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Clinical Analysis of EEG Parameters in Prediction of the Depth of Anesthesia in Different Stages: A Comparative Study

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ABSTRACT

Background: *Evaluation of depth of anesthesia is especially important in adequate and efficient management of patients. Clinical assessment of EEG in the operating room is one of the major difficulties in this field.*

This study aims to find the most valuable EEG parameters in prediction of the depth of anesthesia in different stages.

Materials and Methods: *EEG data of 30 patients with same anesthesia protocol (total intravenous anesthesia) were recorded in all anesthetic stages in Shohada-e-Tajrish Hospital. Quantitative EEG characteristics are classified into 4 categories of time, frequency, bispectral and entropy-based characteristics. Their sensitivity, specificity and accuracy in determination of depth of anesthesia were yielded by comparing them with the recorded reference signals in awake, light anesthesia, deep anesthesia and brain dead patients.*

Results: *Time parameters had low accuracy in prediction of the depth of anesthesia. The accuracy rate was 75% for burst suppression response. This value was higher for frequency- based characteristics and the best results were obtained in ß spectral power (accuracy: 88.9%). The accuracy rate was 89.9% for synch fast slow bispectral characteristics. The best results were obtained from entropy-based characteristics with the accuracy of 99.8%.*

Conclusion: *Analysis of the entropy-based characteristics had a great value in predicting the depth of anesthesia. Generally, due to the low accuracy of each single parameter in prediction of the depth of anesthesia, we recommend multiple characteristics analysis with greater focus on entropy-based characteristics.* ***(Tanaffos 2009; 8(2): 46-53)***

Key words: *Anesthesia, Analysis, Electroencephalogram*

INTRODUCTION

Clinical evaluation of intra-operative EEG for assessment of the depth of anesthesia is very difficult. Therefore, it is important to find ways for better qualitative classification of recorded EEG.

To date, several methods have been proposed for assessment of depth of anesthesia by using time, frequency and bispectral characteristics. Entropy-based characteristics are also used for classification of anesthetic stages (1- 3).

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In order to more accurately determine the depth of anesthesia, we have to evaluate brain waves which are quite different in various stages of anesthesia.

In other words, some characteristics are more common in a special anesthetic stage compared to other stages. Therefore, we have to introduce methods that can use EEG characteristics in their useful ranges. It is important to know that these characteristics can be used for immediate assessment of depth of anesthesia. We want to calculate the drug dose based on the score attributed to the quantitative method we adopt. In order to do so, we must have the least lag with the current patient status (4). In recent years, anesthesiologists have used several monitors to evaluate the depth of anesthesia. These monitors try to quantify cortical electrical activities for determination of the depth of anesthesia and we named it as “depth of anesthesia index”. One of these monitors is BIS which was introduced in 1996. BIS monitors yield a dimensionless index from EEG signals, based on bispectral analysis called bispectral index (2). In 2004 Demeter company introduced CSM which shows cortical status index (CSI). Both these monitors are FDA-approved.

CSI uses 4 different characteristics of time and frequency of EEG signal as the input of ANFIS system.

Clinical studies have shown that there is a significant correlation between CSI and BIS. Also, these two indices have a significant correlation (92% and 93%, respectively) with the clinical depth of anesthesia based on standards such as Observer's Assessment of Alertness/Sedation (OAAS) (5).

EEG signals are results of neuronal electrical activities .Time, frequency, bispectral and high level spectrums are characteristics used for EEG signal analysis. Entropic methods are used for EEG signals as well (6, 7).

In this study we aimed to evaluate EEG signal-derived parameters and choose the best characteristic for differentiation of anesthesia stages. We tried to calculate each characteristic’s significance separately in prediction of the depth of anesthesia. Based on this data it would be possible to analyze multiple characteristics to acquire the best index for future studies. One of the advantages of our study was considering the significance of each characteristic in each of the 4 stages of anesthesia separately as well as its overall accuracy. Other advantages of this study included its prospective design, similar anesthetic protocols in all patients and in our knowledge, being the first to study such an important subject in Iran.

