

## Can obstructive apnea and hypopnea during sleep be differentiated by using electroencephalographic frequency bands? Statistical analysis of receiver-operator curve characteristics

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**Aim:** To investigate whether electroencephalographic (EEG) frequency bands are applicable in distinguishing abnormal respiratory events such as obstructive apnea and hypopnea in patients with sleep apnea.

**Materials and methods:** The polysomnographic recordings of 20 patients were examined retrospectively. EEG record segments were taken from C4-A1 and C3-A2 channels and were analyzed with software that uses digital signal processing methods, developed by the study team. Percentage values of delta, theta, alpha, and beta frequency bands were evaluated through discriminant and receiver-operator curve (ROC) analysis to distinguish between apneas and hypopneas.

**Results:** For the C4-A1 channel, delta (%) provided the highest discriminative value (AUC = 0.563; P < 0.001); on the other hand, alpha (%) gave the lowest discriminative value (AUC = 0.519; P = 0.041). Likewise, whereas for the C3-A2 channel delta (%) gave the highest discriminative value (AUC = 0.565; P < 0.001), alpha produced the lowest discriminative value (AUC = 0.501; P = 0.943).

**Conclusion:** As a result of discriminant analysis, the accurate classification rate of hypopneas was 44.8% and the accurate classification of obstructive apneas was 63.5%. Of the 4 frequency bands, the most significant was delta. The predictive values were not at significance level.

**Key words:** Sleep apnea, digital signal processing, electroencephalography, receiver-operator curve characteristics

### Obstrüktif apne ve hipopne uyku esnasında elektroensefalografik frekans bandları kullanılarak birbirinden ayırt edilebilir mi? Karakteristik işlem eğrisi (receiver-operator curve, ROC) analizi

**Amaç:** Elektroensefalografik (EEG) frekans bandlarının uyku apneli hastalarda obstrüktif apne ve hipopne gibi anormal solunum olaylarını ayırt etmede kullanılıp kullanılmayacağını belirlemek üzere bu çalışmayı planladık.

**Yöntem ve gereç:** 20 hastanın polisomnografik kayıtları retrospektif olarak incelendi. EEG kayıtları C4-A1 ve C3-A2 kanallarından alınarak dijital sinyal işleme yöntemlerini kullanan ve çalışma ekibi tarafından geliştirilen bir yazılım ile incelendi. Delta, teta, alfa ve beta frekans bandlarının yüzde değerleri apne ve hipopneleri ayırt edebilmek amacıyla diskriminant ve ROC analizleri kullanılarak değerlendirildi.

**Bulgular:** C4-A1 delta (%) frekans düzeyi en yüksek diskriminatif değeri sağladı (AUC = 0,563; P < 0,001), ancak C4-A1 alfa (%) düzeyi en düşük diskriminatif değeri verdi (AUC = 0,519; P = 0,041). Benzer şekilde, C4-A2 delta (%)

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frekans düzeyi en yüksek diskriminatif değeri sağlarken (AUC = 0,565; P < 0,001), C4-A2 alfa (%) düzeyi en düşük diskriminatif değeri verdi (AUC = 0,501; P = 0,943).

**Sonuç:** Diskriminant analiz sonucunda, hipopnelerin doğru sınıflandırılma oranı % 44,8 ve obstrüktif olguların doğru sınıflandırılma oranı % 63,5 oldu. Dört farklı frekans bandı içinde en anlamlı frekans delta idi. Ancak, prediktif değerler anlamlı derecede yüksek değildi.

**Anahtar sözcükler:** Uyku apnesi, dijital sinyal işleme, elektroensefalografik, karakteristik işlem eğrisi

## Introduction

Sleep apnea is characterized by frequent breathing cessations during sleep. Apneas are identified when airflow decreases to 10% or less of the baseline flow for at least 10 s (1,2). This syndrome causes severe sleep impairment and is often responsible for the development of other problems such as illusions, memory deficits, difficulty in speaking, concentration disorders, heart problems, hypertension, and daytime fatigue (3,4).

