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Research Article

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Combination of Entropy and Electroencephalograpy for Deep of Hypnosis Monitoring Improvement during General Anesthesia

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Abstract

Background: Deep of hypnosis monitoring based on electroencephalogram (EEG) and end tidal anesthetic concentration (ETAC) of volatile agents are a standard of care in patients under general anesthesia. Entropy and ETAC could reflected the effects of volatile agents as evidence had been showed, but its accuracy for hypnosis monitoring during nociceptive stimulation in patients under neuromuscular block and emergence is controversial.

Methods: Prospective, single-group, double-blinded and observational study was conducted in young female patients scheduled for minor gynecological surgery under general anesthesia. A standard protocol was administered to all patients and deep of hypnosis monitoring using entropy and quantitative EEG (qEEG) was blind to anesthesiologist in charge. Primary outcomes were described changes and discrimination capacity of hypnosis depth of entropy, qEEG and ETAC from induction to emergence. Secondary outcome was described an equation of hypnosis state prediction using entropy, qEEG and ETAC based on its discrimination capacity of hypnosis depth.

Results: 42 patients scheduled for minor gynecological surgery under general anesthesia were included. Combination of frontal electromyogram (fEMG), Response Entropy (RE), delta and theta activities showed an excellent prediction capacity of hypnosis state. Entropy and fEMG showed an excellent discrimination capacity of hypnosis depth from induction to emergence. Delta activity showed a good discrimination capacity of hypnosis state during emergence. Electroencephalogram amplitude during maintenance and median Frequency (MF) during emergence showed an acceptable discrimination capacity of hypnosis depth. Beta/Delta ratio (B/D) during induction and emergence showed an acceptable discrimination capacity of hypnosis depth. During maintenance Burst Suppression corrected for Spectral Edge Frequency ratio (BcSEF) and Beta/Theta ratio (B/T) showed an acceptable discrimination capacity of hypnosis depth. ETAC showed a good discrimination capacity from laryngoscopy to emergence. ETAC variability was poorly explained for entropy. Entropy variability was poorly explained for ETAC and EEG variables.

Conclusions: Our study described an equation for hypnosis state prediction combining fast, intermediate and slow activity. An interesting finding of the present study was that delta activity, MF, amplitude and corrected variables probably reflecting the balance between slow and fast activity could improve deep of hypnosis monitoring, but limitations related to little size and design of this study warrants further validation.

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Introduction

Deep of hypnosis monitoring is a currently recommended standard of care during general anesthesia according to guidelines [1] as an indication of anesthetic drugs effects on brain electrical activity registered for processed electroencephalographic monitors like Bispectral Index (BIS) and entropy. Although end tidal anesthetic concentration (ETAC) could indicate drug concentration in blood and brain [1], previous studies showed that entropy monitoring also reflected effects of sevoflurane (2) and reduces its uptake [3]. Nevertheless, alert state after emergence of general anesthesia is a main challenge for deep of hypnosis monitors because this brain reactivation probably come from subcortical structures [4] not registered for electroencephalographic monitors. Entropy monitor (GE Healthcare®, Helsinki, Finland) analyses space and temporal integration of brain neuronal activity registered for frontal electroencephalogram (EEG) [2,4]. State entropy (SE) and Response Entropy (RE) gives complementary information for deep of hypnosis monitoring [2,4-9]. SE showed dominant band of EEG spectrum, reflecting mainly cortical brain electrical activity [4,5,7,8,10-15] using a time window between 60 to 16 seconds obtaining values from 0 (deep hypnosis state) to 91 (awake state) [8,11,13,14,16,17]. RE showed higher frequency bands including those of frontal electromyogram (fEMG) [4,5,7,8,9,10-13], with a time window between 15 to 1.92 seconds, obtaining values from 0 to 100 [8,11,13,14,16,17]. Entropy correctly reflected all general anesthesia phases according to evidence [4]. RE has advantages for monitoring induction and emergence [11,18], with benefits for potentially reducing time to alert state [2,19,20]. Classic intraoperative awareness associated with increase of higher amplitude bands of fEMG could be faster monitored for RE compared to SE and BIS [18]. A lack of strong evidence related to entropy performance for time to awakening and recall of intraoperative awareness make necessary more powerful studies [21].

Important changes of hypnosis depth during general anesthesia mainly related to imbalance between surgical stimulation and hypnosis drugs concentration probably required a combined approach for accurately monitoring and reducing complications associated to slight or deep anesthesia probably related with higher mortality and costs. Quantitative electroencephalogram (qEEG) and entropy classically showed changes associated to general anesthesia [18, 22]. Corrected electroencephalographic variables reflecting balance between fast and slow activity could have advantages for deep of hypnosis monitoring. This study aims to describe a prediction equation of hypnosis state combining entropy and qEEG variables for deep of hypnosis monitoring improvement during general volatile anesthesia with sevoflurane.

Methods

Study design and population

This prospective, single group, double blind and observational study was conducted in Anesthesia and Critical Care Department of Cruces University Hospital between 2019 and 2020. Female patients between 18 to 60 years, ASA I and II scheduled for minor gynecology surgery after informed consent sign were included (Table 1). Patients with neurological disease, substance abuse history, obesity, negative decision to participate in study or simultaneously participating in another study were excluded. (Table 1). Ethical Committee of Clinical Investigation acceptance was obtained before inclusion of patients.

Anesthesia protocol

A standard monitoring with Non-Invasive Blood Pressure, electrocardiogram and peripheral pulse oximeter (Sp02) was placed when patient arrived at operating room. Pre-oxygenation with 100% of oxygen until reaching an exhaled fraction of oxygen close to 90% and standard intravenous induction with 1 mg of midazolam, 3 ug/Kg of fentanyl, 2 mg/Kg of propofol and 0.15 mg/Kg of cisatracurium was performed in all patients. Then, ventilation with face mask for 180 seconds and orotracheal intubation was made. If difficulties, ventilation with face mask was restarted and a new attempt of intubation was made in 60 seconds. Mechanical ventilation with mixture of air and oxygen for a fraction of inspired oxygen (Fi02) of 50%, tidal volume of 6 ml/Kg, positive end-expiratory pressure (PEEP) between 4 to 6 cm of H_20 and respiratory rate between 10 to 12 breaths per minute was made with adjustments based on anesthesiologist decision. Sevoflurane at 2% was used for anesthesia maintenance with a constant Minimum Alveolar Concentration (MAC) between 0.7 to 1.2 and ETAC was monitored. Additional doses of fentanyl were administered based on anesthesiologist decision. Intravenous analgesia with 50 mg of dexketoprofen or 2 g of metamizole and 1 g of paracetamol prior to emergence and prophylaxis of postoperative nausea and vomiting (PONV) with ondansetron 4 mg intravenous was administered.

Table 1: Inclusion and Exclusion criteria

Inclusion criteria	Female patients Age between 18 and 60 years ASA I and II. Scheduled minor gynecological surgery Signed informed consent
Exclusion criteria	Neurological disease History of substance abuse Obesity (BMI greater than 28) Patient refusal to participate in study Simultaneous participation in another study

BMI: Body Mass Index

Deep of hypnosis monitoring

Deep of hypnosis monitoring using entropy and qEEG was placed for study team and anesthesiologist in charge of operating room was blinded to it. Entropy, qEEG and ETAC were observed before induction throughout surgery and after emergence. Entropy sensor (GE Healthcare®, Datex-Ohmeda Division, Instrumentarium Corp, Helsinki, Finland) was placed over skin of frontal area cleaned with 70% alcohol according to manufacturer recommendations with the first, second and third electrodes on frontal, orbicular and temporal muscles, respectively. Impedance of electrodes with skin was found to be less than 7.5 kΩ. Values of SE and RE were calculated for M-ENTROPY® module of Datex-Ohmeda S/5 anesthesia monitor (GE Healthcare®, Datex-Ohmeda Division, Instrumentarium Corp, Helsinki, Finland) using a scale from 0 to 91 for SE and 0 to 100 for RE. qEEG surface electrodes (Zipprep, Aspect Medical Systems Inc, Norwood, Massachusetts) were placed over skin of frontal area cleaned with 70% alcohol in position Fp1, Fp2, F7, F8 and Fz according to international system 10/20. Impedance of electrodes with skin was less than 10 kΩ. Spectral analysis of qEEG including Spectral Edge Frequency (SEF), Medium frequency (MF), amplitude, Burst Suppression Rate (BSR), relative powers α, β ,δ, θ and fEMG was performed for M-EEG® module of Datex-Ohmeda S/5 anesthesia monitor (GE Healthcare®, Datex Ohmeda Division, Instrumentarium Corp,Helsinki, Finland). A frequency range between 0.5 to 30 Hz was used for qEEG and 60 to 300 Hz for fEMG.

Variables

Baseline variables were age, Heart Rate (HR), Systolic Blood Pressure (SBP), Sp02 and temperature. Intraoperative variables were HR, SBP, ETAC, SE, RE, SEF, MF, BSR, amplitude, fEMG and α, β, δ, θ activity.

