TOPOGRAPHIC EEG BRAIN MAPPING BEFORE, DURING AND AFTER OBSTRUCTIVE SLEEP APNEA EPISODES

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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 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. Since δ waves are linked to learning and plasticity processes, it is hypothesized that decreased δ power during the episode may contribute to the cognitive deterioration in patients with OSAS.

Index Terms— Obstructive Sleep Apnea, Electroencephalogram, Spectral Analysis,Continuous Wavelet transform, Brain Mapping

1. INTRODUCTION

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.

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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 [3]. 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 [3]. The EEG spectral analysis was found to be a very useful tool to assess the EEG power in the four stated EEG frequency ranges [3].

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 maps 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 ocused in the detection of non-visible arousals (related to autonomic activation). Furthermore, topographic EEG brain mapping is introduced as a powerful tool to better visualize spectral changes during OSA episodes across the whole brain in a local basis.

2. METHODS

In this section the data used in this study is described and characterized as well as the methods for analyse them and visualize the results.

2.1. Experimental Setup and Data Acquisition

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* [4].

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

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 to analyze data not only during an OSA (dur) but also before (pre) and after ($post$) the event. Each pre and pos have a duration of 30 seconds. In total, 171 *isolated* OSA and without artifacts, extracted from the 15 mentioned patients, were available and 10773 epochs (171 episodes$\times$3 periods$\times$21 channels) were analyzed. The mean duration of these episodes is 14.54 $\pm$ 6.43 s.

2.2. Data 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 median filter of order $n = 10$ as well as a moving average filter were applied to the signal.

Each signal sample value was then normalized as a function of the signal total power of the corresponding person in order to be possible to compare across various subjects.

It was decided to exclude bursts of K-complex and/or δ activity (lasting between 3 and 7 seconds) occurring at the beginning of $post$ EEG epochs, since they influenced the mean δ power of those epochs and, thus, would conduct to misleading results. This remotion was carefully tested. The arousal artifacts occurred in 31 episodes, so the episodes were separated into 3 groups: (1) one containing those that did not present the arousal artifact (140 episodes), (2) one containing the episodes with the artifact (31 episodes), (3) one containing all the 171 episodes and with the artifact removed in those 31. All the signal processing analysis explained next was performed for the three groups. It was concluded that group (1) presented very similar results to those obtained in group (3). Group (2) presented similar results to the other two groups for all EEG spectral bands except for δ band, where mean $post$ power was much higher and presented an huge standard deviation. Therefore, we concluded that it was reasonable to remove these subcortical arousal artifacts.

In order to obtain the power in δ, θ, α and β bands, the CWT method was applied to each 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 [5]. 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 [5], that in the case of the present study was the Morlet function, defined as:

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

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) [5].

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

2.3. Brain Mapping

In order to have a better insight of the EEG power changes across all brain regions, a topographic EEG brain mapping was performed using the *EEGlab* toolbox for *Matlab*.

After determining the mean power of each EEG pre, dur and $post$ epoch of each EEG signal (the 21 channels), each dur and $post$ epoch power was normalized by simply divide it by the corresponding pre power. These mean power values formed a vector with length *(21$\times$1)*, which was posteriorly analyzed in *EEGlab*.

The brain mapping was first based on the approximation of the head to a semi-sphere. This simplification allows the spherical interpolation of the vector with the respective power values. Ferree [6] described that spherical splines are the best splines to fit to the superior surface of the head.

Let $\vec{r_j}$ denote the location of an electrode on the spherical scalp surface, with $j = 1, ..., 21$, $\vec{r}$ the location of an arbitrary surface point, and $V(\vec{r})$ the potential at that point. Spherical splines estimate the potential $V(\vec{r})$ by:

$$V(\vec{r}) = c_0 + \sum_{j=1}^{N} c_j g_m(\hat{r} \cdot \hat{r_j}) \qquad (2)$$

where c_0 and c_j are constants fit to data. The dot product $\widehat{r} \cdot \widehat{r_j}$ is the cosine of the angle between the interpolation point $\vec{r}$ and electrode location $\vec{r_j}$. The function $g_m(x)$ is given by:

$$g_m(x) = \frac{1}{4\pi} \sum_{n=1}^{\infty} \frac{2n+1}{(n(n+1))^m} P_n(x) \quad (3)$$

where the $P_n(x)$ are the ordinary Legendre polynomials.

