



Distinguishing Obstructive Sleep Apnea Using Electroencephalography Records

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Highlights

- Identifying people with obstructive sleep apnea (OSA) with using EEG.
- The data were analyzed with a new software using Fourier and Wavelet Transforms.
- High success rate of the classifying apnea correctly in a meaningful way

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Abstract

In this study, it was aimed to find out whether electroencephalographic (EEG) frequency bands can be used to distinguish people with obstructive sleep apnea (OSA) from those who do not have it. 11842 different cases taken from 121 patients suffering from OSA were combined with the case study of 30-person control group without sleep apnea. Apneas were highlighted at the respiration-record channels and EEG records which are concurrent with abnormal respiration cases were extracted from C4-A1 and C3-A2. Following that, they were examined with Fourier and Wavelet Transforms using a new software that was developed by us. The percentage values of Delta (0, 5-4 Hz), Theta (4-8 Hz), Alpha (8-13 Hz) and Beta (13-30 Hz) frequency bands were evaluated with the help of t-test and ROC Analysis to differentiate between apneas. The C3-A2 Beta (%) frequency level gave the highest distinguishing asset (AUC=0.662; $p<0.001$); however, the C3-A2 Alpha (%) level yielded the lowest distinguishing (AUC=0.536; $p<0.001$). Similarly, the C4-A1 Alpha (%) level produced the lowest distinguishing asset (AUC=0.536; $p<0.001$) whereas the C4-A1 Beta (%) frequency level gave the highest distinguishing asset (AUC=0.658; $p<0.001$). The chief finding of this study suggests that the EEG rates of patients with OSA differ from those of patients without OSA and following the changes at these channels may give rise to detection of apneas, and the Beta (%) yielded the most meaningful result among four different frequency bands in the study.

1. INTRODUCTION

There is no doubt a good night sleep plays a highly important role in a person's life and it helps to lead a healthy and fruitful life. Therefore, a great deal of effort is put into finding methods in order to help people to overcome their sleep disorders and have better life conditions related to sleep, which inevitably requires to develop new techniques to monitor and assess a good night's sleep [1]. EEG signals, design and implementation of a BCI that straightly relates with the brain. With the expansion of application areas, a wide variety of low-cost EEG devices [2] that can produce and process signals can be developed and used. It is possible to benefit from EEG signals by reducing noise [3] in various ways in the diagnosis of sleep apnea.

In this process, Electroencephalogram (EEG) supplies significant and unrivalled data about the sleeping brain. Polysomnography (PSG), too, has been one of the leading methods for analyzing these sleep data and a chief diagnostic tool in medicine dealing with sleep in over the last 60 years [4]. The standard

interpretation of polysomnographic recordings are used to give a description of macrostructure regarding sleep stages, described according to the criteria Rechtschaffen and Kales put forward (R&K, [5]). R&K scoring criteria have been an invaluable standard which makes it possible to compare the results obtained in laboratories.

Even though it is costly and hard to reach, PSG is still the unmatched standard in diagnosing obstructive sleep apnea (OSA) [6]. Yet, taking into consideration that the disease will prevail (i.e. 1-4% in middle-aged adults [7]) and the practitioners will have increased knowledge of the disease, it is likely that the number of the patients who will turn to laboratories will probably increase. In order to reduce the number of full polysomnographic evaluation, various approaches and strategies were developed to diagnose OSA. Among these were split-night PSG, ambulatory home monitorization, snoring and/or nocturnal oximetry analysis, and craniofacial assessment. Mathematical models and artificial intelligence were also used [6, 8].

A diagnostic system of less sophistication would prove a useful tool if the accuracy of the system could meet standards for the correct diagnosis and grading of OSA severity and if the data analysis was less time-consuming [9, 10]. A simple, relatively cheap and less labor-intensive diagnostic system that enables fast data analysis would be a valuable tool, provided that the system has an adequate accuracy for correct diagnosing and grading of OSA [11]. We hypothesized that EEG frequency band analysis by statistical methods could be used to diagnose OSA. These methods could be a useful to distinguishing people having OSA from those not having this problem. For this aim, we developed a new computer software to obtain the attributes of the EEG segments for statistical analysis.

This study was carried out on the hypothesis that we can detect this disease without using airflow, thor, abdo and SpO2 channels, which are actually used for apnea detection. If successful, we can detect the disease using only EEG. Thus, these 4 channels are not connected to the patient.

