This is a post-peer-review, pre-copyedit version of an article published in IFMBE Proceedings book series (IFMBE, volume 76). The final authenticated version is available online at: https://doi.org/10.1007/978-3-030-31635-8_15

Linear and non-linear analysis of EEG during sleep deprivation in subjects with and without epilepsy

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Abstract. EEG has a central role in the diagnosis of epileptiform abnormalities helpful in diagnosing epilepsy. Since irregularities are random and sporadic events, easily activated in the initial phase of sleep but difficult to observe in a standard EEG examination, sleep deprivation is a frequent condition to be used. Thus, in this study the EEG monitoring of 44 subjects, 14 without epilepsy and 30 with epilepsy, afferent to the IRCCS Centro Neurolesi "Bonino Pulejo" of Messina were examined after sleep deprivation the day before performing the registration. EEGs were recorded according to the international setting system using nineteen channels. The normalized power spectral densities in delta (2-4 Hz), theta (4-8 Hz), alpha (8-13 Hz) and beta (13-30 Hz) band were computed and the non-linear parameters such as beta exponent, fractal dimension and zero crossing were considered. The differences between the sleep and awake were significant in almost all the channels in the beta band and in posterior areas for beta exponent, fractal dimension and zero crossing in normal subjects. In epileptic patients they were significant in all the channels in the delta band and for the non-linear parameters, and in several ones in theta and beta bands. Even if in posterior areas all the spectral and the non-linear parameters showed different values between epileptic and healthy subjects, no significant differences were found. The results suggest that analysis of spectral power as well as of complexity, obtained by non-linear parameters, could be used to identify differences between healthy and epileptic patients.

Keywords: EEG, Epilepsy, Sleep deprivation.

1 Introduction

The electroencephalography (EEG) is a widely used research tool in the investigation of cognitive process and it plays a fundamental role in the diagnosis of epileptiform abnormalities helpful in diagnosing epilepsy [1]. This disease represents a clinical condition in which an early diagnosis is essential, not only to prevent repeated attacks, but also in light of the harmful effects of convulsions on the brain, especially if prolonged.

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However, anomalies are sporadic and random events, difficult to observe in a standard EEG exam, which lasts from 30 to 60 minutes. Indeed, seizures, even in repeated recordings, can be found only in 10-20% of patients with epilepsy and, conversely, a pathological finding can be observed in 1-2% of subjects with no history of epilepsy.

Moreover, the awake and sleep influence neuronal excitability and the sleep affects the frequency of epileptic discharges [2]. The literature reports that 21% of epilepsy patients had seizures exclusively at night [3, 4]. Since the anomalies tend to be activated in the initial phase of sleep, it would be useful for the patient to fall asleep during registration. Unfortunately, it is unusual that patients fall asleep spontaneously during EEG examination so that, frequently the registration follows a sleep deprivation. In fact, in epilepsy clinics, sleep deprivation is reported to be the most common trigger for seizures regardless of the epilepsy syndrome [5, 6].

In order to examine EEG anomalies due to epilepsy, some clinical methods for calculating the proportion of epileptiform activity during sleep have been proposed [7]. In particular, the spike-wave index (SI) measures the percentage of 1-second epochs containing spikes [8], the interictal epileptiform discharges per hour [9] quantifies the occurrence of interictal epileptiform discharges during sleep deprivation, while the spike index [10,11] allows the examination of sleep macro- and micro-structure, being significantly higher in sleep deprivation. Other algorithms for automated spike quantification in raw EEG signals are more recently based on wavelets and machine learning [12]. On the other hand, although quantitative EEG analysis may be based on parameters extracted from EEG power spectral density (PSD), in the literature, only few studies investigated these parameters during sleep in healthy subjects. In particular, at the beginning of the sleep, when the need for recovery is greatest, a power increase in the delta and theta bands and a corresponding power decrease in the beta band are present [13, 15, 16].

