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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

Introduction: Evaluation of the depth of anesthesia is especially important in good and useful handling of the patient. Clinical assessment of EEG in the operating room is one of the major difficulties in this field.
This study tries to find the most valuable EEG parameters in prediction the depth of anesthesia in different stages.

Material and methods: EEG data of 30 patients with same anesthesia protocol (total intravenous anesthesia) were recorded in all anesthetic stages at the SHOHADA-E- TAJRISH hospital.
Quantitative EEG characteristics were classified into 4 categories: time, frequency, bispectral and entropy based characteristics. Their sensitivity, specificity and accuracy in determination of depth of anesthesia were obtained by comparison with the recorded reference signals in awake, light anesthesia, deep anesthesia and brain death patients.

Result: Time parameters had low accuracy in prediction of the depth of anesthesia determination. The accuracy was 75% for burst suppression response. It was higher for frequency based characteristics which the best results were in spectral power. (Accuracy: 88.9%)
The accuracy was 89.9% for synchronized fast slow bispectral characteristics. The best results were obtained from entropy based characteristics which its accuracy was 99.8%.

Conclusion: Entropy based characteristics analysis have a great value in predicting the depth of anesthesia. Generally, due to the low accuracy of each single parameter in prediction depth of anesthesia, we advise multiple characteristics analysis with more persistence on entropy based characteristic.

INTRODUCTION

Clinical evaluation of intra operative EEG for assessment depth of anesthesia determination is very difficult. Finding some ways for better qualitative classification of recorded EEG is especially important.

Until now, for assessment of depth of anesthesia, several methods according to time, frequency and bispectral characteristics have been proposed. Entropy based characteristics are also used for anesthetic stages classification ([1], [2], [3]) .

For increasing accuracy of depth of anesthesia determination we should find brain waves characteristics which are quite different in different stages of anesthesia.

In other words some characteristics are more common in a special anesthetic stage, which are different in other stages. Therefore, we have to introduce methods which can use EEG characteristics in their useful ranges. One of the factors that should be minded is the possibility of use of these characteristics in the immediate assessment of the depth of anesthesia. We want to calculate drug dose on the basis of a score attributed to a quantitative method we adopt, so we must have the least lag with the present patient status ([4]). In recent years, anesthesiologists have used several monitors to evaluate the depth of anesthesia. These monitors try to quantify electrical cortical activities for determination the depth of anesthesia and we named it as depth of anesthesia index. One of these monitors is BIS, introduced in 1996, BIS monitors yield a dimensionless index from EEG signals, based on Bispectral analyses which is called bispecteral index (BI) ($_2$). In 2004 the Demeter company introduced CSM which shows cortical status index (CSI). These 2 monitors enjoy FDA approval.

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

Clinical studies show that there is a great correlation between CSI and Bis. Also Bis and CSI indices have a good correlation (92%, 93% respectively) to the clinical depth of anesthesia based on standards such as OAAS ($_5$).

EEG signals are results of neuronal electrical activities .Time, frequency, bispectral and high level spectrums are characteristics which are used for EEG signal analysis. Entropic methods are used for EEG signals too ($_6$, $_7$).

In this study we tried to consider EEG signal derived parameters and choose the best characteristic for several anesthesia stages' differentiation. We tried to calculate each characteristic's significance in prediction of the depth of anesthesia separately and individually. Based on this data it would be possible to analyze multiple characteristics to acquire the best index in future studies. One of the advantageous of our study is considering the significance of each characteristic in each 4 stages of anesthesia separately and also its overall accuracy. Another advantage of this is a prospective design, similar anesthetic protocols in all patients and it is the first time that such are important subject is studying in Iran.