MATERIALS AND METHODS

In this study, general physiological and anesthetic data plus EEG, depth of anesthesia scores based on CSI parameter, the degree of muscle relaxation and hemodynamic parameters such as blood pressure, heart rate, and arterial blood oxygen saturation of 30 patients were recorded. Other general information such as age, sex, weight, type of surgical operation and date, time and duration of surgery were also recorded. Patients’ EEG waves were recorded by CSM (Danmeter, Denmark) which recorded crude EEG and also the depth of anesthesia based on CSI and EMG as a parameter of muscle relaxation. Muscle relaxation degree was recorded by nerve stimulator (Xavant) and hemodynamic parameters were measured with pulse oxymeter and non-invasive blood pressure monitoring. These patients took no medications before surgery. In operating room, the patients first received their premedication drugs containing 0.03 mg/kg midazolam and 2 ug/kg fentanyl. For induction of anesthesia, we injected thiopental, 4 mg/kg at first and then 1 mg/kg when intubating. Muscle relaxant drug was cisatracurium. In this study, we used propofol 75-100 ug/kg/min and N2O/O2 (as 50% ratio) for maintenance of anesthesia. If the CSI was more than 60 during anesthesia, we used thiopental, 0.5 mg/kg or bolus injection of propofol. Muscle relaxation degree was calculated by nerve stimulator and if TOF was more than one response, cisatracurium was injected. Every one hour, 0.5ug/kg fentanyl was administered to the patients. EEG was done by CSM with 100 Hz frequency. EEG was recorded with 3 superficial electrodes on Fpz position (positive on the middle of forehead), Ts (negative on left mastoid) and reference electrode on F(P1) (left frontal). In order to differentiate anesthesia stages, we described 4 classes of anesthesia: consciousness, light anesthesia, deep anesthesia and isoelectric state. We recorded 15 minutes for each class (overall 60 minutes). Consciousness class reference data included 15 minutes of EEG recorded from 3 healthy awake people (5 minutes each). To avoid blinking artifacts we advised them to close their eyes and concentrate on a special subject. Light anesthesia stage was defined from the time of initial drug injection to intubation and from the discontinuation of drugs until achieving full consciousness based on anesthesiologist's assessment. EEGs of 14 different patients anesthetized according to the above-mentioned protocols were collected to form a 15-minute reference signal for this class.

Anesthetic class data included 15 minutes of EEG signal from the above mentioned 14 patients recorded in phase 3 of anesthesia .Isoelectric class data were recorded from 3 brain dead patients. For classification, we used BISS classifier and accuracy, sensitivity and specificity were calculated by leave one-out for each characteristic in each of the 4 anesthetic classes.

RESULTS

Our under study patients included 10 women and 20 men, with the age range of 15-75 yrs (44.36±19.93 yrs.), and weight range of 50-96 kg (68.64±12.99 kg).

Ninety-five percent spectral edge frequency had the highest association power in predicting deep anesthetic status in comparison with others (accuracy: 91.42%). Sensitivity and specificity of this characteristic were also high (91.11% and 91.52% respectively).

Among frequency characteristics, α and β band powers had the best results. Alpha band power dissociates deep anesthetic class very well. All 3 parameters were in acceptable range for this characteristic: sensitivity: 92%, specificity: 93% and accuracy: 93%. Synch fast slow bispectral characteristic had high specificity in determination of deep anesthesia class (92.7%) and isoelectric status (93.2%). The main parameter used in time-based characteristics was burst suppression response, which had 100% accuracy, sensitivity and specificity in isoelectric class. It showed its significance in differentiating isoelectric class.

Among entropy-based characteristics, Shannon entropy parameter was the only one with 100% accuracy to predict isoelectric class although it was not accurate for other classes.

Spectral entropy scores showed better results, especially in deep anesthesia class (92.72%). Unexpectedly, Renyi entropy showed no better accuracy than spectral entropy, although both were better than Shannon.

In the consciousness class, the approximate entropy parameter had the greatest score (99.02%) followed by the β frequency coefficient with the prediction power of 87.42%. Lempel- Ziv (83.98%), Renyi entropy (81.33%) and β band power (80.17%) characteristics had acceptable results in delineating this class.

In differentiating light anesthesia class, approximate entropy had the best results (accuracy: 98.04%).

Teta (θ) frequency coefficient was also able to dissociate this class from other classes very well (accuracy 96.34%). Followed by these 2 characteristics, β band power showed the best results in light anesthesia class. Teta (θ) band power, Lempel-Ziv and median frequency had acceptable results as well (figure 1-5).

