Entropy Versus Bispectral Index in Evaluation of Anesthetic Depth in Adults

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Abstract

Objective: To compare the sensitivity and specificity of the entropy and Bispectral Index (BIS) values with respect to predicting loss of consciousness and emergence from general anesthesia and to compare the effects of electrosurgical unit on the displayed index values of both monitors during operation.

Methods: Thirty consenting patients, aged 18-65 yr, ASA physical status I or II scheduled for elective abdominal, gynecologic, urologic, or orthopedic surgery expected to last at least 1 h, were studied. The simultaneous state entropy (SE), response entropy (RE) and BIS values were recorded at six time points which coincided with anesthetic and surgical maneuvers: Pre induction (baseline value), Loss of consciousness, Preincision value, 5 minutes after surgery started, Preawakening, 1 minute post awakening.

Results: The BIS, RE, and SE values decreased progressively from preinduction (baseline) values of 96 ± 3, 95 ± 4 and 88 ± 3 to preincision values of 37 ± 13, 35 ± 14 and 30 ± 13, respectively. Although the indices were comparable during the induction period, the SE values were significantly less than the RE and BIS values during the emergence period this is to be expected as SE is scored out of 91 while RE and BIS are scored out of 100. RE and SE are compared with BIS in Bland Altman plots demonstrated a good agreement especially between RE and BIS [average mean difference (95%CI)= -1.1 (-17.5 – 15.4)]. Logistic regression analysis demonstrated that the BIS, RE and SE were all significant predictors of unconsciousness (p <0.01), with area under the Receiver operating characteristics (ROC) curve values of 0.976 ±0.058, 0.965±0.075 and 0.950±0.115 for the BIS, RE and SE, respectively. Finally, the entropy indices were less interfered with by the electrocautery unit during the operation (11% versus 63% for the BIS monitor).

Conclusions: The changes in SE and RE values followed a similar pattern to the BIS values during anesthesia. Use of entropy module is associated with less frequent intraoperative interference (by electromyographic activity and the electrocautery) during general anesthesia.

Key Words: Bispectral index – State entropy – Response entropy.

Introduction

A PATIENT’S hypnotic state can be evaluated in real time using several devices that quantify the electroencephalogram (EEG). Among them, the Bispectral Index monitor (BIS; Aspect Medical Systems, Newton, MA) uses the bispectral analysis of the EEG, while the Entropy Module (GE Healthcare, Helsinki, Finland), based upon spectral entropy, describes the irregularity, complexity, or unpredictability characteristics of a signal [1].

The use of such EEG monitors can decrease drug consumption during anesthesia [2] and lead to a faster recovery from anesthesia [3]. The use of the Bispectral IndexTM (BIS) monitor may decrease the incidence of intraoperative awareness [4,5].

 Whereas the BIS monitor uses different algorithms to calculate the BIS during the different stages of anesthesia, e.g., burst suppression (BS) [6] and frequency power calculation [7], as well as bispectral analysis [8], the Entropy ModuleTM measures depth of anesthesia with a single algorithm, i.e., calculating the Shannon Entropy [9] of the power spectrum called the Spectral Entropy. The Entropy ModuleTM calculates two different Spectral Entropy indicators: The state entropy (SE), computed over the frequency range from 0.8 to 32 Hz, reflecting the EEG-dominant part of the spectrum, in addition to the response entropy (RE), computed over the frequency range of 0.8 to 47 Hz, including both the EEG and electromyographic (EMG) dominant part of the recorded spectrum [1].

The aim of this study was to compare the sensitivity and specificity of the entropy and BIS values with respect to predicting loss of consciousness and emergence from general anesthesia and to compare the effects of electrosurgical unit on
the displayed index values of both monitors during operation.

Patients and Methods

Between January and October 2007, at King Fahad Medical City in Riyadh Saudi Arabia, after local ethics committee approval, written informed consent was obtained from 30 Patients, aged 18-65 yr, ASA physical status I or II scheduled for elective abdominal, gynecologic, urologic, or orthopedic surgery expected to last at least 1h, were studied. Exclusion criteria were a history of any disabling central nervous or cerebrovascular disease, substance abuse, treatment with opioids or any psychoactive medication, or a body weight <70% or more than 130% of ideal body weight. Regional anesthesia was administered (lower-extremity block, epidural or subarachnoid blocks) in either the preoperative area or the operating room, as appropriate.