SEF corrected for BSR (BcSEF), Beta/Theta (B/T) and Beta/Delta (B/D) ratios were corrected EEG variables calculated using follow equations:

Spectral Edge Frequency corrected for Burst Suppression Rate (BcSEF)

BcSEF= SEF95 x (1- BSR /100)

Beta/Theta ratio (B/T)

B/T= % beta band / % theta band

Beta/Delta ratio (B/D)

B/D= % beta band / % delta band

In time 0 (T0) patient was awake, time 1 (T1) was induction of anesthesia, time 2 (T2) was nociceptive stimulation of laryngoscopy, time 3 to 6 (T3-6) was maintenance and time 7 to 8 (T7-8) was emergence.

Clinical variables were awake defined as patient responds to verbal command or sleep when patient does not respond to verbal commands or nociceptive stimulus (jaw pull) in each anesthesia times of induction, laryngoscopy, maintenance and emergence.

Outcomes

Primary outcomes were described changes and discrimination capacity of hypnosis depth of entropy, qEEG and ETAC in each study times. Correlation between entropy, qEEG, ETAC and hemodynamic variables (HR and SBP) and regression analysis to explained variability of ETAC and entropy were another primary endpoints.

Secondary outcome was described an equation of hypnosis state prediction using entropy and qEEG based on its discrimination capacity of hypnosis depth.

Statistical analysis

All baseline and intraoperative variables were stored using Datex-Ohmeda S/5 Collect software (Datex-Ohmeda Division, Instrumentarium Corp,Helsinki, Finland) for offline analysis. Statistical analysis was performed using SPSS 19 software (IBM® SPSS Chicago IL). Sample size was calculated based on previously published data of likelihood of entropy, qEEG variables and ETAC to correctly discriminate hypnosis depth [23,24]. Kolmogorov Smirnov test was used to determine normality of distributions. Mean, median, standard deviation (SD) and interquartile ranges (IQR) of variables were calculated in each study times.

Comparisons of means was performed using t test for normal distributed variables and Wilcoxon test for non-normal distributed variables to determine differences between study times with p value of 5%. Receiver Operating Characteristics (ROC) curves showed discrimination capacity of entropy, qEEG variables and ETAC to monitoring deep of hypnosis in each study times using Wilcoxon or Mann Whitney tests; values higher than 0.7 were considered acceptable and rounding 1 a perfect discrimination capacity. A linear correlation was performed to determine the strength of association between entropy, qEEG, ETAC and hemodynamic variables (HR and SBP) using Rho Spearman test and considering a strong correlation if values rounding + 1 and -1. Linear regression analysis determined capacity of entropy to explained ETAC variability or ETAC and qEEG variables to explained entropy variability.

A logistic regression analysis was performed for described an equation of depth of hypnosis prediction using entropy and qEEG variables. Validity of the model was tested with -2log plausibility, R square of Cox and Snell and R square of Nagelkerke. The overall fit of the model was checked with the Hosmer Lemeshow test.

Results and Discussion

Baseline variables

42 patients were included in this study. Baseline variables were mean SBP of 140 mmHg, HR of 95 bpm and temperature of 36 ºC (Table 2)

Table 2: Baseline variables

AGE (years) Mean (SD)	39 (8)
SYSTOLIC BLOOD PRESSURE (mmHg) Mean (SD)	139.7 (13.2)
HEART RATE (bpm) Mean (SD)	94.76 (1.6)
$Sp0_2$ (%) Mean (SD)	99 (0.47)
TEMPERATURE (ºC) Mean (SD)	36 (0.19)

Comparison of Means

Comparison of means of SBP, HR, ETAC, entropy, qEEG and corrected variables from induction to emergence of general anesthesia were made (Table 3, figures 1 to 16 supplemental content)

Discrimination Capacity

Discrimination capacity of SBP, HR, ETAC, entropy, qEEG and corrected variables from induction to emergence of general anesthesia was observed (Table 4, Figures 1 to 12).

Correlation

Correlations of entropy, SBP, HR, ETAC, qEEG and corrected variables from induction to emergence of general anesthesia were observed (Table 5, figures 13 to 17)

Table 3: Comparison of means of Systolic Blood Pressure, Heart Rate, End Tidal Anesthetic Concentration, Entropy, Quantitative Electroencephalographic and Corrected Variables from induction to emergence of anesthesia

Variable	Induction	Laryngoscopy	Maintenance	Emergence
SYSTOLIC BLOOD PRESSURE (SBP) (95% CI)	↓10,082 (3,953 – 16,210 **p 0.002**	↑-20,975 (-27,618 – -14,332) **p 0.000**	↓22,620 (18,563 – 26,678) **p 0.000**	↑-8,201 (-12,508 – -3,895) **p 0.000**
HEART RATE (HR) (95% CI)	≈ -7,143 (-11,662 – -2,623) **p 0.002**	↑-6,725 (-11,152 – -2,299) **p 0.003**	↓7,855 (4,632 – 11,078) **p 0.000**	↑-5,288 (-8,532 – -2,044) **p 0.000**
END TIDAL ANESTHETIC CONCENTRATION (ETAC) (95% CI)	↑-0,055 (-0,095 – -0,015) **p 0.008**	↑-0,938 (-1,013 – -0,862) **p 0.000**	↓0,109 (-0,023 – 0,240) p 0.104	↓0,439 (0,342 – 0,536) **p 0.000**
STATE ENTROPY (SE) (95% CI)	↓61,976 (59,150 – 64,802) **p 0.000**	↑-26,961 (-30,572 – -23,349) **p 0.000**	↑ -5,565(-7,927 – -3,204) **p 0.000**	↑-21,511 (-23,876 – -19,146) **p 0.000**
RESPONSE ENTROPY (RE) (95% CI)	↓69,968 (67,131 – 72,806) **p 0.000**	↑-27,748(-31,638 – -23,858) **p 0.000**	↑-7,203 (-10,019 – -4,386) **p 0.000**	↑-27,204 (-30,113 – -24,296) **p 0.000**
FRONTAL ELECTROMYOGRAM (fEMG) (95% CI)	↓3,609 (2,883 – 4,334) **p 0.000**	↑-0,125 (-0,651 – 0,401) p 0.639	↓ -0,048 (-0,154 – 0,058) p 0.368	↑-1,840(-2,452 – -1,228) **p0.000**
AMPLITUDE (95% CI)	↑ -11,930 (-15,636 – -8,223) **p 0.000**	↓7,115(3,944 – 10,286) **p 0.000**	↓ 4,261 (2,747 – 5,774) **p 0.000**	↓5,045 (2,628 – 7,463) **p0.000**
ALPHA POWER (95% CI)	↓4,139 (1,455 – 6,823) **p 0.003**	↑-6,591 (-8,464 – -4,718) **p 0.000**	↑-8,976 (-11,345 – -6,607) **p 0.000**	↓8,672 (5,434 – 11,910) **p0.000**
BETA POWER (95% CI)	↓4,806 (2,852 – 6,759) **p 0.000**	↑-3,035 (-4,402 – -1,667) **p 0.000**	↓-0,371 (-1,160 – 0,418) p 0.354	↑-2,824 (-5,466 – -0,183) **p 0.036**

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DELTA POWER (95% CI)	↑-12,287 (-17,174 – -7,400) **p 0.000**	↓15,957 (12,050 – 19,863) **p 0.000**	↓12,702 (9,300 – 16,103) **p 0.000**	↑-9,916 (-14,876 – 4,956) **p 0.000**
THETA POWER (95% CI)	↓3,361 (1,716 – 5,006) **p 0.000**	↑-6,357 (-8,082 – -4,631) **p 0.000**	↑-3,298 (-4,579 – -2,017) **p 0.000**	↓4,053 (2,336 – 5,771) **p 0.000**
SPECTRAL EDGE FREQUENCY (SEF) (95% CI)	↓4,806 (3,234 – 6,377) **p 0.000**	↑-5,052 (-6,122 – -3,983) **p 0.000**	↑-0,895 (-1,460 – -0,330) **p 0.002**	↑-1,382 (-2,301 – -0,462) **p0.004**
MEDIAN FREQUENCY (MF) (95% CI)	↓0,389 (-0,168 – 0,946) p 0.169	↑-0,626 (-1,089 – -0,163) **p 0.008**	↑-1,226 (-1,650 – -0,802) **p 0.000**	↓1,214 (0,383 – 2,044) **p 0.005**
SPECTRAL EDGE FREQUENCY CORRECTED FOR SUPPRESSION RATE (BcSEF) (95% CI)	↓1,808 (0,813 – 2,803) **p 0.000**	↑-3,341 (-4,139 – -2,542) **p 0.000**	↓1,516 (0,519 – 2,514) **p 0.003**	↓3,665 (2,712 – 4,618) **p 0.000**
BETA /THETA RATIO (B/T) (95% CI)	↓0,717 (0,093 – 1,342) **p 0.025**	↑-0,145 (-0,362 –0,072) p 0.187	↑-0,145 (-0,314 – 0,024) p 0.092	↑-1,885 (-3,267 –-0,502) **p 0.008**
BETA/DELTA RATIO (B/D) (95% CI)	≈ 0,019 (-0,040 – 0,077) p 0.530	↑0,000 (-0,049 – 0,049) p 1.000	≈-0,016 (-0,055 – 0,023) p 0.416	↓0,183 (-0,071 – 0,438) p 0,157

