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Bispectral Analysis of EEG Waves Provides an Objective Method of Determining Sedation Level in Intensive Care Unit Patients

Key Terms:

- Bispectral Index (BIS)
- Electroencephalography (EEG)
- Sedation Level
- Ramsay Sedation Score (RSS)
- Spectral Edge Frequency (SEF)
- Median Power Frequency
- Absolute Power (Delta, Theta, Alpha Beta)

Author

Susan Khera

Susan Khera chose to do clinical research in the ICU because it was there that the terminally ill patients could benefit from her research. She not only had the chance to work with patients, but also to work towards a better clinical environment for them. Susan will attend Georgetown University Medical School and hopes to be an obstetrician-gynecologist. She felt that research allowed her to practically apply what she learned in class, to communicate effectively with doctors, and to cultivate a deeper appreciation for all patients.

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Abstract

The primary objective of this experiment was to determine if Bispectral Index (BIS), a multivariate discriminate analysis computed by an electroencephalography (EEG) machine, correlates with Ramsay Sedation Score (RSS), and if it is effective in measuring sedation in Intensive Care Unit (ICU) patients. This study was conducted in the surgical ICU at the Long Beach Veterans Administration Hospital. We studied 30 consenting male adults who were receiving sedative drugs. This was a non-invasive study employing continuous EEG monitoring of patients. A four-channel EEG was recorded for 6 to 8 h using fronto-temporal electrode montage. The BIS score computed by the EEG machine was recorded every half hour. Response to verbal command was measured using RSS every half hour as well. Linear regression analysis showed that BIS correlates well with RSS. BIS may be a more objective and sensitive technique than current methods used to monitor sedation of ICU patients. BIS may be particularly useful in assessing sedation level of patients receiving muscle relaxants as well as patients on ventilators.

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Faculty Mentor

Monitoring any parameter is simple and objective if the monitor gives us a number that everybody can understand. Unfortunately, we do not have any monitor that can do that for assessing sedation levels in ICU patients, and hence the patients in ICU are either over- or under-sedated. The only method available at present is the Ramsey Sedation Score (RSS), which is very subjective and observer-dependent. Susan's project addresses this issue by examining Bispectral Index (BIS), which is the newest variable that converts EEG findings into

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numerical form and gives a number that can be interpreted easily. It is a good idea to gain some experience in research as it can be fun, intellectually stimulating, and gives you some idea whether that is something you will like to do as you progress in your career.◇

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Introduction

Current methods used to evaluate depth of sedation in Intensive Care Unit (ICU) patients are subjective. Presently, the Ramsey Sedation Score (RSS) is the primary method used to determine sedation level (Habibi and Coursin 1996). This technique employs a numerical scale by which an observer can rank the patient's response to verbal commands. The observer evaluates how aware the patients are by calling out their names and prodding the patients. The patient is then scored using the RSS system. The inefficacy of such a system is threefold. First, intubated and unconscious patients cannot be effectively evaluated; because they cannot respond to the observer's command, they will be given a score of 0 to 1, and they may be unnecessarily sedated. Second, RSS is subject to inter-observer variability and is not an objective measure of sedation. Third, RSS can only differentiate into two categories of sedation: responder, score of 4 to 6, and non-responder, score of 0 to 3. Although there are seven levels one can give the patient, it is difficult to assess the difference between 0, 1, 2, or 3 scores as well as between 4, 5, or 6 scores. Thus, RSS is not precise enough to ensure that the patient will get the ideal amount of sedative.

A more objective measure of sedation can be provided using an electroencephalography (EEG) machine that measures the patients brain activity. In the following study, we used Bispectral Index (BIS) analysis of the EEG (Aspect 1992). The EEG machine computes a multivariate discriminate analysis called BIS (Aspect 1992). BIS analysis quantitatively measures consistency between phase and power of EEG waves and computes a single number, BIS. BIS can portray the dynamic structure of EEG that simple linear analysis cannot. Therefore, BIS analysis can depict subtle changes in brain activity (Aspect 1992). Higher doses of anesthetics cause slower, more synchronized EEG patterns that are picked up by BIS analysis. BIS can help one detect cerebral state changes when patients are under anesthesia (Aspect 1992). Previous studies have shown BIS analysis to be a good indicator of depth of anesthesia in healthy volunteers (Glass et al. 1997; Lui et al. 1997). BIS was found to correlate with level of responsiveness and predict the loss of consciousness in volunteers receiving propofol, midazolam, isoflurane, or alfentanil (Lui et al. 1997). Also, BIS was found to correlate with the observer's assessment on an alertness and sedation scale (Glass et al.

Materials and Methods

Subjects and setting:
Following approval by the Institutional Review Board (IRB) of our proposed study, we tested BIS efficacy in monitoring and assessing sedation levels of 30 consenting male patients, aged 46 to 90, in the surgical ICU at the Long Beach Veterans Administration Hospital. Some subjects were on a ventilator; many were receiving some type of sedative or analgesic medication. This was documented, but not controlled for in the study.