Anesthetic regimen:

After arrival in the induction room, an IV catheter was inserted into a larger forearm vein and standard monitors were applied. The EEG was recorded continuously using an Aspect A-2000 BISTM monitor (version XP) and the Entropy ModuleTM (Datex-Ohmeda). The skin of the forehead was prepared with 70% alcohol and the BIS (BIS-XP sensor, Aspect Medical Systems) and the Entropy electrodes were positioned, as recommended by the manufacturers, onto the temporal-frontal area of the patient’s forehead. Measurements were started after the electrode impedance check of each monitor was completed.

Baseline heart rate and mean arterial blood pressure were defined as the mean of three measurements obtained in the operating room before induction of anesthesia. Abnormal heart rate and mean arterial blood pressure were defined as values <75% or >125% of baseline values. After administration of 100% oxygen, anesthesia was induced with IV propofol 2-3mg/kg and IV fentanyl 2-3 µg/kg, injected over 15-30s. After loss of consciousness, oxygen was given by facemask ventilation and patients received IV cisatracurium 0.15mg/kg. After tracheal intubation, the lungs were mechanically ventilated with a tidal volume of 8-10mL/kg, with the ventilatory rate adjusted to maintain an end-tidal carbon dioxide concentration (partial pressure) of 30-40mm Hg. Anesthesia was continued with sevoflurane in 60% nitrous oxide with oxygen, IV cisatracurium 0.03mg/kg/h initially and thereafter adjusted according to train-of-four monitoring.

BIS, RE and SE were recorded at certain time points which coincided with anesthetic and surgical maneuvers.

1- Pre induction (baseline value).
2- Loss of consciousness.
3- Preincision value.
4- 5 minutes after surgery started.
5- Preawakening.
6- 1 minute post awakening.

On termination of surgery the endotracheal tubes were removed under deep anesthesia. No verbal or tactile stimulation were done and preawakening values were taken the moment the patient emerged from anesthesia. Values of BIS and entropy measured at the moments immediately before awakening were beneficial as they predict the impending awakening in the absence of stimulation. Preincision values denoted for the epoch of deep anesthesia whilst the values retrieved one minute post awakening were an estimate monitor of the established awake state. Awakening was defined by eye opening, onset of sustained purposeful movement and phonation.

RE, SE and BIS measurements were separately compared at all previously mentioned times. Each of RE and SE was separately plotted against BIS and correlation was established in a coefficient determined by using the data gathered from the 6 time points mentioned earlier. At a 24h follow-up interview, patients were asked if they had recall of any events during the operation.

Statistical analysis:

Data were collected, coded, tabulated and then analyzed using SPSS® version 12.0. Numerical variables were presented as mean ± standard deviation while categorical variables were presented as number and percentage. One-way analysis of variance was used to analyze normally distributed continuous variables and when a significant difference was noted, the Newman-Keuls test was performed for post hoc comparisons among the three indices. Repeated-measures analysis of variance with a post hoc Bonferroni correction was used to compare the changes in the specific BIS, RE and SE values (versus baseline values). Categorical data were analyzed by the χ² test. The area under the receiver operating characteristic (ROC) curve for each index was determined by plotting the sensitivity (fraction of unresponsive patients who were correctly predicted to be unconscious) against 1-specificity (fraction of responsive patients who
were correctly predicted to be awake) and reflects the discriminating power of the indices. The area under the ROC curve summarizes the predictive power of the index to achieve a high specificity at any given sensitivity \[10\]. An area >0.5 indicates that the measurement is predictive and a measurement with 100% accuracy would have an area of 1.0. However, an area under the ROC of 0.5 has the same predictive value as a coin flip. Bland-Altman plot was used to estimate the agreement between the three indices. All tests were two-sided and a \( p \) value <0.05 was considered statistically significant.

**Results**

One patient was excluded for surgical cancelation. Twenty nine patients, 17 men and 12 women, completed the study. ASA status ranged from I or II (I, \( n=14 \) and II, \( n=15 \)). The average age was 43 ± 12 yr. The average weight and height were 84 ± 12kg and 178 ± 11cm, respectively. Surgery included orthopedic \( (n=11) \), gynecological \( (n=11) \), general \( (n=6) \) and urological \( (n=1) \) procedures. Regional anesthesia was administered by subarachnoid \( (n=12) \), epidural \( (n=10) \) and lower-extremity \( (n=7) \) techniques. After IV induction, either patients were endotracheally intubated \( (n=21) \) or a laryngeal mask airway \( (n=8) \) was placed. The total dosages of propofol and fentanyl were 219 ± 51mg and 129 ± 25 \( \mu g \), respectively. In addition, the average end-tidal concentration of sevoflurane was 2.4% ± 1.5%. Times to eye opening and orientation were 7 ± 3 and 9 ± 3min, respectively. No patient reported intraoperative recall at the 24-h follow-up interview.