Table 4: Discrimination capacity of Systolic Blood Pressure, Heart Rate, End tidal of Anesthetic Concentration, Entropy, Quantitative Electroencephalographic and Corrected Variables from induction to emergence of anesthesia

	INDUCTION	LARYNGOSCOPY	MAINTENANCE	EMERGENCE
SYSTOLIC BLOOD PRESSURE (SBP)	**0,757±0.06**	0,58±0.07	0,457±0.07	0,635±0.07
HEART RATE (HR)	0,515±0,062	0,554±0,066	0,540±0,062	0,603±0,058
END TIDAL ANESTHESIC CONCENTRATION (ETAC)	0,52±0,07	**0,982±0,02**	**1**	**0,884±0,04**
STATE ENTROPY (SE)	**0,997±0,002**	**0,959±0,022**	**0,998±0,022**	**0,844±0,046**
RESPONSE ENTROPY (RE)	**0,999±0,002**	**0,985±0,01**	**1**	**0,862±0,044**
FRONTAL ELECTROMYOGRAM (fEMG)	**0,933±0,04**	**0,941±0.032**	**0,977±0,02**	**0,756±0,06**
AMPLITUDE	**0,829±0,052**	**0,739±0,068**	**0,781±0,06**	0,644±0,072
BETA POWER	0,694±0,062	0,527±0,066	0,557±0,064	0,696±0,062
THETA POWER	0,630±0,066	0,654±0,062	**0,709±0,056**	0,616±0,064
DELTA POWER	0,630±0,064	0,667±0,058	0,696±0,056	**0,808±0,048**
SPECTRAL EDGE FREQUENCY (SEF)	0,695±0,062	0,528±0,066	0,544±0,066	0,635±0,064
MEDIAN FREQUENCY (MF)	0,514±0,068	0,645±0,062	0,7±0,056	**0,759±0,048**
SPECTRAL EDGE FREQUENCY CORRECTED FOR SUPPRESSION RATE (BcSEF)	0,563±0,066	0,563±0,033	**0,766±0,027**	0,509±0,07
BETA/THETA RATIO (B/T)	0,648±0,068	0,589±0,068	**0,711±0,062**	0,579±0,06
BETA/DELTA RATIO (B/D)	**0,711±0,062**	0,537±0,066	0,524±0,058	**0,713±0,064**

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Combined analysis of entropy, qEEG, corrected variables, ETAC and hemodynamic variables

Induction

SE and RE decreasing showed an excellent discrimination capacity of hypnosis state and acceptable correlation with beta waves (Table 3, 4 and 5, Figure 1, 2 and 13A). fEMG decreasing showed an excellent discrimination capacity of hypnosis state without significant correlation with qEEG (Table 3, 4 and 5, Figure 1). qEEG showed a decrease of rapid and medium activity along with a slow waves increased leading to a higher amplitude and decrease of SEF (Table 3), but discrimination capacity was excellent only for amplitude (Table 4, Figure 2 and 3). Fast, medium and slow waves showed a good correlation between them and with SEF (Table 5, Figure 13 C,D,E and F), but correlations with MF was weak (Figure 13 B). BcSEF and B/T significantly decreased but only B/D showed an acceptable capacity for hypnosis depth discrimination (Table 3 and 4). BcSEF showed a good correlation with fast, medium and slow waves (Table 5). ETAC significantly increases but not showed an adequate capacity to hypnosis state prediction nor correlated with qEEG or corrected variables (Table 3,4 and 5). SBP significantly decrease and showing an acceptable discrimination of hypnosis depth but not correlating with entropy, qEEG, corrected variables and ETAC (Table 3, 4 and 5, Figure 1). HR not changed and showing a poor discrimination capacity not correlating with entropy, qEEG, corrected variables and ETAC (Table 3, 4 and 5, Figure 1).

Laryngoscopy

SE and RE increasing showed excellent discrimination capacity of hypnosis depth and a higher correlation with beta activity and SEF (Table 3, 4 and 5. Figure 4, 5, 14A and B). fEMG not significantly changed but showed excellent capacity for deep of hypnosis monitoring without significant correlation with entropy and qEEG (Table 3, 4 and 5, Figure 4). Alpha, beta, theta, SEF and MF increasing with a decrease of delta and less amplitude of qEEG was seen during this phase (Table 3), but discrimination capacity of hypnosis state was only acceptable for amplitude (Table 4, Figure 5 and 6). A good correlation between delta with beta, alpha and theta was seen (Table 5). Beta, alpha and delta had a good correlation with SEF and MF, but theta only showed acceptable correlation with MF (Table 5). BcSEF significantly increases only presenting acceptable correlation with alpha activity (Table 3 and 5) with a poor discrimination capacity of hypnosis depth (Table 4). ETAC significantly increases showing an excellent capacity for hypnosis state discrimination without correlating with entropy, qEEG and corrected variables (Table 3, 4 and 5). SBP and HR significantly increases but showed a poor discrimination of hypnosis depth not correlating with entropy, qEEG, corrected variables and ETAC (Table 3, 4 and 5, Figure 4).

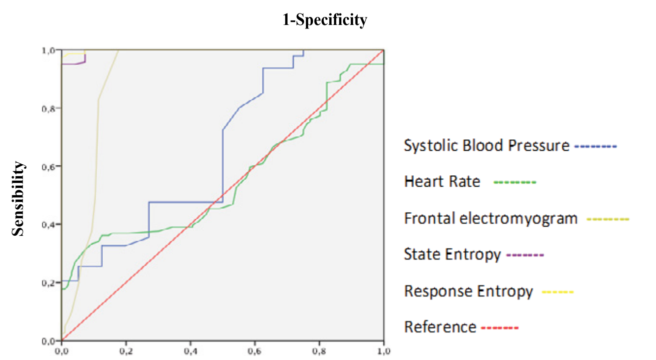

Figure 1: ROC curves of Systolic Blood Pressure, Heart Rate, Frontal Electromyogram and Entropy during induction.

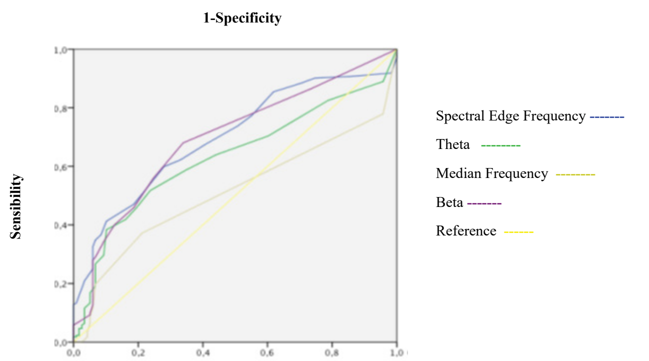

Figure 3: ROC curves of Electroencephalogram variables during induction

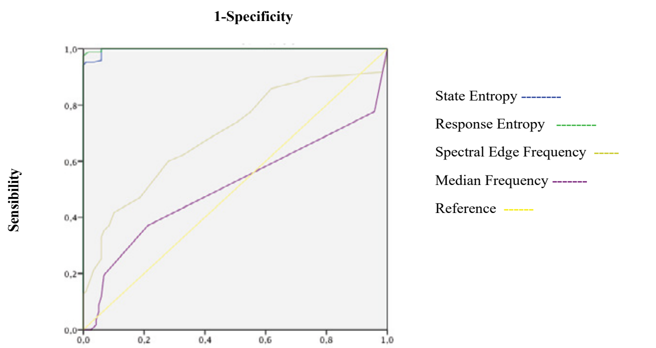

Figure 2: ROC curves of Entropy and Electroencephalogram variables during induction

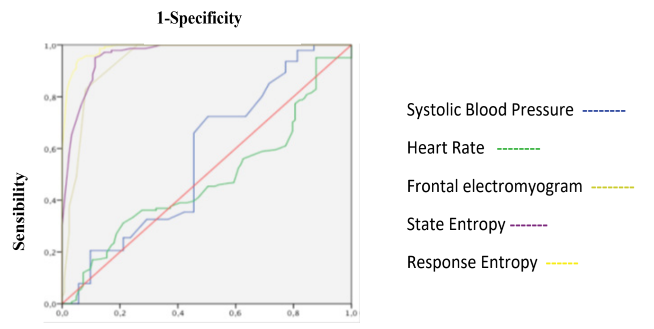

Figure 4: ROC curves of Systolic Blood Pressure, Heart Rate, Frontal Electromyogram and Entropy during laryngoscopy.

