailed two-sample *t-test* against *pre* segments. This test considers as null hypothesis the independency of two samples from normal distributions and that the mean of one is higher than the other. A p-value < 0.05 was considered statistically significant.

All the episodes were tested for E_{dur} and E_{post} against E_{pre} for each frequecy band (ω_b) and channel (c). The binary vector $S_p^{\omega_b}(c)$ was the result of the validation (1 for pass, 0 otherwise). New brain maps were made using topoplot() with each $S_p^{\omega_b}$ as the input vectors. The interpolated values were considered true if they were in the interval $]0.5, 1]$ and false for $[0, 0.5]$. These maps were used as a mask to hide the points that weren't statisticaly significant of the respective mean power maps.

2 Results

2.1 Demographic, respiratory and polysomnographic variables

The resume of the polysomnographic characteristics of the 15 male patients considered in this study are shown in Table 1.

Table 1. Polysomnographic characteristics in 15 OSAS patients.

Parameter	**Mean ± SD**
AHI (hours^{-1})	30.87 ± 13.04
*TST (min)	411.87 ± 109.46
Sleep efficiency (%)	80.07 ± 16.39
TST in NREM1 (% of TST)	16.24 ± 7.18
TST in NREM2 (% of TST)	58.91 ± 9.03
TST in NREM3 (% of TST)	12.63 ± 6.87
TST in REM (% of TST)	12.23 ± 5.88
Number of arousals	105.67 ± 78.23
SpO_2 baseline (%)	94.19 ± 1.32
Nadir SpO_2 (%)	78.67 ± 8.79
Number of desaturations	82.71 ± 64.34

* *TST - total sleep time*

As it is shown, these OSAS patients had low percentages of NREM-3 and REM sleep, higher percentages of stage NREM-1 and NREM-2 sleep, and a high number of arousals, which show a clear disturbed sleep pattern. In terms of hypoxemia, the patients included in the study were severely affected: they were characterized by a mean SpO_2 nadir of less than 80% and a high number of dessaturations.

2.2 EEG analysis

The results (Figures 1 and 2) show a statistically significant generalized δ power decrease during OSA, which is not fully recovered after the episode for all the brain spectra.

For θ waves, there is a statistically significant power decrease only in frontal (F3 and F4) and temporal (T3 and T4) regions during OSA, and in part of the occipital (O1 and O2), temporal (T3 and T4), central (C3 and C4) and frontal (F3, F4, Fp1 and Fpz) regions in *post*.

The EBM for the α and β frequency bands during OSA show a statistically significant power decrease in occipital (O1 and O2), temporal (T3 and T4), central (C3 and C4) and frontal (F3 and F4) regions of the brain, and an increase in all the parietal are for the β band. In *post*, there is an overall slight power increase, which is stronger in the frontal and occipital brain regions. However, statistically, only channels F3, T5 and P4 are significant for β band, and Fp1,