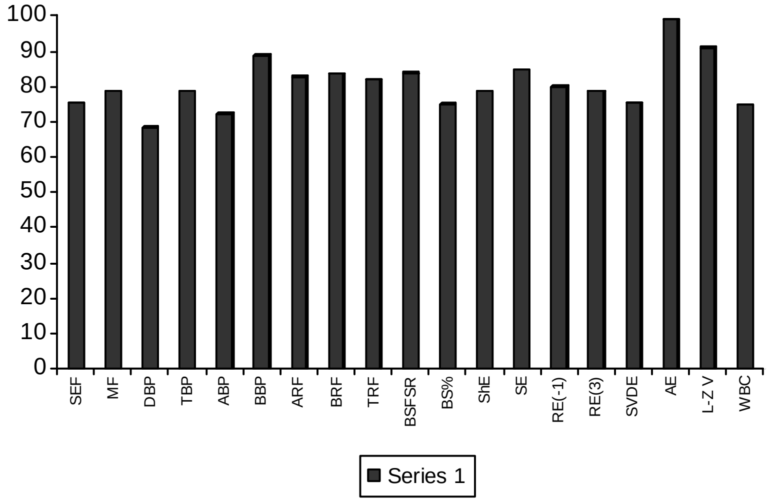

Figure 1. Total accuracy of different EEG characteristics in predicting the depth of anesthesia stages

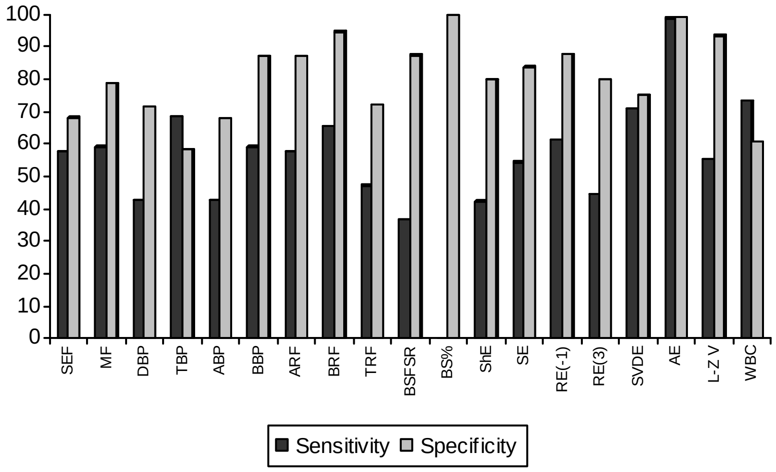

Figure 2. Sensitivity and specificity of different EEG characteristics in predicting the consciousness class

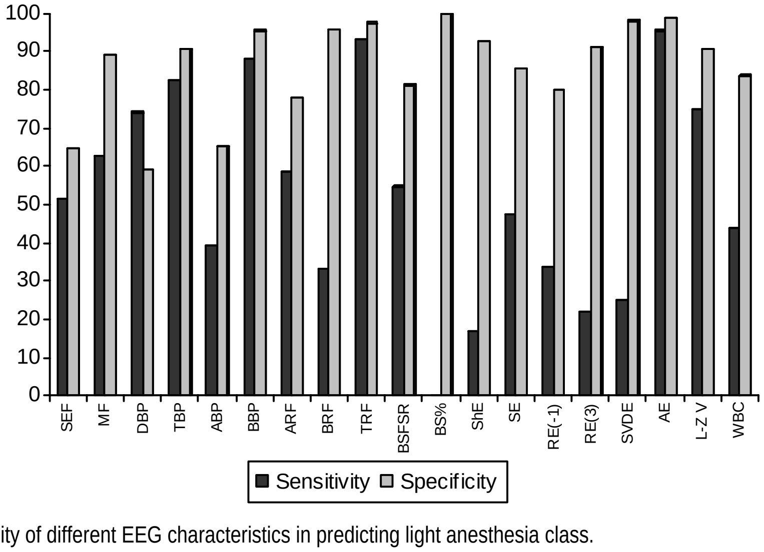

Figure 3. Sensitivity and specificity of different EEG characteristics in predicting light anesthesia class.