There are different types of respiratory abnormalities, namely obstructive apnea, central apnea, mixed apnea, and hypopnea. Distinguishing obstructive hypopnea from apnea can be clinically important because different types of respiratory events may require different treatment approaches (5). Furthermore, for research purposes, this distinction is important for investigating the pathological mechanism of different types of sleep apnea. Conventional full-night polysomnography (PSG) with recording of chest and abdominal movement may overestimate the frequency of hypopnea and thus the severity of the disease, leading to inappropriate treatment of sleep-disordered breathing.

Electroencephalography (EEG) has long been an important clinical tool in the diagnosing, monitoring, and managing of neuronal brain activity. EEG signals contain a wide range of frequency components. However, the range of clinical and physiological interest is between 0.5 and 30 Hz. This range is classified approximately in a number of frequency bands, as follows:  $\delta$  (0.5-4 Hz),  $\theta$  (4-8 Hz),  $\alpha$  (8-13 Hz), and  $\beta$  (13-30 Hz) (6). Since there is no definite criterion used by the experts, visual analysis of EEG signals in the time domain may be insufficient. Large amounts of data are generated by EEG monitoring systems for electroencephalographic changes, such that their complete visual analysis is not routinely

possible. Extracted features such as wavelet transform (WT) coefficients and discrete Fourier transform (DFT) are promising tools in polygraphic sleep studies (7).

We hypothesized that electroencephalographic frequency band analysis by statistical methods could be a useful tool to distinguish accurately between hypopnea and apnea in sleep apnea patients. Therefore, we developed computer software to extract and prepare relevant EEG segments for statistical analysis.

## Methods

### Data collection

This study was performed in a retrospective manner. All study data were obtained from the routine polysomnography archive of the Sleep Laboratory Unit at the Trakya University Education and Research Hospital. The polysomnographic recordings of 20 patients with obstructive sleep apnea syndrome (OSAS) were reviewed, and 4849 obstructive apneas and 1210 obstructive hypopneas were analyzed for study purposes (Table 1).

We used new software, developed by the study team, to collect the abnormal respiratory events and the corresponding EEG segments. We then performed receiver-operator curve characteristic analysis in order to determine the sensitivities and specificities of frequency bands in distinguishing apneas from hypopnea.

### Polysomnography

The polysomnography (PSG) records analyzed in this study were digitized using full PSG techniques with a 44-channel polygraph (Compumedics 44E Series, Australia). The PSG montage included 2 channels of EEG (C3-A2 and C4-A1), left and right

Table 1. General characteristics of study group.

| Patient No. | Number of Hypopneas | Number of Apneas | Age | Weight (kg) | Height (cm) | Neck Circumference (cm) | Sex |
|-------------|---------------------|------------------|-----|-------------|-------------|-------------------------|-----|
| 1           | 85                  | 114              | 51  | 96          | 173         | 43                      | M   |
| 2           | 49                  | 306              | 62  | 84          | 173         | 40                      | M   |
| 3           | 19                  | 91               | 60  | 76          | 167         | 40                      | M   |
| 4           | 55                  | 236              | 40  | 107         | 174         | 47                      | M   |
| 5           | 28                  | 132              | 33  | 96          | 180         | 41                      | M   |
| 6           | 10                  | 65               | 41  | 85          | 175         | 41                      | M   |
| 7           | 2                   | 506              | 67  | 110         | 164         | 39                      | F   |
| 8           | 34                  | 250              | 51  | 106         | 174         | 50                      | M   |
| 9           | 123                 | 278              | 68  | 110         | 166         | 47                      | F   |
| 10          | 102                 | 120              | 55  | 80          | 168         | 43                      | M   |
| 11          | 52                  | 205              | 33  | 88          | 177         | 44                      | M   |
| 12          | 112                 | 120              | 42  | 105         | 166         | 43                      | M   |
| 13          | 79                  | 148              | 38  | 85          | 165         | 37                      | F   |
| 14          | 69                  | 127              | 38  | 122         | 192         | 45                      | M   |
| 15          | 37                  | 8                | 47  | 134         | 168         | 39                      | F   |
| 16          | 127                 | 206              | 63  | 125         | 169         | 41                      | F   |
| 17          | 9                   | 543              | 54  | 116         | 169         | 46                      | M   |
| 18          | 14                  | 675              | 53  | 82          | 168         | 36                      | F   |
| 19          | 125                 | 619              | 58  | 120         | 165         | 46                      | M   |
| 20          | 76                  | 100              | 53  | 102         | 176         | 41                      | M   |
| Total       | 1207                | 4849             |     |             |             |                         |     |