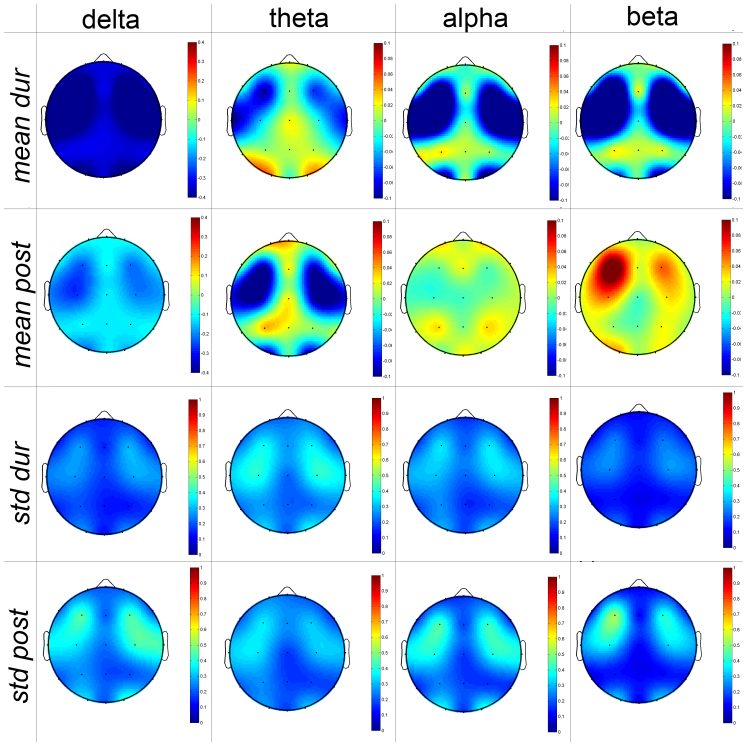

Fig. 1. EBM of the normalized power with *pre* apnea as reference. The sections of the first row represent the mean power values of *dur* apnea for the four frequency bands, and the third row the respective standard deviations. The second row represent the power mean of *post* apnea for the four different frequency bands and the forth row the respective standard deviations. Each brain map has a gauge with a color range from dark red, the highest energy content, to dark blue, the lowest energy content, according to the respective scale.

P4 and Oz for α band. The β and α increases after the OSA episode, specially in the frontal (motor area) and occipital (visual area) regions, are probably due to an arousal mechanism that often accompanies the termination of an apneic event, which are responsible for sleep fragmentation [11].

The SD maps validate the results above described. Note that areas with a higher SD for all frequency bands are those representing pre-motor, motor and visual areas of the brain.

Decreases in δ power preceding arousal and termination of apneic events in both REM and NREM sleep are reported [6, 12]. However, the opposite conclusions were also addressed [13, 14]. Perhaps the difference between their results and the ones obtained in the current study are due to the fact that δ power was assessed only near or even at the apnea termination, so subcortical arousals, including K-complexes and δ bursts, might occur and, thus, contribute to the

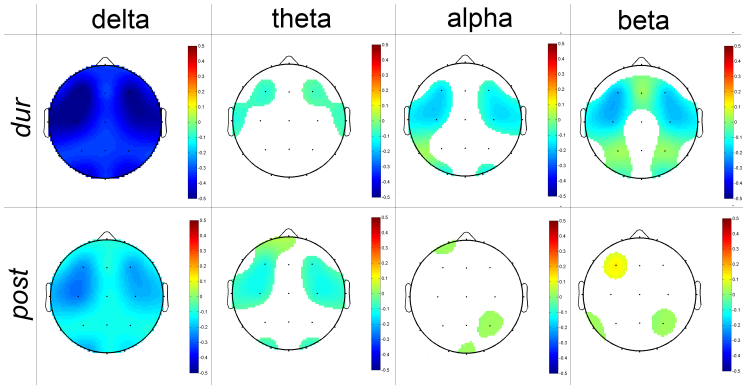

Fig. 2. Statistical significance map. The displayed maps represent the normalized power points that passed the tailed two-sample t-test for *post* and *dur* against *pre* apnea episodes. Each brain map has a gauge with a color range from dark red, the highest energy content, to dark blue, the lowest energy content, according to the respective scale.

reported δ increases. In this work, all OSA episodes were visually examined and δ bursts were removed at the end of OSA episodes, so that they did not influence the mean δ power of *post*.

Please note that there is a power decrease during OSA also in θ, α and β in specific regions - frontal (F3 and F4), temporal (T3 and T4) and central (C3 and C4) regions - which shows a clear decreased EEG activity in these regions that might evidence that this is the most affected brain region during OSA episodes. Since working memory and executive tasks performance are localized at the frontal cortex [2, 11], it is possible that memory impairments reported in OSAS patients are due to a decrease of the brain's activity in this referred specific brain region.

It was suggested for various authors that there is a correlation between δ power changes and the severity of hypoxemia and hypercapnia during the OSA [6, 15]. Moderate hypoxemia has been shown to elicit a depression of absolute power in the EEG δ band [6]. So, it is possible that the detected δ fluctuations may be due to hypoxemia and/or hypercapnia.