In addition to PSD linear method, also non-linear methods have been proposed for the examination of the EEG signal [13, 14, 17, 18]. In particular, Ferri et al [18] studied the non linear dynamic properties of EEG presenting slow-wave forms using a non-linear cross predictor. Moreover, parameters like zero crossing, fractal dimension

and beta exponent have shown to be able to distinguish different compartmental states, sleep and resting states, bringing complementary information with respect to the one carried out by linear analysis [17, 14].

However, no studies, exploring possible differences in PSD parameters as well as in non linear ones between patient with and without epilepsy in sleep deprivation, are available in the literature. In order to fill this gap, the purpose of this study is to quantify as linear and non linear parameters extracted from EEG signals recorded during sleep deprivation changes between subjects with and without epilepsy.

2 *Materials and Methods*

A group of 44 patients who underwent consecutively an EEG monitoring at the IRCCS Centro Neurolesi "Bonino Pulejo" of Messina were retrospectively examined. The sample was composed of 14 subjects without epilepsy (39.0±16 years old) and 30 with epilepsy (39.6±16 years old). In particular, 6 patients were affected by symptomatic focal epilepsy and the remaining 24 were affected by temporal lobe epilepsy. Symptomatic focal epilepsy is determined by a brain injury that usually occurs in a well-defined brain area. Epilepsy diagnosis was based on semiology, clinical history, neuroimaging and EEG findings, according with ILAE recommendations [19]. All the subjects included in this study had given their written consent for the analysis of their clinical data for research purposes.

EEGs were recorded according to the international 10–20 electrode setting system using Ag/AgCl electrodes. Nineteen channels were utilized for the analysis (Fp1, Fp2, F7, F3, Fz, F4, F8, T3, C3, Cz, C4, T4, T5, P3, Pz, P4, T6, O1, O2). All the subjects underwent sleep deprivation the day before performing the registration and no crises have been reported in any subject. At least 10 minutes of waking state condition and other 10 minutes in the sleepiness phase were recorded. The EEG signal, coming from each channel, was sampled at 256Hz and digitally band-pass filtered between 0.4Hz and 40Hz. The Power Spectral Density (PSD) was calculated on segments of 5s each, overlapped of 50% along the whole recording, separately for the two conditions. The power in Delta (2-4 Hz), Theta (4-8 Hz), Alpha (8-13 Hz) and Beta (13-30 Hz) band was then computed and normalized dividing each power for the total power. Beside

spectral factors also the following non-linear parameters were considered: Beta exponent, referred to a so-called 1/f -like behavior of EEG a ubiquitous property of complex biological systems [20], Fractal dimension (FD) computed by Higuchi's algorithm [21] and Zero crossing, measuring the changes in dominant frequency [22]. The power-law beta exponent, was calculated as the slope of the regression line in the relationship between the ln(PSD) and ln(frequency). The Higuchi algorithm is based on the estimation of the mean length of the curve, L(k), by using different time intervals, k. If L(k) is proportional to k^{-FD} the EEG time series is fractal with dimension FD, representing the slope of the line fitting the pairs {ln(1/k); ln(L(k))}.

All parameters were averaged among the subjects of the same group, obtaining one value per parameter and channel. For intra-group analysis, Wilcoxon sign rank sum test was used to evaluate the statistical differences between awake and sleep conditions in each group. For inter-group analysis, Mann-Whitney U test, to assess the difference between epileptic and healthy normal group during awake and sleep conditions, was used. A 95% of confidence level was set with a 5% alpha error. Statistical significance was set at $p<0.05$.

3 Results

Figure 1 shows the normalized spectral power values in the four bands in the 19 EEG channels for healthy and epileptic subjects during awake and sleep. About spectral analysis, the results indicated that all subjects presented higher normalized power in delta band during sleep than during the awake and that the epileptic subjects had lower values than healthy ones. However, the differences between the two conditions were significant in almost all the channels in the beta band in normal subjects (Tab.1) and in the delta, theta, and beta bands in epileptic patients (Tab.2). The differences between normal and epileptic subjects were not significant in all the cerebral areas mainly because of a large inter-subject variability, especially during sleep.