These 4 channels affect the patient's sleep quality, increase the hardware cost, increase the memory space required for recording, increase the CPU workload and create a load on the network. Most changes in the human body are controlled by the brain. We planned such a study to determine whether we could detect these respiratory changes using EEG alone.

2. METHODS

2.1. Data Collection

This research was performed in a retrospective way. All study data were obtained from the routine PSG archive of the Sleep Laboratory. The analyses were carried out on 151 individuals of different age and gender. 121 of these individuals were diagnosed as having OSA and 30 of them were diagnosed without OSA. Of (epoch) EEG recordings, 11842 belonging to the patients and 4584 belonging to the healthy, were analyzed. Statistical information of study groups are shown in Table 1. Since the definition of apnea was a minimum of 10 seconds, 10-second periods from the onset of apnea were used in patients and random 10-second periods in the control group.

Table 1. Statistical informations of control group (21 males 9 females) and experimental group (92 males 29 females)

		Age	Weight (kg)	Height (cm)	Neck diameter (cm)	Apnea epoch count
Apnea Group	<i>Average</i>	61.3	95.7	171	41.8	98
	<i>Standard</i>	11.3	20.4	8.4	3.7	30
	<i>Deviation(σ)</i>					
	<i>Min</i>	37	55	150	30	74

	Max	94	195	192	53	154
		Age	Weight (kg)	Height (cm)	Neck diameter (cm)	Randomly selected non apnea epoch
Control Group	Average	62.1	86.7	170.5	40.4	153
	Standard	12.4	17.1	9.1	4.7	5
	Deviation(σ)					
	Min	32	47	150	31	140
	Max	92	125	185	47	160

Although there are similar studies [12, 13], we used a novel software, built by the study team, to collect the apnea events and the corresponding EEG segments. Then performed statistical analysis in order to determine the sensitivities and specificities of frequency bands in distinguishing between apneas and control.

2.2. Polysomnography

After PSG records are obtained (shown in Figure 1) from patients the records of the study were digitized with full PSG techniques with a 44-channel polygraph (Compumedics 44E Series, Australia). The PSG montage involved left and right electrooculography (EOG) (LOC-A2 and ROC-A1), two channels of EEG (C4-A1 and C3-A2), electrocardiography (ECG) (two derivations, ECG1 and ECG2), chin electromyography (EMG), a thermistor (for upper respiratory tract signals), body position, snoring (microphone), SpO2 (blood oxygen saturation), thoracic and abdominal excursions. The EEG electrodes were incorporated in compliance with the international 10-20 electrode placement system [14], with a high-pass of 0.5 Hz, low-pass filters of 30 Hz and sampling rate of 256 Hz, in the mentioned order. Pulmonary and abdominal respiratory signals were digitized with 128 Hz. The upper respiratory signals were digitized with 256 Hz. All sleep signals were around 8 hours long and were stored on a hard disk in the European data format (EDF) [15].



Figure 1. PSG records sample

The investigator was also used to score respiratory events manually with the help of Standard criteria proposed by the AASM [5, 16]. The decrease in airflow to 10% or less of the baseline flow amplitude for at least 10 s helped recognize apneas in OSAS patients. Each EEG signal was annotated in regard to sleep stages [5]. All annotations were stored on a hard disk in Extensible Markup Language (XML) and text (TXT) files [17, 18].

2.3. Data Processing

Thanks to the program V2 (Version 1 was used for a different study [19]) developed for the study (shown in Figure 2), the recording pieces in the EEG channels overlapping each apnea were gathered in the form of 10-second epochs in C4-A1 and C3-A2 channels. On the other hand, they were chosen at random from the healthy control group. Delta, Theta, Alpha, and Beta sub bands, which are of great importance to the EEG signals, and their spectrum values were obtained through the developed program. These data were stored in the database so that a statistical data analysis could be performed for each case.