\*M: male, F: female

electrooculography (EOG) (LOC-A2 and ROC-A1), chin electromyography (EMG), electrocardiography (ECG) (2 derivations, ECG1 and ECG2), SpO<sub>2</sub> (blood oxygen saturation), a thermistor (for upper respiratory tract signals), thoracic and abdominal excursions, snoring (microphone), and body position. The EEG electrodes were placed according to the international 10-20 electrode placement

system (8), with a sampling rate of 256 Hz and high-pass and low-pass filters of 0.5 Hz and 30 Hz, respectively. The upper respiratory signals were digitized with 256 Hz, and pulmonary and abdominal respiratory signals were digitized with 128 Hz. All sleep signals with a duration of nearly 8 h were stored on a hard disk in the European data format (EDF) (Figure 1).

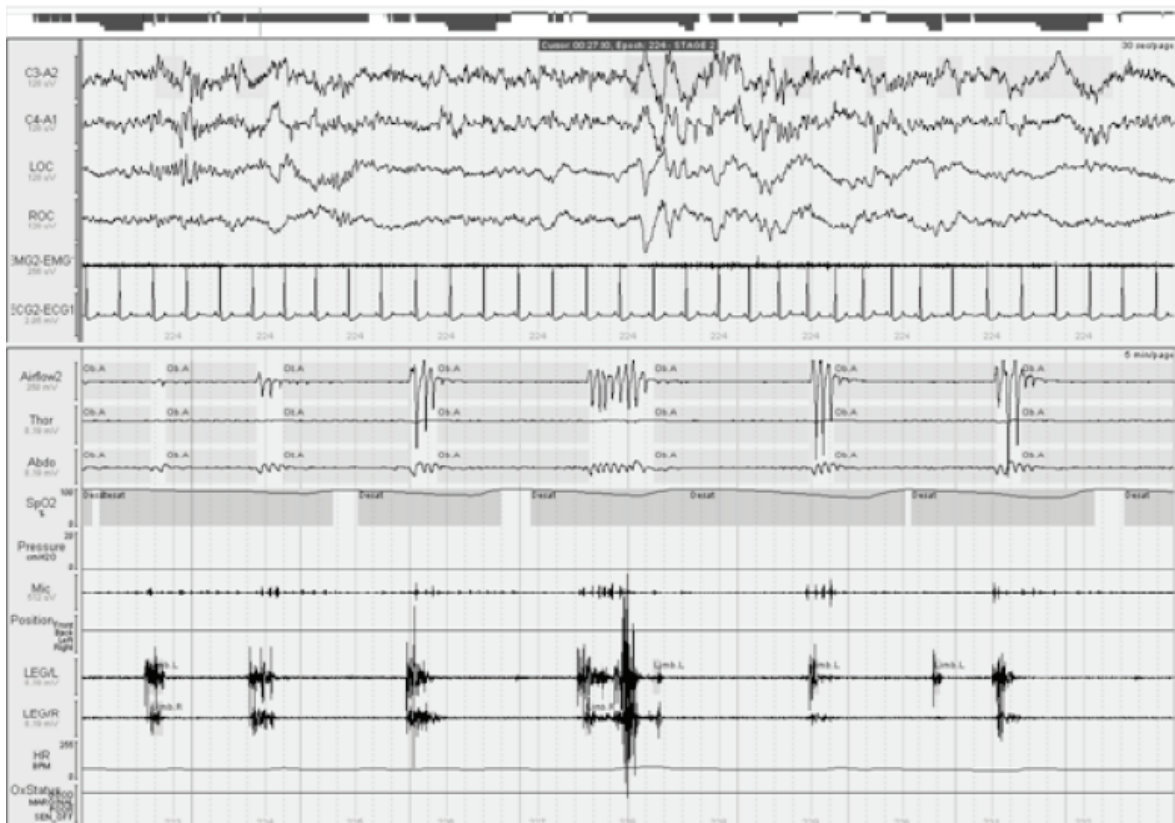


Figure 1. A representative sample of patient polygraphic recordings. Obstructive apneas were marked and corresponding electroencephalographic segments were collected for further analysis.