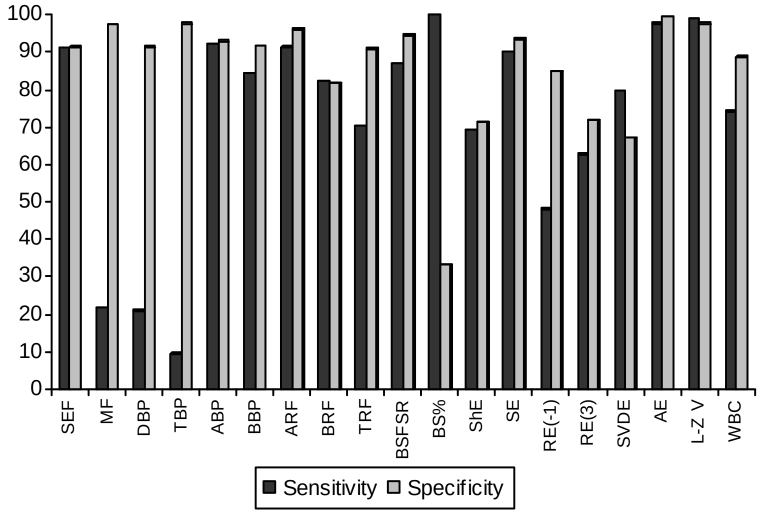

Figure 4. Sensitivity and specificity of different EEG characteristics in predicting deep anesthesia class.

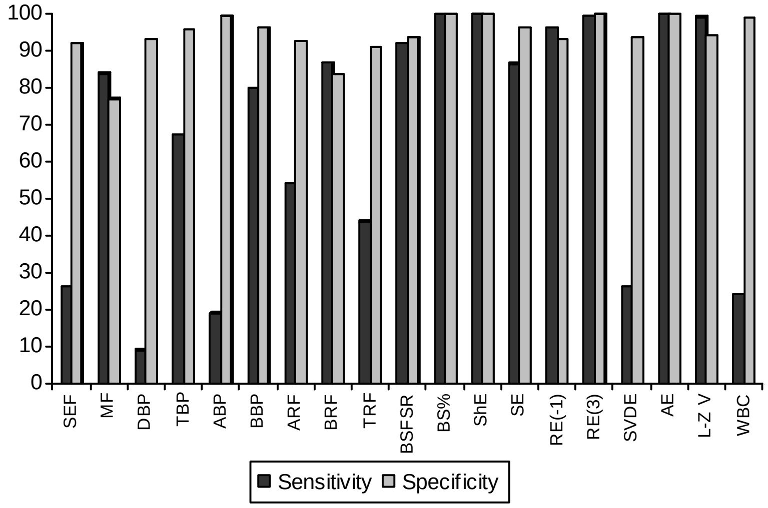

Figure 5. Sensitivity and specificity of different EEG characteristics in predicting the isoelectric class.

Abbreviations of EEG characteristics

SEF:	Spectral Edge Frequency	BS%:	Burst Suppression%
MF:	Median Frequency	ShE:	Shannon Entropy
DBP:	Delta Band Power	SE:	Spectral Entropy
TBP:	Teta Band Power	RE(-1):	Renyi Entropy(-1)
ABP:	Alpha Band Power	RE(3):	Renyi Entropy(3)
BBP:	Beta Band Power	SVDE:	Singular Value Decomposition Entropy
ARF:	Alpha Ratio Frequency	AE:	Approximate Entropy
BRF:	Beta Ratio Frequency	L-Z V:	Lempel-Ziv Entropy
TRF:	Teta Ratio Frequency	WBC:	Wavelet Based Characteristic
BSFSR:	Bispectral Synch Fast Slow Ratio		

DISCUSSION

Spectral edge frequency (SEF) of 95 stands for the frequency below which 95% of the total power of a given signal is located. Some of earlier studies have suggested this characteristic as a marker for regaining consciousness in the recovery room. (7). However, SEF has never been used as a clinical marker in routine practices. In our study, accuracy of SEF 95 was 75.4%.