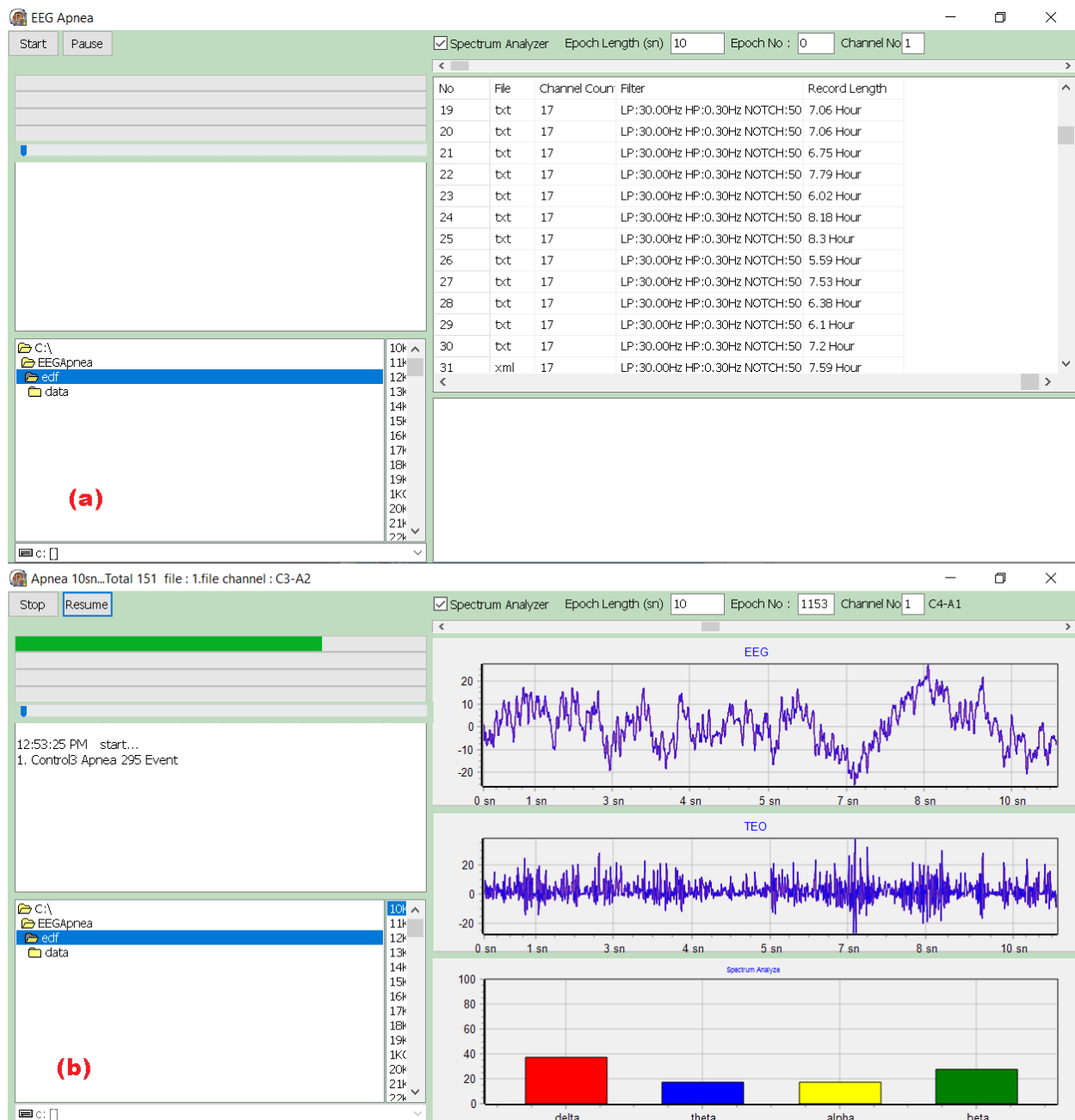


Figure 2. Programming interfaces a) Setup b) Analysis

The stated program is modular in structure and it can operate on the data file and relational database. Considering these basic requirements and the software experiences, a 3-layer structure was modelled as data access, analysis, and database on deciding the most appropriate architectural structure for the program carried out. Furthermore, the layers were put into modules within each other in accordance with the functions of the application. By taking the present software licenses and software skills into account,

Microsoft SQL relational database and Delphi software development tools were used. Figure 3 shows general flow scheme.