3 CONCLUSION

A new approach was carried out for assessing EEG changes during an OSA episode: EBM. This technique was proved to be very useful, since it allowed to draw new conclusions about the visualization of the brain has a whole. It is a reliable tool for the assessment of EEG spectral power changes, of each region, resulted from an obstructive event.

The present study confirms that the majority of OSA, which can be or not terminated by visually scored arousals, are associated with significant spectral

power changes, mainly in δ frequency band, where there is a clear decrease in δ power during OSA. Moreover, it was notice that a power decrease in a specific brain region occurred for all EEG frequency ranges. This sugests that

Future studies include the performance of memory tests to the OSAS patients assessed by the presented analysis in order to correlate the memory impairments with the spectral EEG power changes observed during OSA episodes.

References

1. T. Young and M. Palta and J. Dempsey and J. Skatrud and S. Weber and S. Badr: The occurrence of sleep-disordered breathing among middle-aged adults. N. Engl. J. Med. 328, 1230-1235 (1993)
2. B. Naegel and S. Launois and S. Mazza and C. Feuerstein and J. Ppin and P. Lvy: Which memory processes are affected in patients with obstructive sleep apnea? An evaluation of 3 types of memory. Sleep. 29(4), 533-544 (2006)
3. W. Xu and L. Chi and B. Row and R. Xu and Y. Ke and B. Xu and C. Luo and L. Kheirandish and D. Gozal and R. Liu: Increased oxidative stress is associated with chronic intermittent hypoxia-mediated brain cortical neuronal cell apoptosis in a mouse model of sleep apnea. Neuroscience. 126, 313-323 (2004)
4. T. Hayakawa and M. Terashima and Y. Kayukawa and T. Ohta and T. Okada: Changes in cerebral oxygenation and hemodynamics during obstructive sleep apneas. Chest. 109, 916-921 (1996)
5. J. Muthuswamy and N. Thakor: Spectral analysis methods for neurological signals. J. Neurosci. Methods. 83, 1-14 (1998)
6. J. Walsleben and E. O'Malley and K. Bonnet and R. Norman and D. Rapoport: The utility of topographic EEG mapping in obstructive sleep apnea syndrome. Sleep. 16, 76-78 (1993)
7. C. Iber and S. Ancoli-Israel and A. Chesson and S. Quan: The AASM Manual for the Scoring of Sleep and Associated Events: Rules, Terminology and Technical Specifications. American Academy of Sleep Medicine. Westchester (2007)
8. P. Addison and J. Walker and R. Guido: Time-Frequency Analysis of Biosignals: a wavelet transform overview. IEEE EMB Magazine. 28(5), 14-29 (2009)
9. T. Ferree: Spherical Splines and Average Referencing in Scalp Electroencephalography. Brain Topography. 19, 43-52 (2006)
10. A. Delorme and S. Makeig: EEGLAB: an open source toolbox for analysis of single-trial EEG dynamics including independent component analysis. Journal of Neuroscience Methods. 134, 9-21 (2004)
11. E. Verstraeten: Neurocognitive Effects of Obstructive Sleep Apnea Syndrome. Current Neurology and Neuroscience Reports. 7, 161-166 (2007)
12. H. Bandla and D. Gozal: Dynamic Changes in EEG Spectra During Obstructive Apnea in Children. Pediatric Pulmonology. 29, 359-365 (2000)
13. E. Svanborg and C. Guilleminault: EEG Frequency changes during sleep apneas. Sleep. 19, 248-254 (1996)
14. R. Berry and M. Asyali and M. McNellis and M. Khoo: Within-night variation in respiratory effort preceding apnea termination and EEG delta power in sleep apnea. Journal of Applied Physiology. 85, 1434-1441 (1998)
15. F. Morisson and G. Lavigne and D. Petit and T. Nielsen and J. Malo and J. Montplaisir: Spectral analysis of wakefulness and REM sleep EEG in patients with sleep apnoea syndrome. Eur. Respir. J. 11, 1135-1140 (1998)