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Table 1. Statistical significance of differences between Awake and Sleep in Normal subjects in the six cerebral areas. BB: Beta Band, BE: Beta Exponent, FD: Fractal Dimension, ZC: Zero Crossing.

	Normal: Awake vs Sleep			
	BB	BE	FD	ZC
Fp1, Fp2	n.s.	n.s.	Fp1$^{\#}$	n.s.
F3,F4,Fz,F7, F8	F3***,F4***,Fz***,F7***,F8***	F7$^{\#}$	Fz$^{\#}$,F7$^{\#}$	F7$^{\#}$
T3, T4, T5, T6	T3**,T4**,T5**,T6**	T3**,T4**,T5**,T6**	T3$^{\#}$,T4$^{\#}$,T6$^{\#}$	T3***,T5***,T6***
C3, Cz, C4	C3**,Cz**,C4**	C3$^{\#}$,Cz$^{\#}$,C4$^{\#}$	C3**,Cz**	C3$^{\#\#}$,Cz$^{\#\#}$,C4$^{\#\#}$
P3, Pz, P4	P3***,Pz***,P4***	P3*,Pz*,P4*	P3***	P3*,Pz*,P4*
O1, O2	O1**,O2**	O1*,O2*	O2**	O1$^{\#\#}$,O2$^{\#\#}$

* p<0.01, ** p<0.02, *** p<0.03, #p<0.04, ##p<0.05, n.s. not significant

Table 1. Statistical significance of differences between Awake and Sleep in Epileptic subjects in the six cerebral areas. DB: Delta Band, TB: Theta Band, BB: Beta Band, BE: Beta Exponent, FD: Fractal Dimension, ZC: Zero Crossing.

	Epileptic: Awake vs Sleep					
	DB	TB	BB	BE	FD	ZC
Fp1, Fp2	Fp1*,Fp2*	Fp1$^{\#}$	Fp1**,Fp2**	Fp1*,Fp2*	Fp1*,Fp2*	Fp1**,Fp2**
F3,F4,Fz	F3*,F4*,Fz*	F3$^{\#\#}$,F4$^{\#\#}$	n.s.	F3*,F4*,Fz*	F3***,F4***,Fz***	F3***,F4***,Fz***
F7, F8	F7*,F8*	F7$^{\#\#}$	F7**,F8**	F7*,F8*	F7***,F8***	F7***,F8***
T3, T4	T3**,T4**	T3***,T4***	T3*,T4*	T3*,T4*	T3*,T4*	T3*,T4*
T5, T6	T5**,T6**	n.s.	T5*,T6*	T5*,T6*	T5*,T6*	T5*,T6*
C3, Cz, C4	C3*,Cz*,C4*	C3$^{\#\#}$,C4$^{\#\#}$	C3*,Cz*,C4*	C3*,Cz*,C4*	C3*,Cz*,C4*	C3*,Cz*,C4*
P3, Pz, P4	P3*,Pz*,P4*	P4$^{*\circ}$	P3*,Pz*,P4*	P3*,Pz*,P4*	P3*,Pz*,P4*	P3*,Pz*,P4*
O1, O2	O1*,O2*	O1$^{\#}$,O2$^{\#}$	O1*,O2*	O1*,O2*	O1*,O2*	O1*,O2*

* p<0.01, ** p<0.02, *** p<0.03, #p<0.04, ##p<0.05, n.s. not significant

Theta band showed very few differences between groups and conditions (Fig.1), significant only between awake (lower values) and sleep (higher values) states in about half channels of epileptic patients (Tab.2). The values of the normalized power in alpha band were very similar (no significant difference) in normal and epileptic subjects during sleep and awake (Fig.1) and no significant differences between the two groups both during awake and sleep were found. The beta band showed the highest differences between conditions (Fig.1), significant in almost all the cerebral areas (Tabs.1 and 2). The values were higher in healthy subjects than epileptic ones,

although without significant differences between the two groups, and during awake than sleep.