Respiratory events were scored manually by the same investigator (L.Ö.) using the standard criteria proposed by the AASM (1,2). In OSAS patients, obstructive apneas were identified when airflow decreased to 10% or less of the baseline flow amplitude for at least 10 s; obstructive hypopneas were identified when airflow decreased to 50% with a 3% oxyhemoglobin desaturation or to 30% with a 4% oxyhemoglobin desaturation. Each EEG signal was annotated with respect to sleep stages (9). Sleep staging was performed by using 30-s intervals according to the criteria of Rechtschaffen and Kales, with 6 discrete levels of stage 1, 2, 3, and 4 non-REM sleep, rapid eye movement (REM), and wake. All annotations were stored on a hard disk in Extensible Markup Language (XML) and text (TXT) files.

### Data processing

In this study, a special program, written using the Delphi programming language, was developed for EEG data processing by the study team (Figure 2).

Sleep stage, event type, and desaturation information of abnormal respiratory events of each patient were taken from the file formatted in TXT. Time information (starting time and duration) of abnormal respiratory events of each patient was taken in order from the file formatted in XML. EEG data from the same time of these events in C4-A1 and C3-A2 channels were taken out of the file in the EDF format. The digital data, with a sampling rate of 256, was filtered between 0.5 and 30 Hz.

### ECG filtering in EEG

In general, EEG data contains many artifacts, such as ECG, muscle artifacts, and eye movements. Practical use of EEG is extremely limited due to such inevitable contamination by large amplitude ECG, which brings on erroneous interpretations of the normal records. Therefore, we removed the ECG artifact from the EEG and used this filtered EEG in the Teager energy operator (TEO) (10) for sleep EEG artifact detection. To do this, we subtracted the

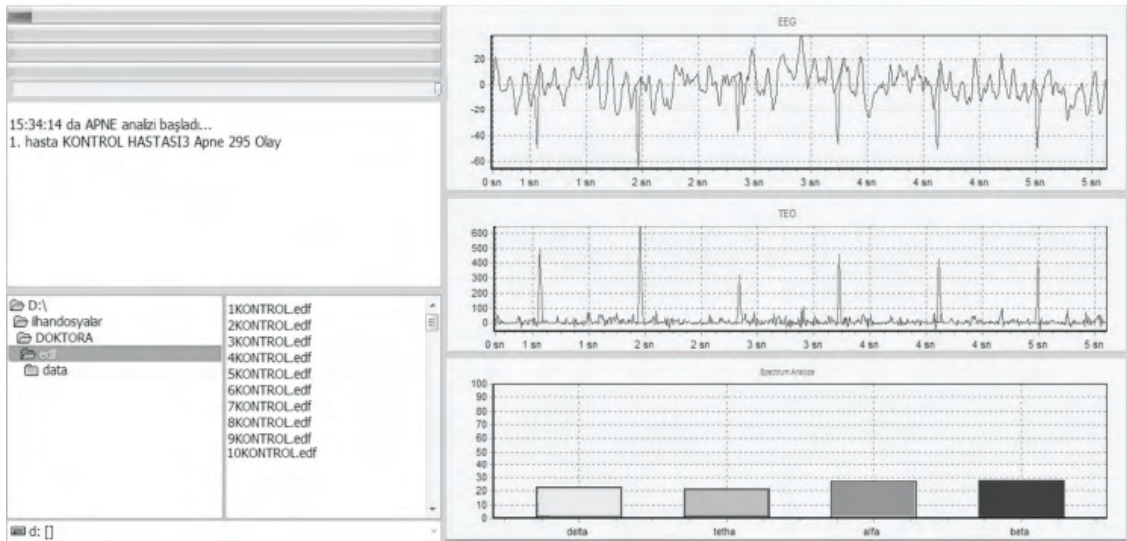


Figure 2. Program interface.

predetermined averaged ECG from the subsequent ECG-contaminated EEG channel (11-13).

$$y(t) = x(t) + z(t)$$

Equation 1. The raw EEG data ( $y$ ), real EEG ( $x$ ), and ECG artifacts ( $z$ ).