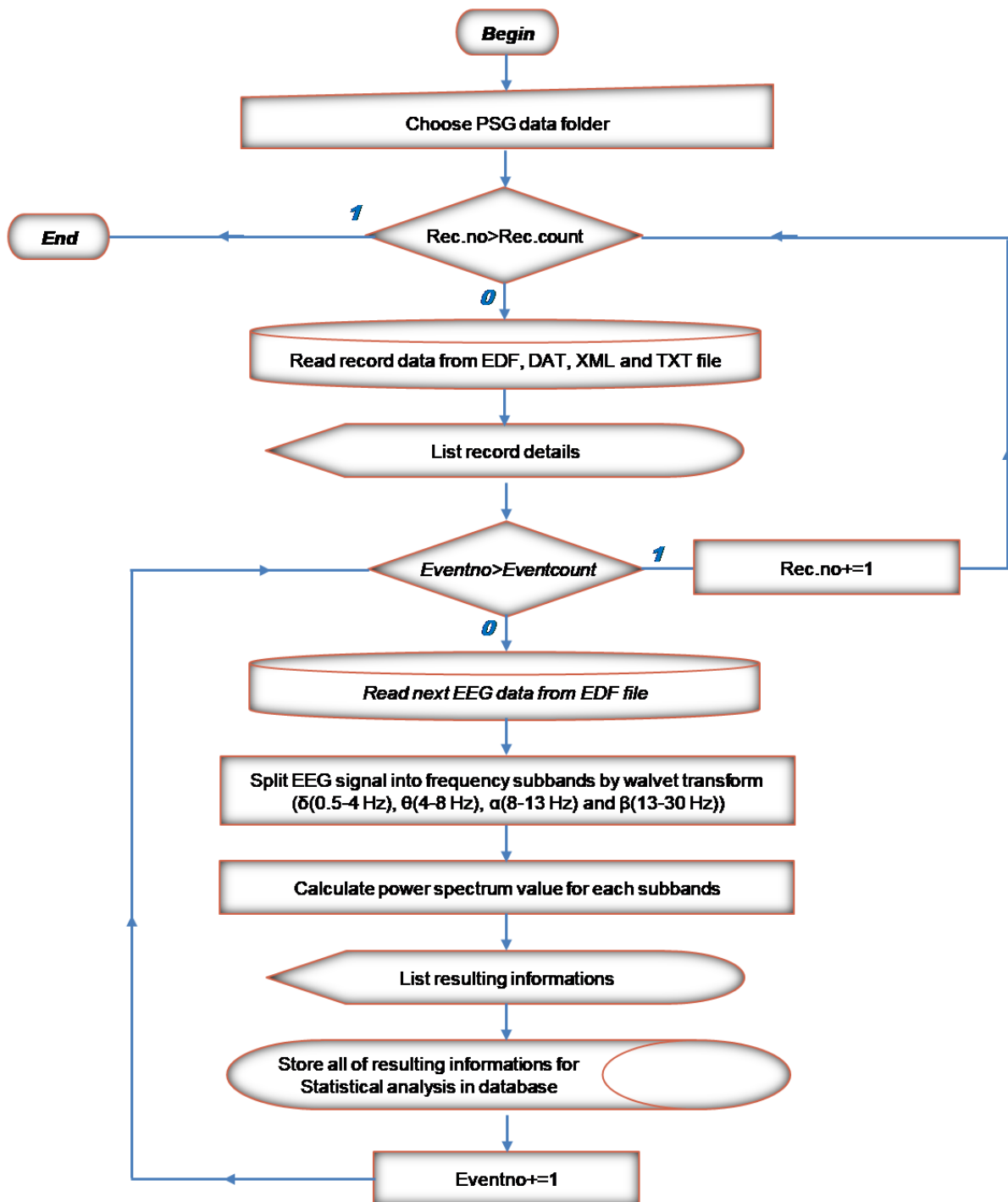


Figure 3. General flow scheme of the study

In the study done, it was decided from the researches done and the techniques used that the discrete Fourier transform (DFT) and the Haar wavelet transform would serve in the most appropriate manner for our purpose. The Haar wavelet transform makes the pretty basic and the fastest transform technique [20].

Many spectral analysis methods in the numeric environment are based on discrete Fourier transforms (DFT) [21]. So we use DFT method for spectral analysis.

DFT is a significant operator that matches a finite series such as $f(k)$, $k = 0, 1, \dots, N-1$, with another finite series like $F(n)$, $n = 0, 1, \dots, N-1$. When normalized sampling frequency is 2π [21]:

$$X_k = \sum_{n=0}^{N-1} x_n e^{-\frac{2\pi i}{N} kn} \quad k = 0, \dots, N \quad (1)$$

The sequence of N complex numbers X_0, \dots, X_{N-1} is transformed into the sequence of N complex numbers X_0, \dots, X_{N-1} by the DFT.