Figure 2 shows the non-linear parameters values in the EEG channels, averaged on healthy and epileptic subjects in the two conditions. The beta exponent values were higher in epileptic subjects, during both awake and sleep conditions, than in healthy subjects, with no significant differences between the two groups. Moreover, the values increased from anterior to posterior areas, in all situations. Significant differences between the two conditions were found in normal subjects, from temporal to occipital areas, and in all the cerebral areas in epileptic patients, with higher values during sleep than awake (Tabs.1 and 2).

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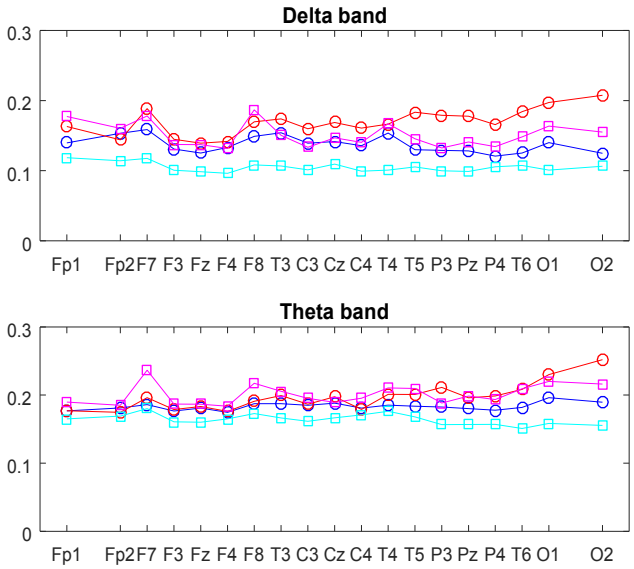

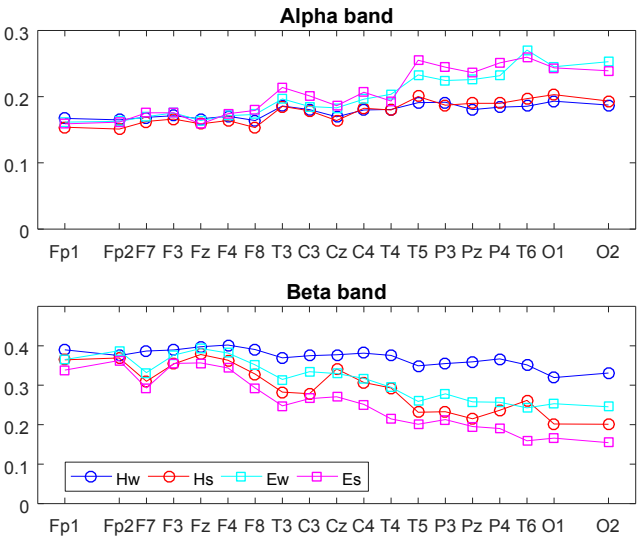

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Fig. 1. Normalized spectral power values in the Theta, Delta, Alpha and Beta bands in the EEG channels, averaged on Healthy (H) and Epileptic (E) subjects during awake (w) and sleep (s) conditions.