The TEO is an energy operator that depends on the derivative of the input signal. It amplifies sudden amplitude changes of the signal. When the Teager operator is applied to a signal, the peak points in the signal become stronger (14). The peak of the ECG is determined from the ECG channel in the polysomnography data by the TEO (13). We calculate the difference of the maximum and minimum value of the ECG and the EEG, respectively, 60 ms before and after the peak point. The ECG channel of the polysomnography data is divided by the mean difference and rescaled to the EEG. By subtracting the estimate of the artifacts,  $z_{est}(t)$ , from the raw EEG,  $y(t)$ , the processed EEG data is obtained as in Equation 2.

$$x_{est}(t) = y(t) - z_{est}(t)$$

Equation 2. The processed EEG ( $x_{est}$ ), the raw EEG data ( $y$ ), and the estimate of the ECG artifacts ( $z_{est}$ ).

$$\psi_{Ts}(n) = \psi_s^2(n) - \psi_s(n-1)\psi_s(n+1)$$

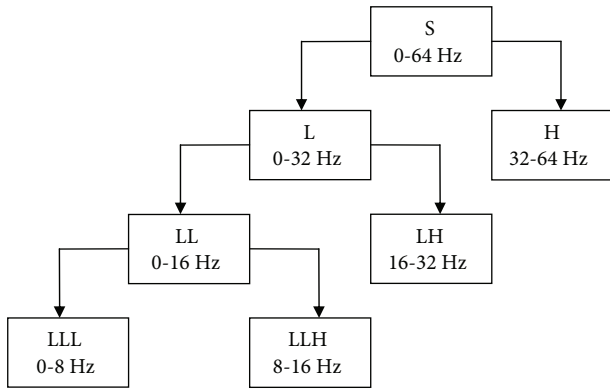
Equation 3.  $\psi_{Ts}$  (Teager energy operator of data),  $\psi_s$  (original data).

## Spectral analysis

In the literature, there are many classifications of EEG signals as noise, quasi-periodic, and even fractal or chaotic signals. Nowadays, the most commonly used methods for signal processing of quasi-periodic signals include techniques like Fourier and wavelet analysis (7). Whereas the Fourier transform provides information about the dominant frequencies, wavelet analysis has the added value of providing time localization of the various frequency components.

The discrete wavelet transform (DWT) is used to decompose a signal into wavelets, small oscillations that are well localized in time. As far as the Fourier transform decomposes a signal into infinite-length sines and cosines, effectively losing all time-localization information, the DWT basic functions are scaled and shifted versions of the time-localized mother wavelet. The DWT is used to construct a time-frequency representation of a signal that offers very good time and frequency localization.

The EEG data, after being filtered, purified of artifacts, and categorized for each abnormal respiratory event, were divided into delta, theta, alpha, and beta frequency bands using the Haar wavelet conversion (15-17) (Figure 3).



Signal (S), Low Frequency (L), High Frequency(H).  
Figure 3. Wavelet decomposition tree.

$$\psi(t) = \begin{cases} 1 & \rightarrow 0 \leq t < 1/2, \\ -1 & \rightarrow 1/2 \leq t < 1, \\ 0 & \rightarrow \text{otherwise.} \end{cases}$$

Equation 4. The Haar wavelet’s mother wavelet function,  $\psi(t)$ .

$$\varphi(t) = \begin{cases} 1 & \rightarrow 0 \leq t < 1, \\ 0 & \rightarrow \text{otherwise.} \end{cases}$$

Equation 5. The Haar wavelet’s scaling function,  $\varphi(t)$ .