Thanks to the Fourier analysis, it is known that a signal is composed of many sinusoidal frequencies. The wavelet, on the other hand, is formed from the shifted and scaled form of the original wavelet. The wavelet transform is achieved from the multiplication of the shifted and scaled form of the wavelet function ψ by the signal during the whole time interval. As a result of the wavelet transform, a multitude of wavelet coefficients are obtained and these make the scale and position functions [22]

$$\psi_{k,s}(t) = 2^{s/2} \psi(2^s t - k) dt. \quad (2)$$

Discrete wavelet transform, choosing subsets of the scales 'k' and positions 's' of the mother wavelet.

In the study, the Haar wavelet transform was applied to the EEG signals between 21 and 24 levels in order to obtain Delta, Theta, Alpha, and Beta sub bands.

2.4. Statistical Analysis

A receiver operating characteristic (ROC) is a technique that is used to choose, organize, and visualize the classifiers depending on their performances. ROC curves are generally used at the stage of giving medical decisions. Recently, ROC is increasingly used in machine learning and data-mining [23].

ROC curves are two dimensional graphics in which true positive is drawn in Y axis whereas false positive is drawn in X axis. A ROC curve also explains the visual relationship between true positives and false positives [23].

The ROC curves were used to distinguish apnea based on EEG frequency band percentages; areas under the curves (AUCs) were computed, and then the AUCs were compared using z statistics.

"t" test is also a method that is widely used in hypothesis tests. By comparing the averages of two groups, it is decided whether the difference between them is coincidental or statistically meaningful. As "t" distribution, which is also known as small sampling, gives opportunity to work with small samples, it allows researchers to carry out their studies with great ease. In cases, where "t" test sample size is small and the standard deviations related to the main mass are unknown; it is an analysis method developed to test the hypotheses aiming to examine

- Whether an average value that belongs to a group is different from the preset value in terms of a variable being examined,
- Whether there is a difference between two independent groups in terms of a variable under examination,
- Whether there is a difference in the reactions of a group under different conditions in terms of a variable under examination [24].

3. RESULTS

The percentage values of Delta, Theta, Alpha and Beta frequency bands were evaluated with ROC analyses for the purpose of distinguishing apneas from non-apnea epochs. While C3-A2 Beta (%) frequency level provided the highest distinguishing value (AUC=0.662; $p<0.001$), C3-A2 Alpha (%) level gave the lowest distinguishing value (AUC=0.536; $p<0.001$).

Similarly, C4-A1 Beta (%) frequency level provided the highest distinguishing value (AUC=0.658; $p<0.001$) whereas C4-A1 Alpha (%) gave the lowest distinguishing value (AUC=0.536; $p<0.001$). Of all the four frequency bands, Beta was determined as the most meaningful frequency band. The positive (Apnea) value in this study is 11842 and the negative (Control) value is 4584.

3.1. C3-A2 Channel

From the curves seen in Figure 4.a, it can be understood that the Beta value (AUC=0.662) below the curve has the highest value and Alpha (AUC=0.536) has the lowest value.