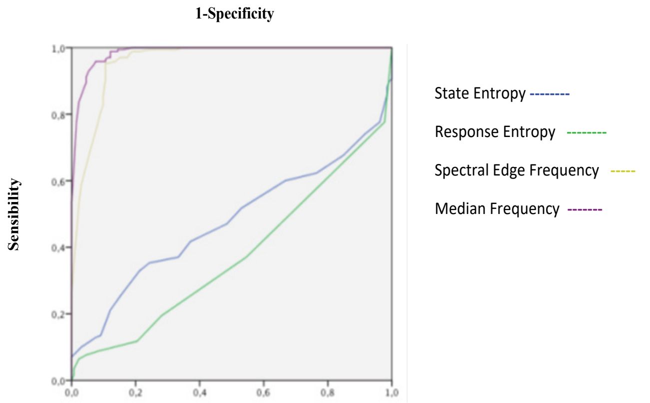

Figure 5: ROC curves of Entropy and Electroencephalographic variables during laryngoscopy.

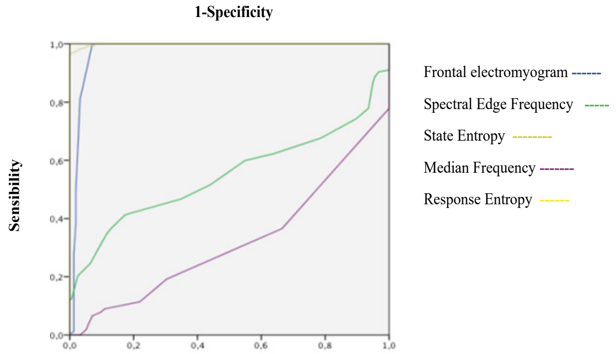

Figure 8: ROC curves of Entropy and Electroencephalographic variables during maintenance

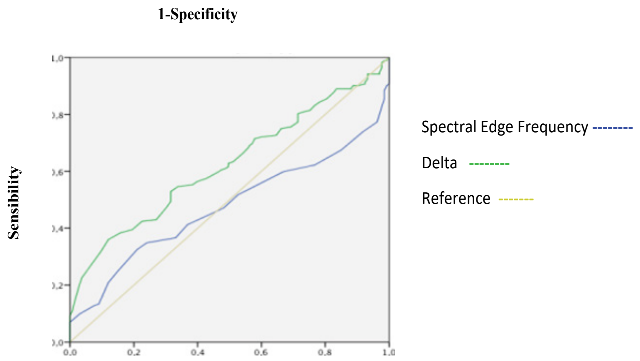

Figure 6: ROC curves of Electroencephalographic variables during laryngoscopy.

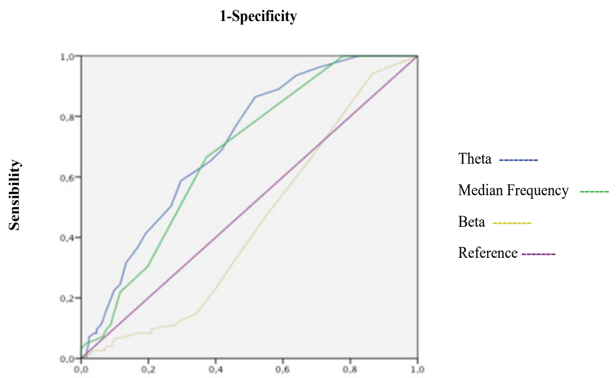

Figure 9: ROC curves of Electroencephalographic variables during maintenance.

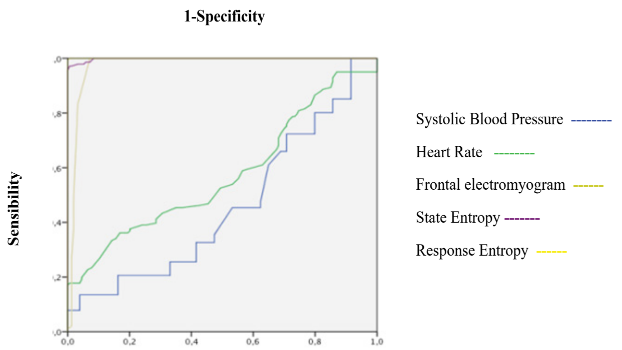

Figure 7: ROC curves of Systolic Blood Pressure, Heart Rate, Frontal Electromyogram and Entropy during maintenance

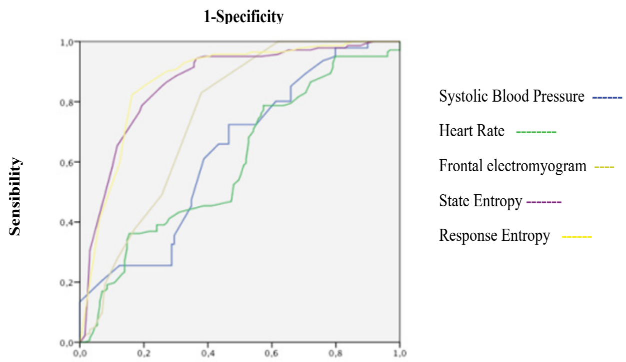

Figure 10: ROC curves of Systolic Blood Pressure, Heart Rate, Frontal Electromyogram and Entropy variables during emergence.

Maintenance

SE and RE increases significantly but showing values reflecting an adequate hypnosis level (40 to 60) presenting an excellent discrimination capacity of hypnosis depth and a good correlation with beta activity and SEF (Table 3, 4 and 5, Figure 7, 8 and 15A). fEMG not significantly changed and showed an excellent discrimination capacity for hypnosis monitoring without significant correlation with entropy and qEEG (Table 3, 4 and 5, Figure 7 and 8). qEEG showed a significant decrease of delta waves and increase of alpha and theta activity without significant changes of beta waves, causing a decrease of EEG amplitude and increasing SEF and MF (Table 3). A good correlation between beta with alpha and delta waves, alpha with delta and beta activity, alpha, beta and delta waves with SEF and MF were seen (Table 5, Figure 15 B and C). Only qEEG amplitude and theta activity showed an acceptable discrimination capacity of hypnosis level (Table 4, Figure 8 and 9). BcSEF significantly decreased showing a

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good discrimination capacity of hypnosis depth and excellent correlation with beta, alpha and delta waves (Table 3, 4 and 5). B/T not significantly changed and showed an acceptable discrimination capacity for hypnosis monitoring (Table 3 and 4). ETAC not significantly changed and showed an excellent discrimination capacity without correlations with entropy, qEEG and corrected variables (Table 3, 4 and 5). SBP and HR significantly decreases but showed a poor discrimination capacity of hypnosis level without correlating with entropy, qEEG, corrected variables and ETAC (Table 3, 4 and 5, Figure 7).

Emergence

SE and RE significantly increases showing an excellent discrimination capacity of hypnosis state without correlating with fEMG and qEEG (Table 3, 4 and 5, Figure 10, 11, 16A and B). fEMG significantly increasing showed an acceptable discrimination capacity of hypnosis depth without correlating with entropy and qEEG (Table 3, 4 and 5, Figure 10 and 16B). qEEG showed an increase of delta and beta waves and decrease of alpha and theta activity, causing a decrease of amplitude and MF and increase of SEF (Table 3). A good correlation between alpha and delta activity, SEF with beta and MF with alpha and delta waves were seen (Table 5).

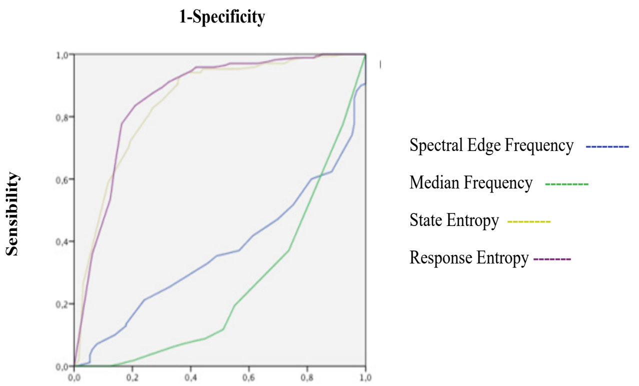

Figure 11: ROC curves of Entropy and Electroencephalographic variables during emergence

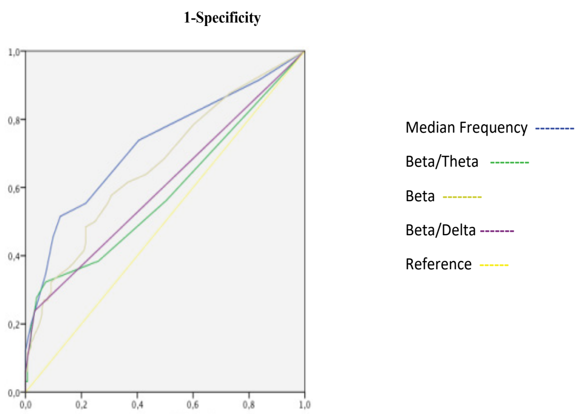

Figure 12: ROC curves of Electroencephalographic variables during emergence.