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

Equation 6. Discrete wavelet transform, choosing subsets of the scales ‘k’ and positions ‘s’ of the mother wavelet.

The data divided into frequency bands were put into windows using the Hamming window technique (18).

$$\omega(n) = 0.54 - 0.46 \cos\left(\frac{2\pi n}{N-1}\right)$$

Equation 7. Hamming window.

The data in the Hamming window were processed using the discrete Fourier transform (19). Frequency

spectrum values of the EEG data were calculated. Percentage distributions of delta, theta, alpha, and beta frequency bands of the calculated values were determined. These final data were stored in a Structured Query Language (SQL) database until statistical analysis.

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

Equation 8. Discrete Fourier transform (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) (20).

### Statistical analysis

The receiver-operating curves (ROC) were used to distinguish obstructive apnea and obstructive hypopnea based on electroencephalographic frequency band percentages; areas under the curves (AUCs) were computed, and then the AUCs were compared using z statistics. The AUC is a measure of the overall discriminatory power of the prognostic variable. A value of 1.0 indicates perfect discrimination, a value of 0.5 random prediction, and a value lower than 0.5 no discriminative power. Sensitivity refers to the fraction of all cases of apnea with positive test results. It measures how well the test identifies those with apneas. Specificity is the fraction of those without apnea that have negative test results. It measures how well the test excludes patients who do not have apnea. To build a predictive model of group membership based on the observed characteristics of each case, a discriminant analysis was performed.

### Results

Electroencephalographic segments corresponding to 4849 obstructive apneas and 1207 obstructive hypopneas recorded from 20 patients were used for the final statistical analysis.

The cut-off point, sensitivity, specificity, AUC, and P-values of C3-A2 and C4-A1 alpha, beta, delta, and theta values are shown in Table 2. In comparing the percentages of the frequency bands, C4-A1 delta (%) gave the highest discriminative value (AUC = 0.563; P < 0.001); on the other hand, C4-A1 alpha (%) gave the

Table 2. Cut-off point, sensitivity, specificity, AUC and P-values of C3-A2 and C4-A1 alpha, beta, delta, and theta values.

|             | Cut-off | Sensitivity | Specificity | AUC   | P      |
|-------------|---------|-------------|-------------|-------|--------|
| C3-A2 alpha | >27.15  | 87.96       | 18.56       | 0.501 | 0.943  |
| C3-A2 beta  | >51.47  | 91.92       | 16.82       | 0.524 | 0.010  |
| C3-A2 delta | >1.32   | 82.45       | 29.16       | 0.565 | <0.001 |
| C3-A2 theta | >16.08  | 90.31       | 19.47       | 0.540 | <0.001 |
| C4-A1 alpha | >28.32  | 86.06       | 22.62       | 0.519 | 0.041  |
| C4-A1 beta  | >37.93  | 89.46       | 20.38       | 0.542 | <0.001 |
| C4-A1 delta | >2.3    | 74.68       | 36.54       | 0.563 | <0.001 |
| C4-A1 theta | >22.66  | 85.61       | 24.86       | 0.548 | <0.001 |

lowest discriminative value (AUC = 0.519; P = 0.041). Likewise, whereas C3-A2 delta (%) gave the highest discriminative value (AUC = 0.565; P < 0.001), C3-A2 alpha produced the lowest discriminative value (AUC = 0.501; P = 0.943). The ROC curves of the C3-A2 and C4-A1 bands are shown in Figures 4 and 5.