Measurements:
An Aspect A-1000 EEG monitor was used to monitor patients' brain electrical activity in real time. A four-channel EEG recording was performed using ZipPrep electrodes placed in a fronto-temporal montage for 6 to 8 h. Other parameters monitored were EKG, pulse oximeter, heart rate, and blood pressure. BIS was computed by the EEG and recorded every half hour. Patients' response to verbal commands was measured every half hour as well. The research assistant assessed patients' response to verbal commands by calling out the patient's name, and then shaking and prodding if the patient was asleep. The patient was given a score based on the RSS (Table 1). The patients with lower scores (0 to 3) were pooled into one group called the "non-responders." Patients with higher scores (4 to 6) were pooled into a second group termed the "responders." All of the data was documented on a computer, including any new medications, treatments, or muscle movements the patient underwent during the study period. This was done to account for any drastic changes in EEG patterns.

Table 1
Ramsay Sedation Scale (Adapted from Habibi and Coursin 1996)

Response to verbal command	Numerical Score
Agitated	6
Responds readily to name spoken in a normal tone	5
Lethargic response to name spoken in normal tone	4
Responds only after name is called loudly and/or repeatedly	3
Responds only after mild prodding or shaking	2
Does not respond to mild prodding or shaking	1
Does not respond to test stimulus	0

Analysis:
The EEG data recorded during the study period was downloaded to a computer that synchronized all parameters. EEG parameters that were processed include BIS, spectral edge frequency (SEF), median power frequency (MPF), absolute power of

1997). However, we wanted to determine if BIS correlates with RSS, and if it is a good indicator of sedation levels in ICU patients.

Our data suggest that BIS correlates well with RSS measurements of response to verbal command. Hence, BIS can be used to monitor and assess sedation level in ICU patients. BIS is a more objective, precise tool of assessing levels of anesthesia than RSS alone.

all frequencies (delta, theta, alpha, beta), and low EMG (Table 2).

Statistical analysis included Levene's test for equality of variance and independent samples t-test for equality of means. A $p < 0.05$ was considered statistically significant. Linear regression analysis for correlation of RSS with BIS was performed as well. Data from the left and

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right side of the brain were combined because there was no statistically significant difference evident between the two brain hemispheres.

Table 2
Power Spectrum Variables (Adapt Tech Overview 1992)

Variable Name	Description
Bispectral Index (BIS)	Quantifies the overall bispectral properties (frequency, power, phase)
Spectral edge frequency (SEF)	Represents the highest significant frequency in the current EEG spectrum. Usually represents 95% of all the power.
Median power frequency (MPF)	Measure the frequency in the current spectrum at which half the power is above and half is below.
Absolute delta power	Measures the power in the delta frequency range–0.5-3.75 Hz
Absolute theta power	Measures the power in the delta frequency range–4.0-7.75 Hz
Absolute alpha power	Measures the power in the delta frequency range–8.0-13.5 Hz
Absolute beta power	Measures the power in the delta frequency range–13.75-30.0 Hz

Results

Data collected from the two fronto-temporal channels were used in the statistical analysis. Means and standard deviations for all processed EEG parameters are shown in Table 3. BIS, SEF, MPF, Absolute alpha, Absolute beta, and EMG data were significantly different between the responders and non-responders. Linear regression analysis demonstrates that BIS correlates with RSS (Figure 1). Ramsay Sedation Scores between 0 and 3 indicate deeply sedated patients ("non-responders") and correspond to lower BIS scores (55 to 70). Similarly, less sedated patients ("responders") have higher RSS (4 to 6) and higher BIS (70 to 100) scores.

Table 3
Means and standard deviations for all EEG parameters.

Parameter	Non-responders	Responders	p-value
BIS	66.1+/-14.0	90.0+/-9.0	0.000
SEF	12.7+/-2.1	18.8+/-5.6	0.000
MPF	3.0+/-0.9	4.7+/-2.1	0.000
Adelta	54.4+/-2.8	55.5+/-5.1	0.325
Atheta	50.4+/-3.4	52.4+/-4.0	0.026
Aalpha	46.8+/-2.6	49.6+/-3.0	0.000
Abeta	43.1+/-2.9	49.5+/-3.8	0
EMG	34.6+/-7.9	48.2+/-7.8	0

The correlation of other EEG parameters with RSS was also computed (Table 4). Of all parameters, BIS correlated the best.

Table 4
Correlation of EEG parameters with RSS.