Delta activity and MF showed a good discrimination capacity of hypnosis state (Table 4, Figure 12). BcSEF significantly decreased and showed a poor discrimination capacity of hypnosis depth (Table 3 and 4). B/D showed no significant changes but an acceptable discrimination of hypnosis state (Table 3 and 4, Figure 12). Good correlations between beta activity with B/D and B/T was seen (Table 5). ETAC significantly decreases showing an excellent capacity for hypnosis monitoring without correlations with entropy, qEEG and corrected variables (Table 3, 4 and 5). SBP and HR significantly increases showing a poor discrimination capacity without correlating with entropy, qEEG, corrected variables and ETAC (Table 3, 4 and 5, Figure 10).

Linear Regression Analysis

ETAC variability

A linear regression analysis was performed to determine if entropy could explain ETAC variability.

ETAC=1.555 – (0.13) SE R^2: 0.183 ($p < 0.001$)

ETAC=1.569 –(0.13) RE R^2: 0.213 ($p < 0.001$)

Entropy variability

A linear regression analysis was performed to determine entropy variability explained for ETAC and qEEG.

SE=72.315 – 3.63 (ETAC) + 3.501 (fEMG) + 0.36 BSR – 0.34 Delta – 0.44 Theta R^2: 0.532 $p < 0.001$

RE=73.586 –5.127 (ETAC)+4.524 (fEMG)+0.398 BSR – 0.319 Delta – 0.386 Theta R^2: 0.540 $p < 0.001$

Linear regression showed that ETAC variability was poorly explained for entropy. Entropy variability was explained in half of cases for ETAC, BSR, delta and theta activity.

Prediction of Hypnosis Depth Equation

A logistic regression analysis was used for hypnosis depth (awake versus sleep) prediction equation using entropy and qEEG.

$$\text{HYPNOSIS DEPTH} = \frac{1}{1+e^{-(0{,}062\,\text{delta}+0{,}128\,\text{RE}+0{,}049\,\text{theta}+0{,}123\,\text{fEMG}-25{,}158)}} \quad R^2: 0.818\ p < 0.001$$

This model explains 81.8% of the variability of the clinical variable awake or sleep.

ROC of this model showed an Area Under Curve (AUC) of 0.999 ($p < 0.001$) which means that this equation could correctly predicts 99% of the time clinical status as awake or sleep (Figure 17).

Logistic regression showed that delta and theta activity, fEMG and RE could predict 81% of hypnosis state variability and 99% of the time could correctly predict hypnosis state.

Citation: Alberto Martinez Ruiz, Blanca Escontrela, Itxaso Merino Julian. Combination of Entropy and Electroencephalograpy for Deep of Hypnosis Monitoring Improvement during General Anesthesia. Journal of Radiology and Clinical Imaging 5 (2023): 53-68.

Table 5: Correlations of Entropy, Systolic Blood Pressure, Heart Rate, End-Tidal Anesthetic Concentration, Quantitative electroencephalogram and Corrected Variables from induction to emergence of anesthesia

	INDUCTION	LARYNGOSCOPY	MAINTENANCE	EMERGENCE
Entropy, Quantitative Electroencephalogram and Corrected Variables	**SE-Beta r 0.714 p0.000**	**SE-Beta r 0.828 p0.000**	**SE-Beta r 0.784 p0.000**	SE-Beta r0.305 p0.000
	SE-Delta r-0.628 p 0.000	SE-Delta r -0.674 p0.000	SE-Delta r -0.671 p0.000	SE-Delta r0.015 p0.867
	SE-Theta r0.489 p0.000	SE-Theta r 0.593 p0.000	SE-Theta r 0.193 p0.016	SE-Theta r-0.362 p0.000
	SE-Alpha r0.542 p0.000	SE-Alpha r 0.458 p0.000	SE-Alpha r 0.619 p0.000	SE-Alpha r-0.183 p0.038
	RE-Beta r 0.716 p 0.0000	**RE-Beta r 0.818 p0.000**	**RE-Beta r0.774 p0.000**	RE-Beta r0.033 p0.713
	RE-Delta r -0.642 p 0.000	RE-Delta r -0.656 p0.000	RE-Delta r-0.649 p0.000	RE-Delta r0.247 p0.005
	RE-Theta r 0.491 p0.0000	RE-Theta r 0.575 p0.000	RE-Theta r 0.171 p0.033	RE-Theta r-0.326 p0.000
	RE-Alpha r 0.574 p0.0000	RE-Alpha r 0.442 p0.000	RE-Alpha r0.591 p0.000	RE-Alpha r-0.293 p0.001
	SE-SEF r 0.636 p0.000	**SE-SEF r 0.824 p0.000**	**SE-SEF r0.767 p0.000**	SE-SEF r0.421 p0.000
	SE-MF r 0.354 p0.000	SE-MF r 0.574 p0.000	SE-MF r0.540 p0.000	SE-MF r0.034 p0.706
	SE-BcSEF r 0.548 p0.000	SE-BcSEF r 0.346 p0.000	SE-BcSEF r0.604 p0.000	SE-BcSEF R-0.228 p0.007
	SE-B/T r 0.499 p0.000	SE-B/T r 0.439 p0.000	SE-B/T r0.462 p0.000	SE-B/T r0.383 p0.000
	SE-B/D r 0.302 p0.000	SE-B/D r 0.245 p0.005	SE-B/D r.0.317 p0.000	SE-B/D r0.133 p0.133
	RE-SEF r 0.659 p0.000	**RE-SEF r 0.820 p0.000**	**RE-SEF r0.753 p0.000**	RE-SEF r0.185 p0.036
	RE-MF r 0.336 p0.000	RE-MF r 0.549 p0.000	RE-MF r0.526 p0.000	RE-MF r-0.180 p0.041
	RE-BcSEF r 0.553 p0.000	RE-BcSEF r 0.326 p0.000	RE-BcSEF r0.589 p0.000	RE-BcSEF r-0.015 p0.865
	RE-B/T r 0.482 p0.000	RE-B/T r 0.437 p0.000	RE-B/T r0.459 p0.000	RE-B/T r0.174 p0.050
	RE-B/D r 0.305 p0.000	RE-B/D r 0.235 p0.000	RE-B/D r 0.314 p0.000	RE-B/D r-0.035 p0.694
Frontal Electromyogram, Entropy, Quantitative Electroencephalogram and Corrected Variables	SE r -0.129 p0.157	SE r 0.129 p0.138	SE r0.305 p0.000	SE r0.264 p0.003
	RE r -0.106 p0.244	RE r 0.138 p0.113	RE r0.299 p0.000	RE r0.576 p0.000
	Beta r 0.021 p 0.825	Beta r 0.042 p 0.627	Beta r 0.230 p 0.004	Beta r -0.190 p 0.030
	Alpha r 0.191 p 0.038	Alpha r 0.011 p 0.899	Alpha r 0.097 p 0.228	Alpha r -0.312 p 0.000
	Theta r 0.061 p 0.514	Theta r 0.107 p 0.221	Theta r 0.122 p 0.132	Theta r -0.108 p 0.219
	Delta r -0.109 p 0.240	Delta r -0.045 p 0.606	Delta r -0.163 p 0.042	Delta r 0.339 p 0.000
	BcSEF r 0.074 p 0.416	BcSEF r 0.021 p 0.807	BcSEF r 0.223 p 0.005	BcSEF 0.368 p 0.000
	B/T r -0.014 p 0.884	B/T r -0.130 p 0.135	B/T r 0.131 p 0.105	B/T r -0.067 p 0.449
	B/D r 0.074 p 0.426	B/D r -0.115 p 0.189	B/D r -0.055 p 0.493	B/D r -0.221 p 0.011