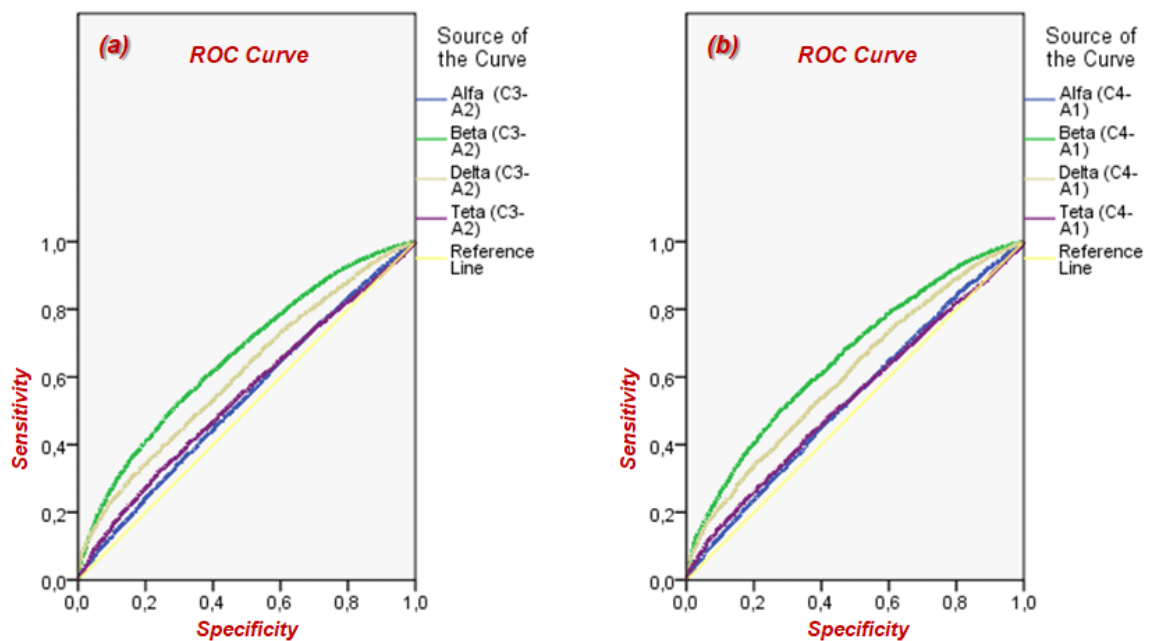


Figure 4. ROC curves a) C3-A2 channel b) C4-A1 channel

According to the results in Table 2, of all 4 bands in the EEG signals, Beta has the highest value in distinguishing the individuals with apnea from those without apnea, and Alpha has the lowest distinguishing value in doing so. As a result of the ROC analysis, the areas which were obtained for all the frequency bands and were remained below the curve, were found statistically meaningful ($p<0.001$).

Table 2. ROC Curve results

		AUC	Standard error	P	95% confidence interval	
					lower bound	upper bound
C3-A2 channel	Alpha(C3-A2)	0.536	0.005	<0.001	0.526	0.545
	Beta (C3-A2)	0.662	0.005	<0.001	0.653	0.671
	Delta (C3-A2)	0.61	0.005	<0.001	0.601	0.619
	Theta (C3-A2)	0.547	0.005	<0.001	0.537	0.556

C4-A1 channel	Alpha(C3-A2)	0.536	0.005	<0.001	0.526	0.546
	Beta (C3-A2)	0.658	0.005	<0.001	0.649	0.667
	Delta (C3-A2)	0.609	0.005	<0.001	0.6	0.618
	Theta (C3-A2)	0.538	0.005	<0.001	0.528	0.547

3.2. C4-A1 Channel

From the curves present in Figure 4.b, it can be seen that the value remaining below the curve, Beta (AUC=0.658), has the highest value and Alpha (AUC=0.536) has the lowest value.

According to the result in Table 2, of all 4 bands in the EEG signals, Beta has the highest value in distinguishing the individuals with apnea from those without apnea, and Alpha has the lowest distinguishing value in doing so. As a result of the ROC analysis, the areas which were obtained for all the frequency bands and were remained below the curve were found statistically meaningful ($p<0.001$).

3.3. T-Test

In the group statistics table, how many cases there are in each group, their average values (frequency band averages of the EEG signals), their standard deviations and standard error values can be seen in Table 3. it can be seen that Delta and Theta averages of the control group are higher and their Alpha and Beta averages are lower than those of the apnea group in both EEG channels.

Table 3. Group statistics analyzed below, for each of 8 subjects, C and A, denoting respectively control group and apnea group

	Groups	N	Average	Standard Deviation	Standard Error Average
Delta (C3-A2)	Control	4584	42.2	10.5	0.2
	Apnea	11842	38.0	10.4	0.1
Theta (C3-A2)	Control	4584	19.1	3.8	0.1
	Apnea	11842	18.5	4.1	0.0
Alpha (C3-A2)	Control	4584	14.0	3.8	0.1
	Apnea	11842	14.6	4.1	0.0
Beta (C3-A2)	Control	4584	24.6	6.7	0.1
	Apnea	11842	28.9	7.3	0.1
Delta (C4-A1)	Control	4584	43.4	10.6	0.2
	Apnea	11842	39.2	10.5	0.1
Theta (C4-A1)	Control	4584	18.9	3.8	0.1
	Apnea	11842	18.4	4.2	0.0
Alpha (C4-A1)	Control	4584	13.8	3.9	0.1
	Apnea	11842	14.4	4.2	0.0
Beta (C4-A1)	Control	4584	23.9	6.7	0.1
	Apnea	11842	28.0	7.3	0.1

The analysis results show a meaningful difference in distinguishing the apnea (according to the individuals with and without apnea) from the EEG channels. As for this, it can be stated that both C3-A2 and C4-A1 Beta bands are more successful. When apnea was compared with the control frequency bands, a statistically meaningful difference was found in all bands ($p<0.001$).