2.4. Statistical Analysis

Powers corresponding to pre, dur and $post$ for each EEG frequency domain were compared by a tailed two-sample *t-test*. 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.

3. RESULTS & DISCUSSION

3.1. 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.

3.2. EEG analysis

Applying the CWT method to the referred 10773 epochs, mean normalized EEG power for δ, θ, α and β frequency band was computed for each EEG channel.

This is the second study applying topographic EEG brain mapping to assess spectral power changes during OSA. The first one remotes to 1993 and had a very poor resolution [7]. Fig. 1 displays the brain maps for normalized mean δ, θ, α and β power, during and after the 171 OSA episodes, and the corresponding maps of SD. With this technique, we can easily visualize which specific region is affected during an apneic event and, thus, we consider a promising method for studying neurophysiological aspects of brain function during OSA.

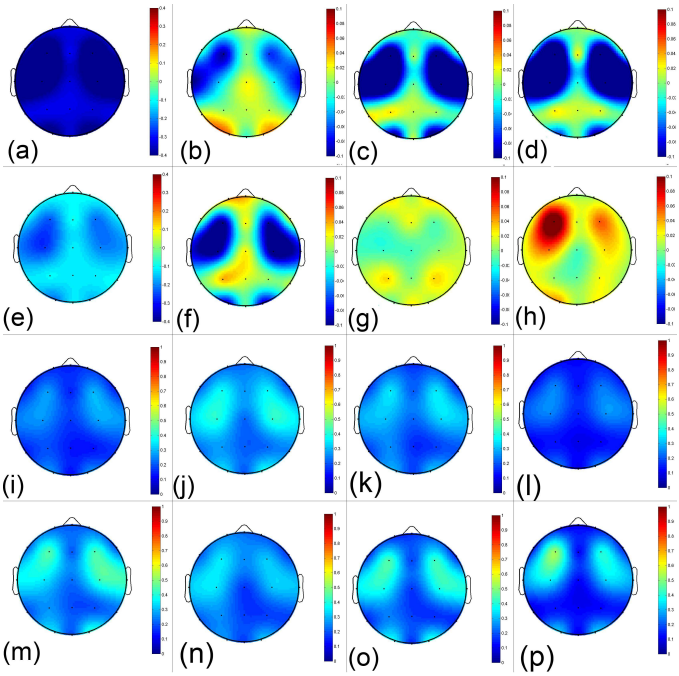

Fig. 1. Topographic brain maps of the normalized power with *pre* apnea as reference. The sections of the first row (a, b, c and d) represent the mean power values of *dur* apnea for δ, θ, α and β, respectively, and the third row (i, j, k and l) the standard deviations. The second row (e, f, g and h) represent the power mean of *post* apnea for δ, θ, α and β, respectively, and the forth row (m, n, o and p) for 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.

The results 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 topographic brain maps 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, 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 [8].

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 [7, 9]. However, the opposite conclusions were also addressed [10, 11]. 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 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 during OSA episodes.

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 [7, 12]. Moderate hypoxemia has been shown to elicit a depression of absolute power in the EEG δ band [7]. So, it is possible that the detected δ fluctuations may be due to hypoxemia and/or hypercapnia.

The relationship between δ waves and memory has not yet been well established, however Tonini & Cirelli [13] recently presented a hypothesis about the function of sleep - the synaptic homeostasis hypothesis - which proposes that learning and synaptic plasticity during wakefulness promotes an increase of slow wave activity during subsequent sleep. Thus, the role of sleep would be to downscale synaptic strength to a baseline level that is sustainable in terms of energy and gray matter space consumption, supply of nutrients, and is beneficial for learning and memory. Therefore, and according to this hypothesis, in the presence of sleep deprivation and reduced slow wave (δ) activity, as it occurs in OSAS, the downscaling promoted by slow wave sleep is reduced, which can lead to a "cerebral overloading" with excessive energy and space consumption, and thus, the ability of the brain to acquire new information decreases. Indeed, there are several studies demonstrating deficits in procedural, declarative and working memory in patients with OSAS [2].

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.

4. CONCLUSION

A new approach was carried out for assessing EEG changes during an OSA episode: topographic EEG brain mapping. 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. It is hypothesized that these fluctuations contribute to the patient's daytime symptoms, including memory impairments, since a decreased δ power could prevent downscaling of increased learning related synaptic strength to a baseline level, occurring a "cerebral overloading".

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