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	Beta-Delta r -0.814 p0.000	**Beta-Delta r-0.845 p 0.000**	**Beta-Delta r-0.833 p0.000**	Beta-Delta r-0.647 p0.000
	Beta-Alpha r 0.711 p0.000	Beta-Alpha r 0.695 p0.000	**Beta-Alpha r 0.758 p0.000**	Beta-Alpha r0.276 p0.001
	Beta-Theta r 0.611 p0.000	Beta-Theta r 0.651 p0.000	Beta-Theta r 0.329 p0.000	Beta-Theta r-0.220 p0.012
	Alpha-Delta r -0.933 p0.000	**Alpha-Delta r-0.886 p0.000**	**Alpha-Delta r-0.931 p0.000**	**Alpha-Delta r-0.824 p0.000**
	Alpha-Theta r -0.701 p0.000	Alpha-Theta r0.613 p0.000	Alpha-Theta r 0.389 p0.000	Alpha-Theta r0.463 p0.000
	Delta-Theta r -0.869 p0.000	**Delta-Theta r-0.840 p0.000**	Delta-Theta r-0.588 p0.000	Delta-Theta r-0.374 p0.000
	Beta-SEF r 0.862 p0.000	**Beta-SEF r 0.953 p0.000**	**Beta-SEF r0.951 p0.000**	**Beta-SEF r0.918 p0.000**
	Beta-MF r 0.461 p0.000	**Beta-MF r 0.725 p0.000**	**Beta-MF r0.707 p0.000**	Beta-MF r0.649 p0.000
	Alpha-SEF r 0.943 p0.000	**Alpha-SEF r 0.710 p0.000**	**Alpha-SEF r0.847 p0.000**	Alpha-SEF r0.244 p0.005
	Alpha-MF r 0.460 p0.000	**Alpha-MF r 0.703 p0.000**	**Alpha-MF r 0.744 p0.000**	**Alpha-MF r0.754 p0.000**
	Delta-SEF r -0.952 p0.000	**Delta-SEF r-0.856 p0.000**	**Delta-SEF r-0.888 p0.000**	Delta-SEF r-0.577 p0.000
	Delta-MF r -0.542 p0.000	**Delta-MF r-0.863 p0.000**	**Delta-MF r-0.855 p0.000**	**Delta-MF r-0.941 p0.000**
Quantitative Electroencephalogram and Corrected Variables	**Theta-SEF r 0.763 p0.000**	Theta-SEF r0.661 p0.000	Theta-SEF r0.379 p0.000	Theta-SEF r-0.151 p0.084
	Theta-MF r 0.539 p0.000	**Theta-MF r0.770 p0.000**	Theta-MF r0.531 p0.000	Theta-MF r0.266 p0.002
	Beta-BcSEF r 0.851 p0.000	Beta-BcSEF r0.562 p0.000	**Beta-BcSEF r0.950 p0.000**	Beta-BcSEF r0.052 p0.558
	Beta-B/T r 0.655 p0.000	Beta-B/T r0.542 p0.000	Beta-B/T r0.534 p0.000	**Beta-B/T r0.851 p0.000**
	Beta-B/D r 0.324 p0.000	Beta-B/D r0.329 p0.000	Beta-B/D r0.340 p0.000	**Beta-B/D r0.712 p0.000**
	Alpha-BcSEF r0.941 p0.000	**Alpha-BcSEF r0.702 p0.000**	**Alpha-BcSEF r0.848 p0.000**	Alpha-BcSEF r0.027 p0.758
	Alpha-B/D r 0.316 p0.000	Alpha-B/D r0.217 p0.012	Alpha-B/D r0.312 p0.000	Alpha-B/D r0.174 p0.047
	Alpha-B/T r 0.447 p0.000	Alpha-B/T r0.230 p0.008	Alpha-B/T 0.441 p0.000	Alpha-B/T r0.017 p0.844
	Delta-BcSEF r-0.938 p0.000	Delta-BcSEF r0.561 p0.000	**Delta-BcSEF r-0.890 p0.000**	Delta-BcSEF r-0.040 p0.651
	Delta-B/T r-0.418 p0.000	Delta-B/T r-0.243 p0.000	Delta-B/T r-0.400 p0.000	Delta-B/T r-0.306 p0.000
	Delta-B/D r -0.314 p0.001	Delta-B/D r-0.332 p0.000	Delta-B/D r-0.334 p0.000	Delta-B/D r-0.557 p0.000
	Theta-BcSEF r 0.737 p0.000	Theta-BcSEF r0.342 p0.000	Theta-BcSEF r0.381 p0.000	Theta-BcSEF r0.190 p0.030
	Theta-B/T r 0.082 p 0.388	Theta-B/T r-0.075 p0.394	Theta-B/T r-0.329 p0.000	Theta-B/T r-0.603 p0.000
	Theta-B/D r 0.278 p0.000	Theta-B/D r0.104 p0.235	Theta-B/D r-0.116 p0.149	Theta-B/D r-0.149 p0.090

Hemodynamic variables (SBP and HR), Entropy, Quantitative Electroencephalogram, Frontal Electromyogram, Corrected Variables and End-Tidal Anesthetic Concentration	SBP-HR r 0.021 p0.831	SBP-HR: r 0.106 p 0.226	SBP-HR: r 0.376 p 0.000	SBP-HR: r 0.469 p 0.000
	SBP-SE: r 0.197 p0.031	SBP-SE: r 0.149 p 0.079	SBP-SE: r 0.067 p 0.399	SBP-SE: r 0.009 p 0.913
	SBP-RE: r 0.122 p0.186	SBP-RE: r 0.159 p 0.061	SBP-RE: r 0.072 p 0.363	SBP-RE: r 0.031 p 0.715
	SBP-Beta: r 0.096 p0.320	SBP-Beta: r 0.018 p 0.835	SBP-Beta: r -0.123 p 0.130	SBP-Beta: r -0.256 p 0.003
	SBP-Alpha: r -0.157 p0.101	SBP-Alpha: r -0.131 p 0.133	SBP-Alpha: r -0.338 p 0.000	SBP-Alpha: r -0.256 p 0.003
	SBP-Theta: r -0.173 p0.071	SBP-Theta: r 0.059 p 0.500	SBP-Theta: r 0.228 p 0.005	SBP-Theta: r 0.048 p 0.583
	SBP-Delta: r 0.084 p0.381	SBP-Delta: r 0.021 p 0.814	SBP-Delta: r 0.193 p 0.016	SBP-Delta: r 0.232 p 0.008
	SBP-SEF: r -0.037 p0.701	SBP-SEF: r -0.025 p 0.771	SBP-SEF: r -0.216 p 0.007	SBP-SEF: r -0.224 p 0.010
	SBP-MF: r 0.047 p0.624	SBP-MF: r 0.026 p 0.765	SBP-MF: r -0.025 p 0.755	SBP-MF: r -0.208 p 0.017
	SBP-fEMG: r -0.381 p0.000	SBP-fEMG: r 0.010 p 0.909	SBP-fEMG: r 0.012 p 0.880	SBP-fEMG: r -0.166 p 0.059
	SBP-BcSEF: r -0.075 p0.413	SBP-BcSEF: r-0.187 p 0.026	SBP-BcSEF: r -0.210 p 0.008	SBP-BcSEF: r -0.223 p 0.008
	SBP-B/T: r 0.312 p0.001	SBP-B/T: r 0.108 p 0.214	SBP-B/T: r -0.438 p 0.000	SBP-B/T: r -0.225 p 0.010
	SBP-B/D: r -0.064 p0.504	SBP-B/D: r 0.015 p 0.864	SBP-B/D: r -0.208 p 0.010	SBP-B/D: r 0.017 p 0.843
	SBP-ETAC: r -0.345 p 0.000	SBP-ETAC: r 0.055 p 0.514	SBP-ETAC: r -0.089 p 0.263	SBP-ETAC: r -0.078 p 0.361
	HR-SBP: r 0.021 p0.831	HR-SBP: r 0.106 p 0.226	HR-SBP: r 0.376 p 0.000	HR-SBP: r 0.469 p 0.000
	HR-SE: r -0.157 p0.114	HR-SE: r 0.304 p 0.000	HR-SE: r -0.46 p 0.557	HR-SE: r 0.041 p 0.638
	HR-RE: r -0.202 p0.041	HR-RE: r 0.288 p 0.001	HR-RE: r -0.036 p 0.651	HR-RE: r 0.145 p 0.091
	HR-Beta: r -0.342 p0.001	HR-Beta: r 0.206 p 0.022	HR-Beta: r -0.104 p 0.200	HR-Beta: r -0.404 p 0.000
	HR-Alpha: r -0.351 p0.001	HR-Alpha: r 0.014 p 0.877	HR-Alpha: r 0.035 p 0.661	HR-Alpha: r -0.373 p 0.000
	HR-Theta: r 0.063 p0.548	HR-Theta: r 0.296 p 0.001	HR-Theta: r 0.283 p 0.000	HR-Theta: r 0.091 p 0.304
	HR-Delta: r 0.228 p0.029	HR-Delta: r -0.159 p 0.080	HR-Delta: r -0.110 p 0.173	HR-Delta: r 0.418 p 0.000
	HR-SEF: r 0.266 p0.010	HR-SEF: r 0.171 p 0.058	HR-SEF: r -0.140 p 0.082	HR-SEF: r -0.342 p 0.000
	HR-MF: r 0.097 p0.358	HR-MF: r 0.200 p 0.027	HR-MF: r 0.221 p 0.006	HR-MF: r -0.405 p 0.000
	HR-fEMG: r -0.149 p0.149	HR-fEMG: r 0.039 p 0.667	HR-fEMG: r -0.243 p 0.002	HR-fEMG: r 0.151 p 0.085
	HR-BcSEF: r -0.137 p0.170	HR-BcSEF: r -0.030 p 0.731	HR-BcSEF: r -0.131 p 0.096	HR-BcSEF: r 0.122 p 0.154
	HR-B/T: r -0.433 p0.000	HR-B/T: r -0.013 p 0.890	HR-B/T: r -0.242 p 0.002	HR-B/T: r -0.310 p 0.000
	HR-B/D: r -0.149 p0.157	HR-B/D: r -0.088 p 0.334	HR-B/D: r -0.049 p 0.543	HR-B/D: r -0.174 p 0.047
	HR-ETAC: r 0.253 p0.010	HR-ETAC: r 0.126 p 0.150	HR-ETAC: r 0.108 p 0.172	HR-ETAC: r 0.136 p 0.109