The analysis of Delta (C3-A2) revealed that, the frequency values of the control group were statistically higher (42.2-38=4.2) in comparison to those of the apnea group ($p<0.001$). The analysis of Theta (C3-A2) revealed that, the frequency values of the control group were statistically higher (19.1-18.5=0.6) in

comparison to those of the apnea group ($p < 0.001$). The analysis of Alpha (C3-A2) revealed that, the frequency values of the control group were statistically lower ($14.0-14.6=-0.6$) in comparison to those of the apnea group ($p < 0.001$). The analysis of Beta (C3-A2) revealed that, the frequency values of the control group were statistically lower ($24.6-28.9=-4.3$) in comparison to those of the apnea group ($p < 0.001$). The analysis of Delta (C4-A1) revealed that, the frequency values of the control group were statistically lower ($43.4-39.2=4.2$) in comparison to those of the apnea group ($p < 0.001$). The analysis of Theta (C4-A1) revealed that, the frequency values of the control group were statistically higher ($18.9-18.4=0.5$) in comparison to those of the apnea group ($p < 0.001$). The analysis of Alpha (C4-A1) revealed that, the frequency values of the control group were statistically lower ($13.8-14.4=-0.6$) in comparison to those of the apnea group ($p < 0.001$). The analysis of Beta (C4-A1) revealed that, the frequency values of the control group were statistically lower ($23.9-28.0=-4.1$) in comparison to those of the apnea group ($p < 0.001$).

In Table 4, t- test was conducted in terms of the averages of these two groups which were classified according to apnea. Here is given a great number of statistics like F, sig, t and so on. The value we should check here for comparison is Sig value. As this value is lower than 0.05 ($1-\alpha = 1-0.95=0.05$), the hypothesis that the apnea can be distinguished from the EEG channels cannot be refused due to the fact that the values obtained from the test results are within the scope of reliability.

Table 4. The printout of t-test results for C4-A1/ C3-A2, 1 and 2 denoting respectively equal variances assumed and equal variances not assumed

		<i>Levene's Test for Equality of Variances</i>		<i>t-test for Equality of Means</i>				<i>95% Confidence Interval of the Difference</i>		
		<i>F</i>	<i>Sig.</i>	<i>t</i>	<i>df</i>	<i>Sig. (2-tailed)</i>	<i>Mean Diff.</i>	<i>Std. Error Diff.</i>	<i>Lower</i>	<i>Upper</i>
C4-A1	Delta	1		23.139	16424	0.000	4.2386	0.1832	3.8796	4.5977
		2	4.818	0.028	23.038	8261.131	0.000	4.2386	0.184	3.8780
	Theta	1		6.804	16424	0.000	0.4872	0.0716	0.3469	0.6276
		2	39.832	0.000	7.087	9081.882	0.000	0.4872	0.0688	0.3524
	Alpha	1		-8.126	16424	0.000	-0.5838	0.0718	-0.7246	-0.4429
		2	8.155	0.004	-8.353	8826.849	0.000	-0.5838	0.0699	-0.7208
Beta	1		-33.164	16424	0.000	-4.1421	0.1249	-4.3869	-3.8973	
	2	46.711	0.000	-34.495	9055.163	0.000	-4.1421	0.1201	-4.3775	-3.9067
C3-A2	Delta	1		23.162	16424	0.000	4.2055	0.1816	3.8496	4.5614
		2	2.795	0.095	23.127	8309.440	0.000	4.2055	0.1818	3.8491
	Theta	1		8.532	16424	0.000	0.6003	0.0704	0.4624	0.7382
		2	32.489	0.000	8.831	8958.143	0.000	0.6003	0.0680	0.4671
	Alpha	1		-8.089	16424	0.000	-0.5626	0.0696	-0.6990	-0.4263
		2	12.538	0.000	-8.308	8811.787	0.000	-0.5626	0.0677	-0.6954
Beta	1		-34.017	16424	0.000	-4.2432	0.1247	-4.4877	-3.9987	
	2	34.733	0.000	-35.296	9007.119	0.000	-4.2432	0.1202	-4.4789	-4.0076

According to the result of Table 5, the average of the control group composed of 30 individuals without apnea involving 4584 cases is 24.6 and that of the apnea group composed of 121 individuals with 11842 cases is 28.9. The standard deviation for the control group was found 6.7. Standard error is the standard deviation related to the sample (Std error mean) and this can be obtained through the division of the standard deviation by the square root of the sample size ($6,7/\sqrt{4584}$).