Schwender and co-workers investigated the significance of spectral power analysis with increasing doses of some anesthetic drugs and they described the frequency characteristic (SEF and relative power of frequency bands) in different doses of drugs as median and standard deviation (6, 7). Kuizenga and co-workers studied EEG signal changes with statistical analysis of frequency characteristics (8). It is shown that by increasing the depth of anesthesia, β band power decreases and θ and Δ band power increase, α band power slightly decreases as well, and by increasing the depth of anesthesia, total power will increase. The frequency band power parameters mentioned above have not yet been of any clinical use (6).

In our study, β band power was better than others (88.4%) and the accuracy related to Δ band power was 68.4%.

Although frequency band power has not been used clinically, frequency index which shows power ratios in frequency bands has many clinical uses for assessing the depth of anesthesia. Among all the instruments for measuring the depth of anesthesia, only CSM and BIS are FDA approved and both use frequency coefficients in their analysis algorithm (5, 6).

In our study, frequency coefficients demonstrated higher accuracy than frequency band powers and β frequency coefficient showed the best results (83.5%).

Bispectral analysis measures the phase relationship between different parts of frequency.

The physiologic meaning of phase relationship has not been determined yet, but in a simple model, it is thought that strong phase relationship is inversely correlated with neural pacemaker compartments. Other advantages include eliminating Gaussian noise sources and increment of signal to noise ratio in EEG signal determination of non linear characteristics which may be important in signal production (9, 10).

To our knowledge, our study is the first in Iran to show the significance of bispectral analysis in determining the depth of anesthesia. Bispectral analysis accuracy in determination of the depth of anesthesia was 83.8% which was higher than that of frequency coefficient based methods.

The highest accuracy of synch fast slow index was in determination and prediction of deep anesthesia and isoelectric signal (92.7% and 93.2% respectively) but its accuracy was low in prediction of consciousness or light anesthesia (74.8% and 74.6% respectively). Time characteristics on EEG signal have not been of much clinical use. The only time characteristic with considerable clinical use in measuring the depth of anesthesia, especially deep anesthesia stage is burst suppression response. Our study revealed that burst suppression had low accuracy in determining the depth of anesthesia (75%) but it's accuracy, sensitivity and specificity in isoelectric phase determination were 100% as were the similar values for relative approximate entropy (accuracy 100%) and Shannon entropy (accuracy 100%) .

Entropy can be an analytic determinant of dynamic EEG signal changes. Neurophysiologic evidences support this idea that entropy indices are markers for optimal brain function. As brain becomes unconscious we will see a decrease in available microstate numbers for neuronal groups; therefore, entropic changes in EEG signal information may show true change in brain function (11, 12).

Although the accuracy of Shannon entropy, spectral entropy , Renyi entropy(-1), Renyi entropy(3), singular value decomposition entropy and wavelet-based characteristic entropy was disappointing, very good results yielded from approximate entropy and Lempel-Ziv entropy (99% and 91%, respectively). Shannon entropy and approximate entropy had accuracy, sensitivity and specificity equal to 100% in isoelectric state. As other studies showed, entropic characteristics provided more complete information than EEG signal (13-15).

As shown in results, most problems arose in prediction of consciousness state and light anesthesia and the most accurate results were obtained in isoelectric state. None of the parameters had acceptable accuracy in predicting the state of consciousness; the best parameter for this goal was approximate entropy which had 98.9% sensitivity, 99.1% specificity and total accuracy of 99%. In isoelectric state we had at least 3 parameters with 100% accuracy (burst suppression response, Shannon entropy and approximate entropy) and at least 5 parameters with more than 90% accuracy [Renyi entropy(-1), Renyi entropy(3), Lempel-Ziv entropy , spectral entropy and synch fast slow] .

The reason may be due to the simplicity of isoelectric analysis by parametric methods in comparison with EEG analysis in a conscious state which is obviously more complex. As the depth of anesthesia decreases, the signal complexity and its analysis difficulty increase. The effectiveness of parameters in deep anesthesia state is higher than in consciousness and lower than isoelectric state. Therefore, more parameters are required to be evaluated in order to obtain better results.

By analyzing the EEG signal parameters, we understood that designing a system for determining the depth of anesthesia is difficult and complex and we should find better parameters for each stage of anesthesia. In our study, the total accuracy of entropy-based characteristics, especially approximate entropy and Lempel-Ziv entropy was more than other parameters. However, suitable choice of parameters can help us in more delicate determination of depth of anesthesia.

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