MATERIAL AND METHODS

In this study general physiological and anesthetic data of 30 patients plus EEG brain waves, 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 were recorded. Other general information such as age, sex, and weight, the type of surgical operation, date, time and duration of surgery were also recorded. Patients EEG waves were recorded by CSM (Danmeter, Denmark). The CSM 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 a nerve stimulator (Xavant) and hemodynamic parameters with pulse oximeter and non invasive blood pressure monitoring. These patients had no medications before surgery. After coming to operating room they received their premed drugs containing 0.03 mg\kg midazolam and 2 ug\kg fentanil. For induction of anesthesia we injected thiopental, 4 mg\kg at first, then 1 mg\kg at intubation time. The Muscle relaxant drug was cisatracorium. In this study for maintenance, we used propofol 75-100 ug\kg\min and N2O\O2 (as 50% ratio). If the CSI were more than 60 during anesthesia, we used thiopental, 0.5 mg\kg or bolus injection of propofol. Muscle relaxation degree was calculated with a nerve stimulator and if TOF was more than one response, cisatracorium was injected. Every one hour 0.5ug\kg fentanyl gave to patients. EEG was done by CSM and with 100 Hz frequency. The EEG was recorded with 3 superficial electrodes on Fpz position (positive in the middle of forehead), Ts (negative on left mastoid) and reference electrode on F(P1) (left frontal). For differentiating different stages of anesthesia we described 4 classes of anesthesia: awakeness, light anesthesia, deep anesthesia and isoelectric. We recorded 15 minutes for each class, overall 60 minutes. Awakeness class reference data, included 15 minutes EEG recorded from 3 healthy awake people (5 minutes each). For omitting blinking artifacts we advised them to close their eyes and concentrate on a special subject. Light anesthesia stage is defined from the time of initial drug injection to intubation and from the discontinuation of drugs until full awakeness of patients based on anesthesiologist assessment. EEG of 14 different patients anesthetized with the above protocols are gathered together to have a 15 minutes reference signal for this class.

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

RESULTS

Our patients included 10 women and 20 men, with the age range 15-75 yrs old (mean 44.36, SD: 19.93), weight range 50-96 kg (mean 68.64, SD: 12.99).

95% spectral edge frequency had the highest association power in predicting deep anesthetic status in comparison with others (accuracy: 91.42%). Sensitivity and specificity is also high with this characteristic (91.11%, 91.52% respectively).

Among frequency characteristics which band power; and band power had the best results. band power dissociates deep anesthetic class very well. All 3 parameters are acceptable. Sensitivity: 92%, specificity: 93%, accuracy: 93%. Synch fast slow bispectral characteristic has great specificity in determination of deep anesthesia class (92.7%) and isoelectric status (93.2%). The main parameter which is used in time based characteristics is burst suppression response, which has 100% accuracy, sensitivity and specificity in isoelectric class. It shows its significance in differentiating isoelectric class.

Among entropy based characteristics the Shannon entropy parameter is the only one which has 100% accuracy to predict the isoelectric class although it is not accurate in other classes.

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

In the awake class approximate entropy parameter had the greatest scores (99.02%). After this characteristic, the frequency coefficient had more prediction power in this class (87.42%). Lempel- Ziv (83.98%), Renyi entropy (81.33%) and band power (80.17%) characteristics had acceptable results in delineating of this class.

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

 frequency coefficient was also able to dissociate this class from other classes very well (accuracy 96.34%). After these 2 characteristic, band power had the best results in light anesthesia class. Band power, Lempel-Ziv and median frequency had acceptable results too.

Figure 1

Sheet 1: Patients` general information

	Sex	Age	Wt	Type of Surgery
1	M	70	60	Prostatectomy
2	M	39	80	Vasovasestomy
3	F	74	80	Hernia
4	M	67	70	Umbelical Hernia
5	M	16	50	Hernia
6	M	31	75	Unilateral Varicoselectomy
7	M	45	70	Unilateral Varicoselectomy
8	M	34	50	B.K(LL)Amputation
9	M	50	64	Hernia
10	M	22	76	Z Plasty
11	F	46	68	Bladder Herniation
12	F	65	61	Bladder Herniation
13	M	66	58	TURT
14	F	23	96	Hernia
15	F	15	50	TOS
16	F	32	90	TL
17	M	40	60	Hernia
18	F	30	51	Hernia
19	M	75	70	TURP
20	M	69	81	TU
21	M	22	70	Thyroidectomy
22	M	45	80	TUL
23	M	35	74	Hernia
24	F	45	63	TOS
25	M	65	75	Amputation
26	M	64	76	Gastrectomy
27	M	35	80	Hernia
28	F	29	65	TL
29	F	50	74	Bladder Herniation
30	M	43	82	Thyroidectomy

Figure 2

Sheet 2: EEG characteristics abbreviation

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

Figure 3

Diagram 1: Total accuracy of different EEG characteristics in predicting depth of anesthesia stages.