P-values of pairwise comparisons of the AUCs of C3-A2 alpha, beta, delta, and theta values

are shown in Table 3. Classification results of discriminant analysis for C3-A2 alpha, beta, delta, and theta values are shown in Table 4. As a result of discriminant analysis, the accurate classification rate of hypopneas was 44.8% and the accurate classification of obstructive cases was 63.1%. Overall, 59.4% of the original grouped cases were correctly classified by using discriminant analysis. P-values of

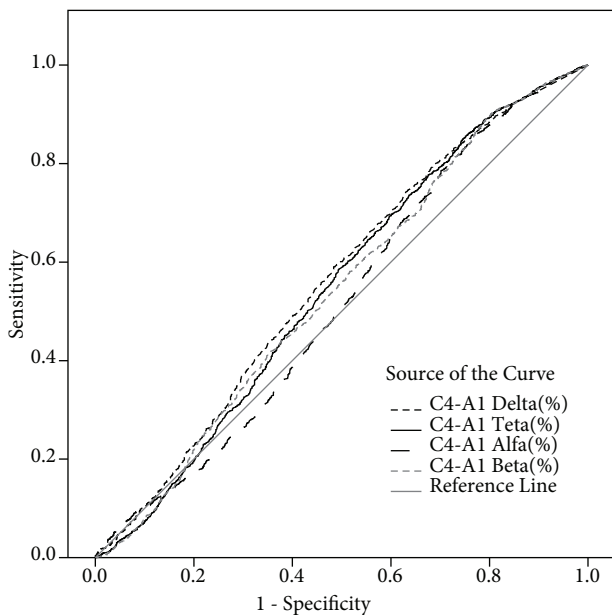


Figure 4. Receiver-operator characteristic curves (ROC) of C4-A1 EEG channels.

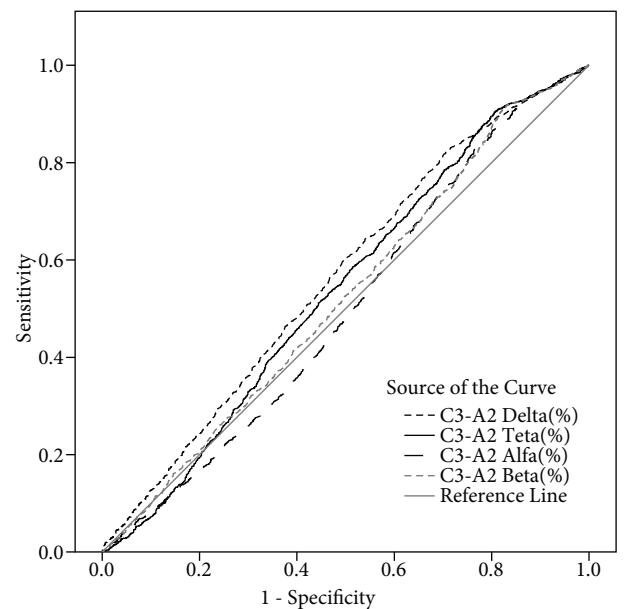


Figure 5. Receiver-operator characteristic curves (ROC) of C3-A2 EEG channels.

Table 3. P-values of pairwise comparisons of AUCs of C3-A2 alpha, beta, delta, and theta values.

|             | C3-A2 beta | C3-A2 delta | C3-A2 theta |
|-------------|------------|-------------|-------------|
| C3-A2 alpha | 0.043      | <0.001      | 0.006       |
| C3-A2 beta  | -          | <0.001      | 0.008       |
| C3-A2 delta | -          | -           | 0.002       |

Table 4. Classification results of discriminant analysis for C3-A2 alpha, beta, delta, and theta values.

|          |                   | Predicted Group Membership |                   | Total |
|----------|-------------------|----------------------------|-------------------|-------|
|          |                   | Hypopnea                   | Obstructive Apnea |       |
| Original | Hypopnea          | 541 (44.8)                 | 666 (55.2)        | 1207  |
|          | Obstructive Apnea | 1791 (36.9)                | 3058 (63.1)       | 4849  |

n (%)

pairwise comparisons of the AUCs of C4-A1 alpha, beta, delta, and theta values are shown in Table 5. Classification results of discriminant analysis for C4-A1 alpha, beta, delta, and theta values are shown in Table 6. As a result of discriminant analysis, the

accurate classification rate of hypopneas was 31.5%, and the accurate classification of obstructive cases was 76.8%. Overall, 67.7% of the original grouped cases were correctly classified by using discriminant analysis.