Parameter	% Correlation
BIS	1
SEF	25
MPF	9
Absolute alpha	20
Absolute beta	40
Absolute delta	21
Absolute theta	39

Discussion

The primary conclusion of this experiment is that BIS correlates well with RSS. In the past, the only method of assessing sedation was the RSS system. RSS is subjective because different observers may give the same patient different scores. Furthermore, RSS is not precise in determining sedation because it is difficult to differentiate if a responder has a score of 4, 5, or 6. Likewise, it is difficult to distinguish if a non-responder is a 0, 1, 2, or 3. Therefore, RSS can differentiate a responder from a non-responder, but it fails to provide a precise measurement of the patient's level of sedation.

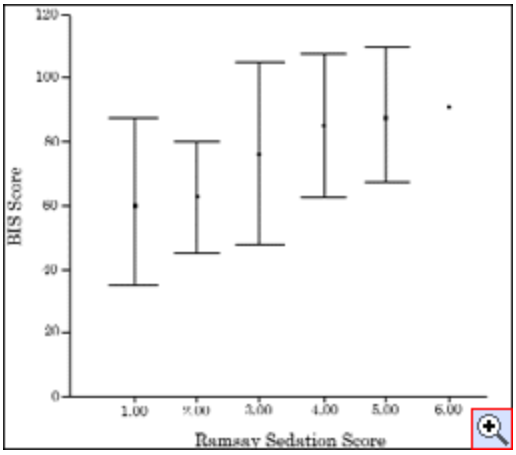

Figure 1
Linear Regression analysis of BIS with RSS. This graph shows the range of BIS at each RSS number. Central point represents the mean BIS score at each RSS number.

On the other hand, BIS is more precise than RSS because BIS can distinguish a deeply sedated non-responder from a lightly sedated non-responder. Such patients would have different BIS scores, but their RSS may be the same. Using only RSS, one may over-sedate the patient, giving more sedative than is necessary to make the patient comfortable. However, for a patient who is being continuously monitored by an EEG machine, the drug can be titrated to a dose that maintains the patient's BIS score between 60 and 80. At this point, the patient will be slightly sedated and comfortable. A BIS score of less than 60 is probably an indication of over-sedation, since this score correlates with RSS numbers of 3 or less (Figure 1).

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Current sedation assessment methods are subject to variability depending upon the observer (Habibi and Coursin 1996). RSS is not sensitive or specific enough to determine agitation and over-sedation (Habibi and Coursin 1996). Furthermore, evaluation using RSS is hard to duplicate in a busy ICU since it can be time-consuming and can agitate the patient (Habibi and Coursin 1996). On the contrary, BIS is an objective, non-invasive method of continuously monitoring the patients sedation level.

Finally, RSS cannot be used to evaluate sedation levels in intubated patients (Polland 1993). Many patients in the ICU require mechanical ventilation and/or muscle relaxants. Patients who are on ventilators and who receive muscle relaxants cannot communicate effectively. RSS is an inadequate method of determining sedation level in such patients since the patients cannot respond (Polland 1993; Spencer et al. 1994). BIS would be a good alternative for intubated patients and/or patients who are receiving muscle relaxants. An EEG would provide non-invasive, continuous monitoring of sedation levels without requiring the patient to respond verbally. Apparently, using BIS analysis could be the vehicle of providing objective sedation assessment in both intubated and non-intubated patients. Using BIS analysis, doctors and nurses may be able to achieve the ideal level of sedation that "provides a degree of sleepiness from which the patient is easily aroused and remains cooperative and responsive to commands" (Habibi and Coursin 1996).

The usefulness of other EEG parameters in determining sedation has also been investigated (Lui et al. 1996). Our results also showed that SEF, MPF, Absolute alpha, Absolute beta, and EMG are statistically different between responders and non-responders. However, these parameters are not as specific as BIS; similar to RSS, they may only be able to differentiate between responders and non-responders (Lui et al. 1996). Also, the other power spectrum variables did not correlate with RSS as well as BIS did (Table 4). According to a previous study, these simple EEG analyses are not effective; little correlation was found between MPF, SEF, and sedation score in critically ill patients (Spencer et al. 1994). Similarily, another study concluded that BIS provided the best correlation with the sedation scaling system used, and that only BIS consistently increased as anesthetic wore off (Spencer et al. 1994). Other EEG parameters do not correlate with RSS as well as BIS and hence, are not as effective in measuring sedation BIS is definitely useful in a clinical setting and may become the new method of monitoring depth of anesthesia in the ICU and possibly even in the operating room.

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(Polland 1993; Spencer et al. 1994).

Other objective measures of sedation are also being investigated. One study found that cardiac beat-to-beat variability (RR variability) correlates well with RSS in ICU patients (Haberthur et al. 1996). It is an objective, continuous method that can be used to monitor intubated patients (Haberthur et al. 1996). More research needs to be done on alternative methods of assessing sedation in an objective manner. Presently, BIS can be used effectively to determine sedation in ICU patients. Other clinical uses of BIS are also being studied. For example, one study concluded that BIS can be used to measure effects anesthetics have on EEG wave patterns (Billard et al., 1997).

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