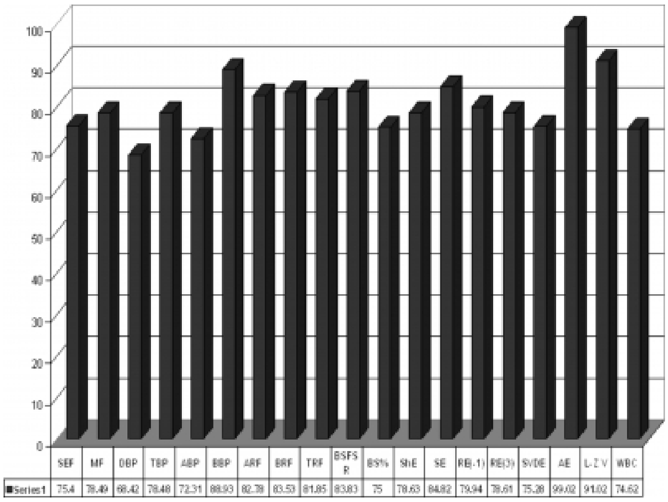


Figure 4

Diagram 2 : Sensitivity and specificity of different EEG characteristics in predicting awakeness class.

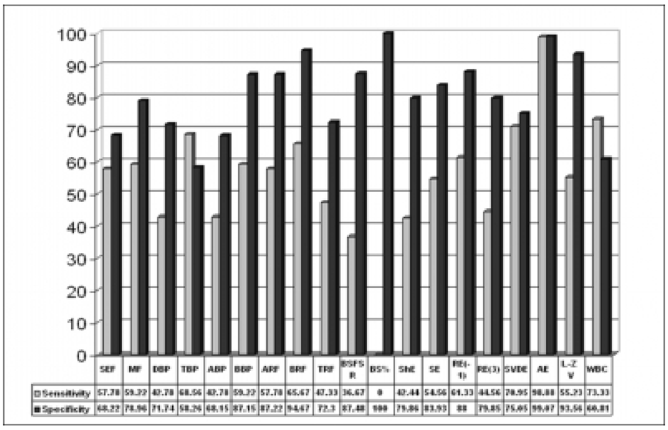


Figure 5

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

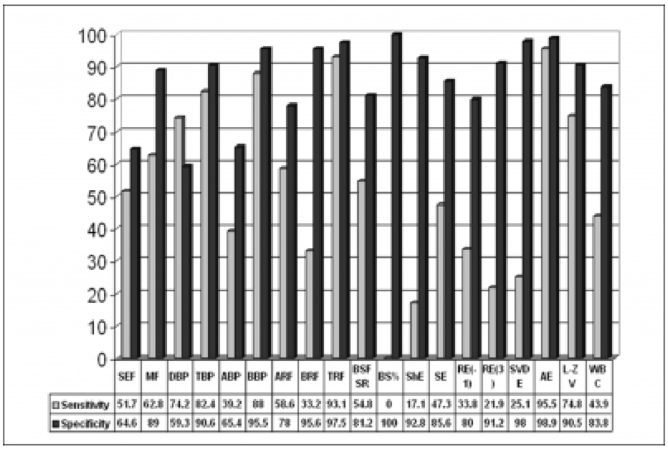


Figure 6

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

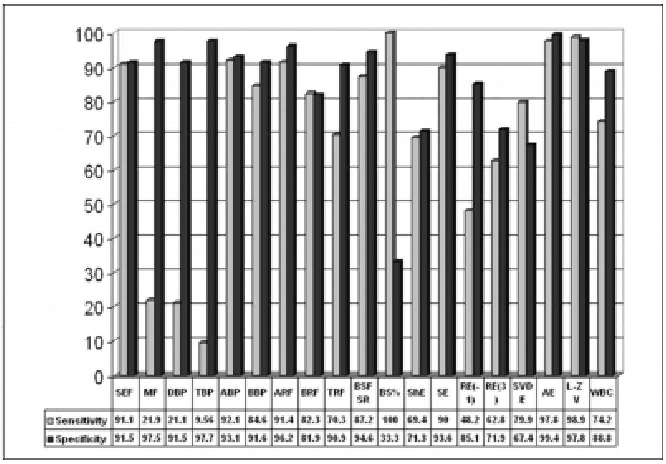
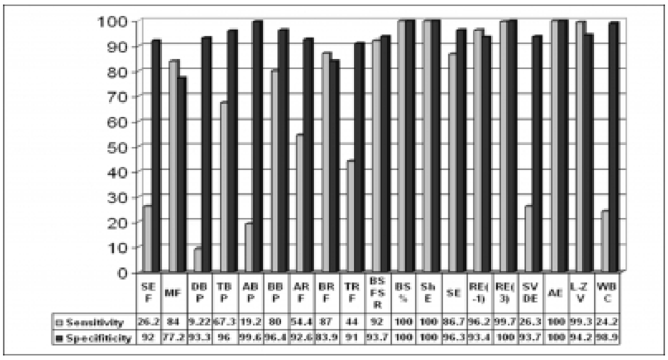


Figure 7

Diagram 5: Sensitivity and specificity of different EEG characteristics in predicting isoelectric class.



DISCUSSION

Spectral edge frequency (SEF) 95 is the frequency that 95% of EEG power located below this frequency. Some of earlier studies suggest this characteristic as a marker for awakeness of anesthesia in recovery room. ([7]). Although SEF never used as a clinical marker in routine works. In our study, accuracy of SEF 95 was 75.4%. Dchwender and co-workers investigated the significance of spectral power analysis with increasing doses of some anesthetic drugs and they described 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 considered EEG signal changes with statistical analysis of frequency characteristics. ([8]) It is shown that by increasing depth of anesthesia, □ band power decreases and □ and □ band power increase , □ band power decreases slightly too ,and by increasing the depth of anesthesia , total power will increase. The frequency band power parameters mentioned above, have not been of any clinical use yet ([6]).

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

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

In our study, frequency coefficients had better accuracy than frequency band powers and □ frequency coefficient had the best results (83.5%).

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

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

Our study is the first study in Iran which tries to show the significance of bispectral analysis in depth of anesthesia determination. Bispectral analysis accuracy in determination the depth of anesthesia was 83.8%, which was more accurate than frequency coefficient based methods.

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