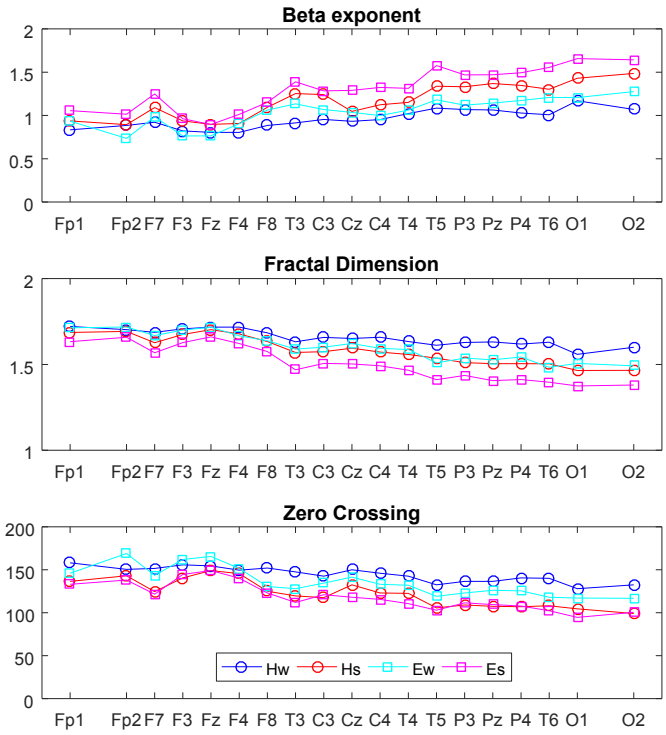

Fig. 1. Non-linear parameters values in the EEG channels, averaged on Healthy (H) and Epileptic (E) subjects during awake (w) and sleep (s) conditions.

The fractal dimension and the zero crossing showed a similar behavior and an inverse one in respect to that of the beta exponent with higher values in healthy subjects than epileptic patients in both conditions and higher values during awake than sleep. These differences between the two states were significant in almost all the cerebral areas for both parameters (Tabs.1 and 2) while the differences between the two groups were not significant.

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4 Discussion

The features found in this study confirm some previous results present in the literature about changes due to sleep in respect to awake in healthy subjects. In particular, during sleep the relative power in lower frequency bands (delta and theta) significantly increased, confirming the effect of prior wakefulness on the sleep EEG, while in beta band significantly decreases in respect to awake, reflecting sleep arousal level [15, 16]. Furthermore, a similar behavior was found in epileptic patients in which relative powers in delta e theta bands significantly increased during sleep with lower values than in normal subjects. Moreover, in beta band, the values significantly decreased from awake to sleep and from anterior to posterior cerebral areas with higher values present in healthy subjects. However, the differences between normal and epileptic subjects, greater in the posterior cerebral areas, especially in beta band, were not significant probably because of the high inter-subject variability present in both groups and the relatively low number of examined cases. On the other hand, in alpha band no significant differences were found between waking and sleeping nor between the two groups of subjects, with values very similar in all cases except in the parietal-occipital areas in which epileptic subjects showed higher, but not significantly, values than normal ones.

The three non-linear parameters presented a similar behavior between awake and sleep conditions with significant differences in all the channels for epileptic patients and predominantly from temporal to occipital areas for healthy subjects. As for the spectral parameters also for the non-linear ones, differences between the two groups were not significant. In particular, beta exponent showed higher values in epileptic patients than in normal subjects and during sleep, with increasing values from anterior to posterior areas, inversely reflecting the behavior found in particular in the beta band which power decreased from frontal to occipital areas. On the contrary, fractal dimension, measuring the level of complexity of the cerebral system, presented a trend opposed to that of beta exponent, as expected due to the law of self-similarity [21], showing higher values in normal subjects, especially in the anterior areas, and during awake, confirming the results reported in [14] for normal subjects. Zero crossing presented a behavior analogous to that of fractal dimension with slightly

decrease from anterior to posterior areas as expected since the relative power in beta band decreases in favor of the power in lower frequencies (in particular alpha e theta bands) which are greater in the posterior areas than in the anterior ones.

In conclusion, this paper compared for the first time the spectral powers in the various cerebral areas in normal subjects with those in epileptic patients, highlighting in the last ones a behavior similar to normal for what concerns the differences between sleep and awake and between the various areas. A lower power in the delta, theta and beta bands and a greater power in the alpha band were found in epileptic patients than in normal subjects. Furthermore, non-linear analysis allowed us to highlight a greater complexity of brain activity in normal subjects than in epileptic patients and in waking than in sleeping, higher in frontal than in occipital areas. Further studies on a larger number of subjects are needed to confirm and provide significance for the differences found between normal and epileptic subjects.

Acknowledgements

Work partially supported by the Master in Clinical Engineering, University of Trieste.

Conflict of interest

The authors declare that they have no conflict of interest.

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