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End-Tidal Anesthetic Concentration, Hemodynamic variables (SBP and HR), Entropy, Quantitative Electroencephalogram, Frontal Electromyogram and Corrected Variables.	ETAC-SBP: r -0.345 p0.000	ETAC-SBP: r 0.055 p 0.514	ETAC-SBP: r -0.089 p 0.263	ETAC-SBP: r -0.078 p 0.361
	ETAC-HR: r 0.253 p0.010	ETAC-HR: r 0.126 p 0.150	ETAC-HR: r 0.108 p 0.172	ETAC-HR: r 0.136 p 0.109
	ETAC-SE: r -0.220 p0.013	ETAC-SE: r -0.346 p 0.000	ETAC-SE: r -0.210 p 0.007	ETAC-SE: r -0.372 p 0.000
	ETAC-RE: r -0.220 p0.013	ETAC-RE: r -0.358 p 0.000	ETAC-RE: r -0.197 p 0.012	ETAC-RE: r -0.309 p 0.000
	ETAC-Beta: r -0.163 p0.077	ETAC-Beta: r -0.354 p 0.000	ETAC-Beta: r -0.237 p 0.003	ETAC-Beta: r -0.229 p 0.009
	ETAC-Alpha: r 0.148 p0.109	ETAC-Alpha: r -0.178 p 0.040	ETAC-Alpha: r -0.316 p 0.000	ETAC-Alpha: r -0.009 p 0.921
	ETAC-Theta: r 0.041 p0.656	ETAC-Theta: r -0.057 p 0.512	ETAC-Theta: r -0.187 p 0.020	ETAC-Theta: r 0.272 p 0.002
	ETAC-Delta: r -0.065 p0.481	ETAC-Delta: r 0.208 p 0.010	ETAC-Delta: r 0.280 p 0.000	ETAC-Delta: r 0.085 p 0.336
	ETAC-SEF: r 0.030 p0.746	ETAC-SEF: r -0.410 p 0.000	ETAC-SEF: r -0.327 p 0.000	ETAC-SEF: r -0.243 p 0.005
	ETAC-MF: r -0.097 p0.298	ETAC-MF: r -0.260 p 0.003	ETAC-MF: r -0.030 p 0.714	ETAC-MF: r -0.077 p 0.383
	ETAC-fEMG: r 0.403 p0.000	ETAC-fEMG: r -0.108 p 0.215	ETAC-fEMG: r -0.060 p 0.460	ETAC-fEMG: r -0.015 p 0.869
	ETAC-BcSEF: r 0.090 p0.315	ETAC-BcSEF: r -0.170 p 0.044	ETAC-BcSEF: r -0.378 p 0.000	ETAC-BcSEF: r 0.144 p 0.091
	ETAC-B/T: r -0.156 p0.099	ETAC-B/T: r -0.295 p 0.001	ETAC-B/T: r-0.043 p 0.591	ETAC-B/T: r -0.283 p 0.001
	ETAC-B/D: r -0.047 p0.613	ETAC-B/D: r -0.096 p 0.273	ETAC-B/D: r 0.080 p 0.325	ETAC-B/D: r -0.147 p 0.093

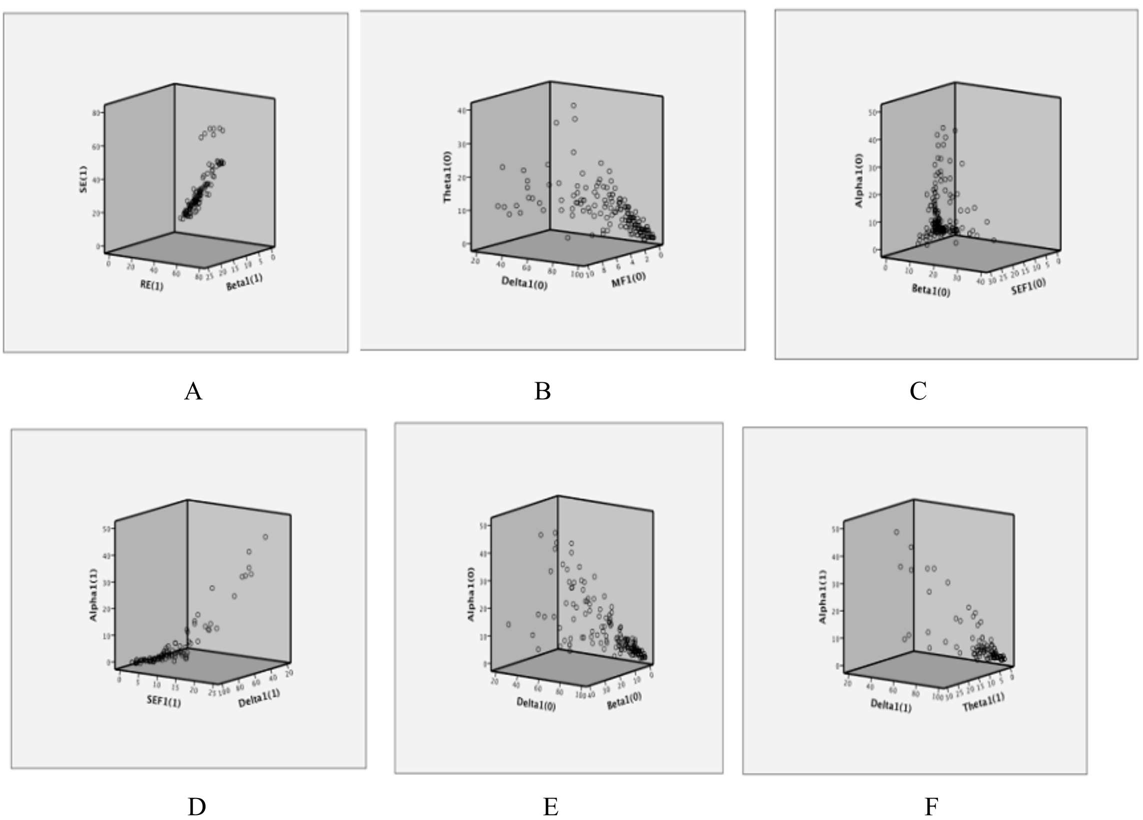

Figure 13: Correlations during induction A.-Entropy and beta activity. B.-Median Frequency, delta and theta activity. C.-Spectral Edge Frequency, alpha and beta activity. D.-Spectral Edge Frequency, alpha and delta activity. E.-Alpha, beta and delta activity. F.-Alpha, theta and delta activity

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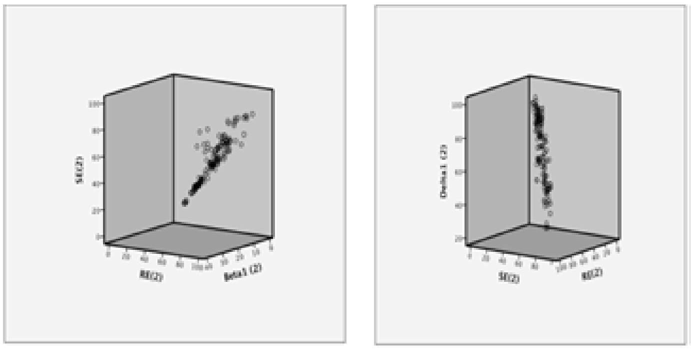
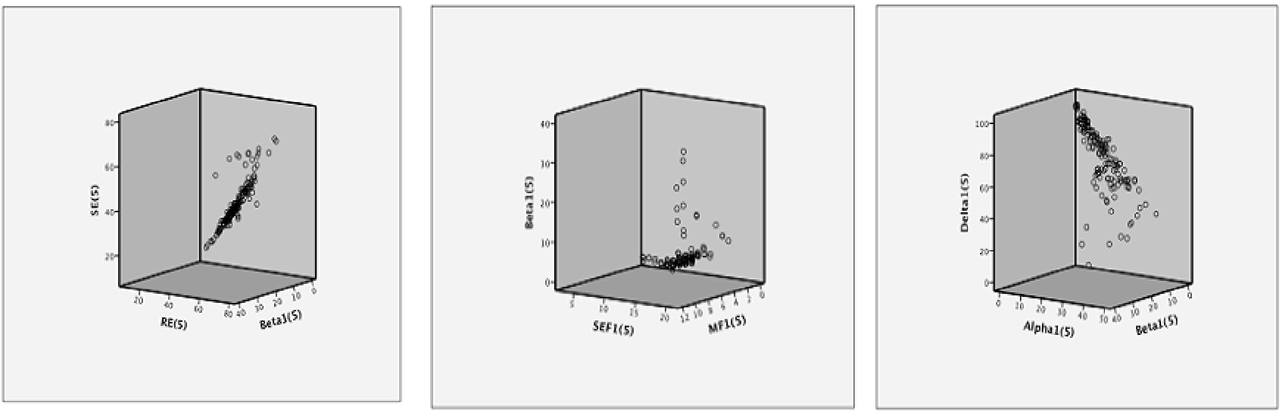


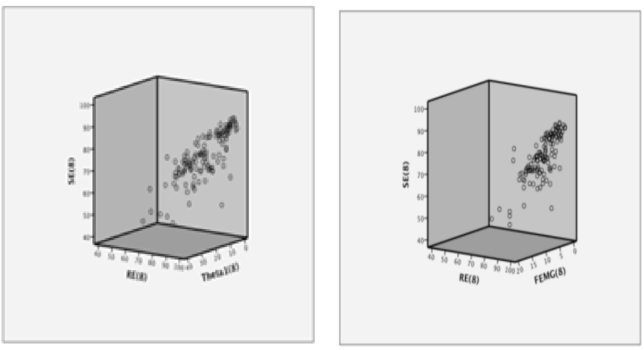
A B

Figure 14: Correlations during laringoscopy A.-Entropy and beta activity B.-Entropy and delta activity.