The BIS, RE, and SE values decreased progressively from preinduction (baseline) values of 96 ±3, 95 ±4 and 88 ±3 to preincision values of 37 ±13, 35±14 and 30 ±13, respectively (Table 1).

Table (1): Perioperative changes in the response entropy (RE), state entropy (SE) and bispectral index (BIS) values.

<table>
<thead>
<tr>
<th>Time points measured</th>
<th>BIS</th>
<th>RE</th>
<th>SE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pre induction (baseline value)</td>
<td>96 ±3</td>
<td>95 ±4</td>
<td>88 ±3*</td>
</tr>
<tr>
<td>Loss of consciousness</td>
<td>75 ±15</td>
<td>53 ±27†</td>
<td>50 ±25†</td>
</tr>
<tr>
<td>Preincision value</td>
<td>46 ±3</td>
<td>45 ±4</td>
<td>43 ±3</td>
</tr>
<tr>
<td>5 minutes after surgery started</td>
<td>44 ±3</td>
<td>43 ±4</td>
<td>41 ±3</td>
</tr>
<tr>
<td>Preawakening</td>
<td>91 ±3</td>
<td>92 ±4</td>
<td>81 ±3*</td>
</tr>
<tr>
<td>1 minute post awakening</td>
<td>97 ±3</td>
<td>95 ±4</td>
<td>85 ±3*</td>
</tr>
</tbody>
</table>

Values are expressed as mean ± SD.

\( *p \leq 0.05 \) versus BIS and RE values.

\( †p \leq 0.05 \) versus BIS.

Although the indices were comparable during the induction period, the SE values were significantly less than the RE and BIS values during the emergence period (Table 1) this is to be expected as SE is scored out of 91.

A similar degree of inter-patient variability was observed in the BIS, RE and SE values. During the maintenance period, the SE values tended to be lower than the RE and BIS values (Fig. 1).

![Fig. 1: Changes in the bispectral index (BIS), response entropy (RE) and state entropy (SE) values during the perioperative period.](image)

\( *p \leq 0.05 \) versus BIS and RE values; †\( p \leq 0.05 \) versus BIS; ‡\( p \leq 0.05 \) versus baseline values.

RE (Fig. 2) and SE (Fig. 3) are compared with BIS in Bland Altman plots demonstrated a good agreement especially between RE and BIS [average mean difference (95%CI)=−1.1 (−17.5–15.4)]. These agreements are more evident at higher values of entropy and BIS (evident by lower scattering on the figures at these levels).

Logistic regression analysis demonstrated that the BIS, RE and SE were all significant predictors of unconsciousness \( (p <0.01) \), with area under the Receiver operating characteristics (ROC) curve values of 0.976±0.058, 0.965±0.075 and 0.950±0.115 for the BIS, RE and SE, respectively (Fig. 4). No significant differences among the three indices.

Receiver operating characteristics (ROC) curves. The area under Entropy (RE and SE) curve was similar to the area under the BIS curve (Fig. 4).
Lasty, the time required to apply the electrode strip (10±4s) and obtain the baseline index values (41-45s) were not significantly different with the two monitoring systems (Table 2).

Table (2): Times to apply and display the entropy and bispectral index (BIS) values and interference with the signal during use of the electrocautery unit.

<table>
<thead>
<tr>
<th></th>
<th>BIS</th>
<th>Entropy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Time to apply the electrode (s)</td>
<td>10±4</td>
<td>10±4</td>
</tr>
<tr>
<td>Time to display the index values (s)</td>
<td>45±34</td>
<td>41±32</td>
</tr>
<tr>
<td>Electrocautery artifact (%)</td>
<td>63</td>
<td>11*</td>
</tr>
</tbody>
</table>

Values are expressed as mean ± SD.
*p≤0.05 versus BIS values.