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

In our study we used Shannon entropy, spectral entropy, Renyi entropy (-1), Renyi entropy (3), singular value decomposiopn entropy, approximate entropy, Lempel-Ziv entropy, wavelet based characteristic entropy.

Although accuracy of Shannon entropy , spectral entropy , Renyi entropy(-1), Renyi entropy(3), singular value decomposiopn entropy, wavelet based characteristic entropy were disappointing but very good results yielded from approximate entropy , Lempel-Ziv entropy (99% and 91% respectively). Shannon entropy and approximate entropy have accuracy, sensitivity and specificity equal to 100% in isoelectric state. As the other studies showed, entropic characteristics have more complete information of EEG signal ([13], [14], [15]).

As shown in results chart the most problems arise in prediction of awakeness and light anesthesia and the most accurate results are in isoelectric state. None of parameters had acceptable accuracy in predicting the awake state; 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, approximate entropy) and at least 5 parameters with more than 90% accuracy [Renyi entropy(-1), Renyi entropy(3), Lempel-Ziv entropy , spectral entropy , synch fast slow] .

The reason may be the simplicity of isoelectric analysis by parametric methods in comparison with awakeness EEG analysis which obvious is more complex. As the depth of anesthesia decreases, the signal complexity and its analytic difficulty increases. The effectiveness of parameters in deep anesthesia state is better than awakeness and lower than isoelectric. So we need more parameters for getting best results.

CONCLUSION

With analysis of EEG signal parameter we understand that designing a predicating system for determining the depth of anesthesia is difficult and complex and we should find better parameters for any stage of anesthesia. In our study total accuracy in entropy based characteristic, especially approximate entropy and Lempel-Ziv entropy were better than other parameters but suitable choice of parameters can help us in more delicate determination of the depth of anesthesia.

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