A B C

Figure 15: Correlations during maintenance A.-Entropy and beta activity B.-Spectral Edge Frequency, Median Frequency and beta activity C.-Alpha, beta and delta activity



A B

Figure 16: Correlations during emergence A.-Entropy and theta activity. B.-Entropy and frontal electromyogram

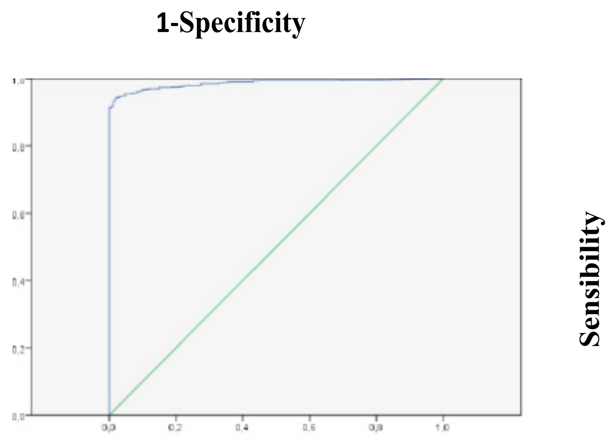


Figure 17: ROC curve of hypnosis depth prediction equation

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Conclusion

This study aims to describe a prediction equation for deep of hypnosis monitoring during general volatile anesthesia with sevoflurane. Our patients were a typical population without significant neurologic diseases, medium age with a situation of normotension and normotermia to avoid possible confounder factors interfering with deep of hypnosis monitoring accuracy using entropy and qEEG.

Several factors related to design must be highlighted. Prospective, single group and observational design in young patients under general anesthesia of short duration probably make possible to describe in a real theater the changes of hypnosis depth resulting of induction, laryngoscopy, maintenance and emergence. Nociceptive stimulation influence for deep of hypnosis monitoring is controversial and was observed in this study during laryngoscopy, classically described as one of the highest pain stimuli during general anesthesia. Effects of neuromuscular paralysis resulting of administration of NMBA during induction to make oro-traqueal intubation easier in accordance to universal recommendations probably resulted in a lack of frontal muscles contraction and fEMG reduction likely influencing deep of hypnosis monitoring.

Entropy, qEEG and ETAC showed expected changes during induction, laringoscopy, maintenance and emergence of general anesthesia. Entropy and qEEG reflected significant changes, increasing hypnosis depth during induction followed for classical awareness probably because of intense nociceptive stimulation of laryngoscopy, increasing of intermediate activity resulted of moderate surgical stimulation during maintenance and fast activity in emergence when anesthesia agents were withdrawal. Entropy showed an excellent discrimination capacity during all anesthesia phases. An acceptable discrimination capacity of qEEG intermediate theta activity during maintenance and slow delta activity in emergence were interesting findings of this study not previously published as far as we know. Significant correlations between entropy with qEEG fast activity from induction to maintenance is another interesting finding of our study, probably indicating that fast activity decreasing as hypnosis deepens according to gold standard qEEG could be reflected for a faster monitoring with entropy, as evidence has been previously showed (18). ETAC showed significant changes during induction, laryngoscopy and emergence as a result of our study protocol including volatile anesthetic administration immediately after oro-traqueal intubation. ETAC had a higher discrimination capacity from laryngoscopy to maintenance, and linear regression analysis showed that entropy does not influence variability of ETAC, probably indicating that entropy and ETAC should be complementary deep of hypnosis monitoring during balanced general anesthesia with volatile hypnotic agent.

Corrected variables could have advantages for deep of hypnosis monitoring reflecting balance between fast and slow activity. In this study, BcSEF showed significant changes from induction to emergence of general anesthesia indicating hypnosis deepens during induction followed for a light anesthesia in laryngoscopy probably because of classic awake and a deep hypnosis level during maintenance probably because of effects of volatile anesthesia increasing BSR and decreasing SEF and paradoxically during emergence when anesthesia agent was withdrawal, but discrimination capacity was acceptable only in maintenance time. B/T reflected a higher hypnosis depth during induction probably resulting of beta activity decreased and theta waves increased because effects of intravenous propofol, followed for a lower hypnosis level only significant during emergence because increasing of beta waves and decreasing of theta activity secondary to hypnotic agent withdrawal, but discrimination capacity was only acceptable during maintenance probably reflecting a lower hypnosis level because of surgical stimulation during this time. B/D not significantly changed from induction to emergence probably resulting of a balance between beta and delta activity during these phases, but discrimination capacity was acceptable in induction and emergence probably indicating the importance of beta and delta activity for deep of hypnosis monitoring especially during induction and emergence. Acceptable discrimination capacity of BcSEF and B/T during maintenance and B/D during induction and emergence were interesting findings of our study not published as far as we know, probably useful for deep of hypnosis monitoring improvement.

fEMG is a source of interference for deep of hypnosis monitoring as evidence had showed [10]. In this study, fEMG significantly decrease during induction because of a lack of frontal neuromuscular activity resulting of action of NMBA administered in this phase for endotraqueal intubation facilitation in laryngoscopy time. fEMG increases during emergence because a frontal neuromuscular activity recovery at the end of surgical procedure to achieve awake and a safe extubation. A very interesting findings of our study were an excellent discrimination capacity of deep of hypnosis state of fEMG from induction to maintenance, decreasing but being good during emergence time and a contribution of fEMG for clinical status of awake vs sleep prediction according to our equation. A lack of correlation with SE and RE along with a lower capacity of fEMG to explained variability of SE and RE according to linear regression in this study was very interesting also, not expected because entropy algorithm includes fEMG band in RE value.

Hemodynamic variables influence for deep of hypnosis monitoring are controversial. In this study, SBP significantly decrease during induction probably because of propofol administration and maintenance resulting of moderate surgical stimulation balanced for effects of volatile anesthetics along with opioids according to anesthesiologist in charge decision without influence of deep of hypnosis monitoring using EEG variables. SBP and HR significantly increased in laryngoscopy and emergence probably because of higher nociceptive stimulation of sympathetic system during these phases. SBP showed only an acceptable discrimination capacity during induction without showed significant correlations with entropy and EEG variables. HR not significantly changed during induction probably resulting of a lack of reflex tachycardia after regular doses of propofol given according to study protocol reflecting our current hospital practice. HR significantly decreased during maintenance probably because of moderate surgical stimulation under effects of volatile and opioid drugs. HR showed a poor discrimination capacity in all phases without correlating with entropy and EEG variables. These results taken together seems to indicate that SBP and HR showed effects of nociceptive stimulation during laryngoscopy and emergence, but its poor discrimination capacity of hypnosis level make these variables not useful for deep of hypnosis monitoring improvement.

Variables influencing changes of entropy and ETAC during general anesthesia in this study should reflect potentially tools for deep of hypnosis monitoring improvement. fEMG and ETAC influence for entropy monitoring has been described earlier [2,4-17], but in this study interestingly nor fEMG or ETAC could explained variability of entropy values. EGG slow and intermediate activity could indicate transition to a deeper hypnosis level but are less important for entropy monitoring algorithm according to our results and previously published papers [2,4-17]. In present study ETAC variability was not explained for entropy unlike evidence had showed earlier [2]. We analyzed prediction capacity of hypnosis state of entropy and variables that showed a poor prediction capacity of entropy variability also with a limited value for deep of hypnosis monitoring in our days. Combination of RE, fEMG, delta and theta activity showed an excellent discrimination capacity of hypnosis state in present study. This was a very interesting finding of our study not published as far as we know that reflects the importance of include fast, intermediate and slow activity for deep of hypnosis monitoring improving.

This study has limitations because its little size and single group of female young patients under short anesthesia for scheduled gynecology procedures. For this reason, our results needs to further confirmation for larger studies.

In conclusion, this study showed that entropy had an excellent discrimination capacity of hypnosis state from induction to emergence of general anesthesia. Corrected EEG variables B/D during induction and emergence or BcSEF and B/T during maintenance reflecting balance between slow and fast activity showed a good discrimination capacity with potential for deep of hypnosis monitoring improvement. Combination of fEMG, RE, delta and theta activities showed an excellent discrimination capacity of hypnosis state highlighting the importance of include fast, intermediate and slow activity for a more accurate deep of hypnosis monitoring during general anesthesia. Our interesting findings needs further investigation in larger studies to assess performance of EEG corrected variables, entropy and EEG fast, slow and intermediate activity for deep of hypnosis monitoring improvement.

Supplementary Files Link

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