Table 5. P-values of pairwise comparisons of AUCs of C4-A1 alpha, beta, delta, and theta values.

|             | C4-A1 beta | C4-A1 delta | C4-A1 theta |
|-------------|------------|-------------|-------------|
| C4-A1 alpha | 0.056      | 0.003       | 0.035       |
| C4-A1 beta  | -          | 0.017       | 0.247       |
| C4-A1 delta | -          | -           | 0.102       |

Table 6. Classification results of discriminant analysis for C4-A1 alpha, beta, delta, and theta values.

|          |                   | Predicted Group Membership |                   | Total |
|----------|-------------------|----------------------------|-------------------|-------|
|          |                   | Hypopnea                   | Obstructive Apnea |       |
| Original | Hypopnea          | 380 (31.5)                 | 827 (68.5)        | 1207  |
|          | Obstructive Apnea | 1127 (23.2)                | 3722 (76.8)       | 4849  |



The main findings of this study were that the rates in EEG frequency bands could differ according to the type of related abnormal respiration event and that the obstructive apneas could particularly be determined by following the changes in these bands. Of the 4 frequency bands, the most meaningful was delta, although the predictive value was not as high as was expected.

## Discussion

Using electroencephalographic frequency bands to determine the presence of obstructive apneas or hypopneas is a promising area of research in the sleep field. The main finding of this study was that the rate of accurate classification of hypopneas or apneas was not significantly high in obstructive sleep apnea patients. The most useful frequency band was delta in distinguishing obstructive apneas from hypopneas.

There are several important characteristics of the study. First, for the purpose of this study, we developed new computer software to extract relevant electrophysiological signal segments. This software enabled us to collect signal trace data in EDF format. Most of the digital computerized polysomnography systems provide and/or transform signal data into the EDF format. Thus, this software can be used in compliance with these polysomnography systems to process biosignals. In this study, we examined more than 6056 abnormal respiratory events, of which 4849 were obstructive apneas and 1207 were hypopneas.

The program that was written was designed in a modular structure so that it can be used in similar studies, and it can also shorten the duration of analysis on a large scale. One of the most important limitations of the program was that the analyses were performed on raw data, and therefore this caused a labor-intensive study, the occupation of computer system resources, and wasted time. This limitation was later overcome by inserting a module that allowed the data to be read in EDF and XML formats. Furthermore, the program had initially been designed as a closed system for a continuous analysis. Later, it was modularized to serve different purposes by setting different parameters without depending

on a single analysis. We also added several other filters, such as a band-pass filter and ECG filter, to the preexisting high-pass and low-pass filters. Thus, with this program, besides the data obtained from the EEG channel, the data taken from the other channels (EMG, ECG, EOG, SpO<sub>2</sub>, thermistor, thoracic and abdominal excursions, microphone, and body position) could also be analyzed by entering the required information. It was designed to analyze not only apneas but also the other events (respiratory, leg movements, arousals, pH, SpO<sub>2</sub>, ECG, etc.). Initially, we manually excluded score sheets with artifacts from the analysis. Then, through the artifact module that was later inserted, the data were automatically processed with an artifact filter before analyzing, and if a great amount of artifacts were detected, these parts were automatically excluded from the analysis. The artifact module provided important time savings and decreased the workload.

There are some limitations of the study that deserve comment. First, we did not compare event-free EEG segments to apnea-related EEG segments in terms of frequency bands. Although the hypothesis of the study was to distinguish apneas from hypopneas, comparison of quiet sleep periods and sleep periods with respiratory events would give better evidence for the benefits of using EEG. Second, coping with artifacts is a major concern when studying electrophysiological signals. Artifacts resulting from gross body movements and sweating might interfere with frequency analysis.

The method has better results than those reported by many previous studies. We believe that the proposed system can be an efficient tool to assist the experts by facilitating the analysis of a patient's information and reducing the time and effort required to make accurate decisions about their patients.

## Acknowledgement

The study was presented as a poster presentation at the Second National Sleep Disorders Congress, which was held in Cyprus 17-21 March 2010, and was awarded the 2nd best poster presentation award.

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