Discussion

Since its introduction in 1996, BIS monitoring has gained increasing popularity in daily anesthesia practice. Spectral entropy is another EEG monitor designed to help the clinician assess the depth of hypnosis. The Entropy monitor displays two variables. SE is computed over the frequency range from 0.8 to 32Hz; it includes the EEG-dominant part of the spectrum, and therefore primarily reflects the cortical state of the patient. RE is computed over a frequency range from 0.8 to 47Hz; it includes both the EEG-dominant and electromyogram-dominant parts of the spectrum. On the monitor display, SE values vary between 0 (suppressed EEG activity) and 91 (indicating an awake state). RE values vary between 0 and 100. The recommended range for adequate anesthesia for both parameters is from 40 to 60 [11] as it is for BIS [12]. When the SE is in the recommended range for adequate anesthesia, but the RE increases 5-10U more, this indicates patient responsiveness to surgery and can be interpreted as a sign of uncovered nociception [13]. The BIS is capable of monitoring the level of consciousness during sedation [14] and general anesthesia [15].

In this study the BIS, RE and SE values decreased progressively from preinduction (baseline) values of 96±3, 95±4 and 88±3 to preincision values of 37±13, 35±14 and 30±13 respectively, i.e. the pattern of changes in the entropy and BIS values was similar during the induction, maintenance and emergence periods in our study. Similarly Bruhn J et al., 2001 demonstrated that the EEG effects of propofol were similarly quantified by both the BIS and Entropy monitors [16].

As expected, the SE values were always less than the RE values because the maximum SE value is 91 (versus 100 for the RE and BIS values).
In this study BIS, RE and SE display greater index values before the induction of anesthesia (awake) 96±3, 95±4 and 88±3 respectively and upon recovery of consciousness 97±3, 95±4 and 85±3 respectively compared with the index values during the maintenance anesthetic period 44±3, 43±4 and 41±3 respectively. Similarly Paul F et al., 2006 [17] studied thirty patients scheduled for major laparoscopic surgery procedures, simultaneous state entropy (SE), response entropy (RE) and BIS values were recorded at specific time intervals during the induction, maintenance and emergence periods in patients administered a standardized general anesthetic technique demonstrated that the SE and RE values correlated with the BIS value during the induction (r=0.77 and 0.78, respectively) and emergence (r=0.86 and 0.91, respectively) periods.

There was no difference between both monitors with respect to their sensitivity to the residual effects of anesthetic drugs administered during the maintenance period, as BIS, RE and SE returned to their preinduction baseline values (97±3, 95±4 and 85±3 respectively) upon reorientation of the patient to person and place.

Recent studies involving anesthetized and paralyzed patients demonstrated that the anesthetic or analgesic-sparing effect associated with cerebral monitoring can also contribute to reduced recovery times and an improved quality of recovery [18].

In our study the Entropy module experienced significantly less interference (i.e., artifact) compared with the BIS monitor, during use of the electrocautery unit (11% versus 63% electrocautery artifact, respectively). This observation is consistent with findings in comparative studies involving the BIS monitor and patient state analyzer [15]. Bruhn and coworkers [19] reported that the entropy parameters were superior to EEG spectral edge frequency regarding robustness against artifacts.

In this study logistic regression analysis demonstrated that the BIS, RE and SE were all significant predictors of unconsciousness (p<0.01), with area under the Receiver Operating Characteristics (ROC) curve values of 0.976±0.058, 0.965±0.075 and 0.950±0.115 for the BIS, RE and SE, respectively. The entropy indices have similar sensitivity and specificity to the BIS value with respect to changes in the level of consciousness. Moreover, RE and SE compared with BIS in Bland Altman plots demonstrated a good agreement especially between RE and BIS [average mean difference (95% CI)=−1.1 (−17.5−15.4)]. These agreements are more evident at higher values of entropy and similarly Paul and coworkers [17] demonstrated that the area under the receiver operating characteristic curve for detection of consciousness indicated a similar performance of the SE (0.93±0.04) relative to the RE (0.98±0.04) and BIS (0.97±0.04).

Finally, given the comparable costs of the two monitoring units and disposable electrode strips, these data would suggest that the Entropy module is a cost-equivalent alternative to the BIS monitor.

The principle limitation of our study is the involvement of a small group of patients undergoing surgical procedures using a highly standardized anesthetic technique. The intraoperative masking was not possible.

In conclusion, the changes in SE and RE values followed a similar pattern to the BIS values during anesthesia. The entropy indices have similar sensitivity and specificity to the BIS value with respect to predicting loss of consciousness and emergence from general anesthesia. Use of the spectral entropy (Entropy) module is associated with less frequent intraoperative interference (by electromyographic activity and the electrocautery) with the displayed indices than the bispectral index (BIS) monitor when used during general anesthesia. In contrast to the extensive clinical experience with the BIS monitor there is a more limited clinical database for the Entropy algorithm. Further comparative studies involving the Entropy module are clearly required.

References
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