According to the result of Table 5, the average of the control group is 23.9 and the average of the apnea group is 28.0. The standard deviation for the control group was found 6.7.

Table 5. C3-A2 / C4-A1 t- test results of the Beta frequency band percentages of EEG band according to the healthy individuals and the individuals with apnea

	Groups	N	X	SS	Sd	t	p
C3-A2	Control	4584	24.6	6.7	16424	-34.017	0.000
	Apnea	11842	28.9	7.3			
C4-A1	Control	4584	23.9	6.7	16424	-33.164	0.000
	Apnea	11842	28.0	7.3			

Although there are similar studies in the literature, more than 16000 events belonging to the control group consisting of 121 patients and 30 healthy individuals were examined in this study. All the data in the study were obtained by a specialist doctor in a real laboratory environment, instead of a ready-made database. In addition, a special software has been developed for the study under the guidance of a specialist doctor. The first version of the software was used in our previous study [19]. However, in the first version, unlike this study, there is 20 patient data and no control group. The hypothesis in that study [19] is to distinguish between obstructive sleep apnea syndrome (OSAS) and obstructive hypopneas with EEG data. The aim of this study is to distinguish individuals with apnea from individuals without apnea using only EEG. This study differs from the previous [19] study both in terms of dataset and hypothesis. In this respect, the results obtained from the present study will contribute to the literature.

4. CONCLUSION

Doing researches about sleep using the EEG frequency bands to detect sleep apnea is a promising field. The main finding of this research is that the success rate of the classifying apnea correctly is high in a meaningful way and at the end of the study it was found out that Beta band proved to be the most useful band and gave the most meaningful result in distinguishing apnea from the EEG bands.

Although there are some restrictions on the study, it is clear that it has more strong points. During the study, firstly a new software was developed to extract the electrophysiological bands. This software can process signal data in EDF format. Most of the PSG systems store the signal data they digitalize in EDF format or they can convert these data into this type of file. Therefore, this software can work in harmony with the PSG systems to process the biosignals. Moreover, more than 16000 different cases, 11842 of which were recorded from 121 patients suffering from OSA and 4584 of which were recorded from 30 healthy individuals, were analyzed. In addition, previously done studies were examined and the results were obtained following the scientific criteria and international standards for sleep scoring at each stage of the study. Likewise, obtaining results through the use of the detailed statistics beyond the descriptive statistics is another remarkable point that underlies the strong points of the study.

Moreover, the software written was built in a modular way so that it could be used in similar research and could help reduce the analysis period. At the beginning, the most important drawback of the program was that the data were received as raw data and then analyzed and this caused waste of a great amount of capacity and time. In the following period, this obstacle was removed by changing the data access module in a way that it could read the data in EDF and XML formats. Furthermore, the program was initially designed for only one analysis. However, thanks to the different parameter inputs, filter, and different analysis methods added later, the program evolved from a single analysis application into a modular structure that can be used for different purposes. For example, besides the data taken from the EEG

channels, the data taken from other different channels (EMG, ECG, EOG, SpO₂, Thermostat, Thoracic and Abdominal excursions, microphone and body position etc.) can be analyzed by entering the required parameters. In addition, it was designed to analyze not only apnea but also other cases (respiratory, periodic leg movements during sleep, arousals, pH, SpO₂ and ECG etc.).

The restrictions on the study can be explained as follows. Firstly, while the EEG analysis was being conducted, event-related potentials (ERP) and sleep phases were not taken into consideration. Nonetheless, if the sleep phases and event-related potentials are considered in distinguishing apnea in the study's hypothesis, more successful results can be obtained. In addition, the recordings were taken from a PSG device using 2 channel EEG. The result may be more successful when the number of EEG channels is increased.

In conclusion, the study carried out gave meaningful results. The software developed has proved to be a reliable mean of preventing experts from wasting time and effort in data analysis and it helps to give right decisions about patients. It also can be used in different signal analyses due to its modular structure. In the future, it is aimed to add various modules such as machine learning to the software for the purpose that a model can be formed to predict apnea and a different treatment method can be developed. Accordingly, the studies are being carried out within the scope of the target at project level.

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CONFLICT OF INTEREST

No conflict of interest was declared by the authors.

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